ROBUST FREQUENCY-SELECTIVE KNOWLEDGE-BASED PARAMETER ESTIMATION FOR NMR SPECTROSCOPY

Naveed R. Butt[†], *Andreas Jakobsson*[†] *and Samuel D. Somasundaram*[‡]

[†] Karlstad University, Department of Electrical Engineering, SE-651 88 Karlstad, Sweden.
[‡] King's College London, Division of Engineering, Strand, London WC2R 2LS, UK.
Email: naveed.butt@kau.se, andreas.jakobsson@ieee.org, sdsomasundaram@hotmail.com

ABSTRACT

In many magnetic resonance spectroscopy (MRS) applications, one strives to estimate the parameters describing the signal to allow for more precise knowledge of the analyte. Typically, MRS signals are well modelled as a sum of damped sinusoids that has properties that are partly known a priori. FREEK, a recently proposed subspace-based parameter estimation method allows for inclusion of such prior knowledge. More specifically, FREEK assumes that there is a constant frequency spacing (say Δ) between the damped sinusoids, which is *exactly known*. However, any errors in this prior knowledge will affect the accuracy of the estimates. Herein, we present an extension of FREEK, making it robust to such errors by allowing Δ to lie in a small interval and utilizing a robust estimate of Δ in the estimation of the remaining parameters. The proposed approach is numerically shown to provide robust estimates of the sinusoidal parameters at various noise levels in the presence of mismatch between the actual and the assumed spacing.

1. INTRODUCTION

Magnetic resonance spectroscopy (MRS) is a non-invasive analytical technique able to provide biochemical signatures of various analytes. The technique is widely used in medical diagnosis and several biochemical studies [1, 2]. From a signal processing perspective, MRS signals can most commonly be represented as sums of damped sinusoids whose individual parameters, such as frequency, amplitude, and damping, provide direct information about the identity, concentration and dynamics of the molecules of the analyte (see, e.g., [3]). Accurate estimation of these parameters is, therefore, a well-known and important problem in MRS applications, and several parameter estimation methods exist in the literature [4–10]. Among these, subspace-based methods, e.g., HSVD [4], HTLS [6] etc., are particularly attractive because of their high level of automation, requiring minimal user involvement or expertise. However, these methods do not take into account the generally a priori known relations between the parameters of groups of signal modes, commonly referred to as *multiplets* [11–13]. Further, several MRS applications allow the user to concentrate on only a small band of the frequency spectrum. This reduces both the out-of-band interference and the computational cost, since only the frequency-selected data is considered [14, 15].

Recently, a number of singular value decomposition (SVD) based algorithms have been proposed in literature with the aim of incorporating some or all of the aforementioned features. In particular, the KNOB-SVD [13] algorithm allows for inclusion of prior knowledge, SELF-SVD [16] extends HSVD to frequency-selected version and FREEK [15] combines the features of the KNOB-SVD and SELF-SVD algorithms. Specifically, for a multiplet of interest, FREEK assumes that the modes have the same damping constant and that there is a constant spacing (say Δ) between them, which is *exactly known*. The main disadvantage of this approach is that any error in the assumed Δ would lead to a reduced accuracy of estimation for all the parameters. Herein, we present and extension of the FREEK algorithm, aiming at making it robust to such errors by allowing a certain degree of uncertainty in Δ. The proposed robust algorithm, here termed the Robust Frequency-selective Knowledge-based SVD (RobFKS), allows Δ to lie in a small interval and utilizes a robust estimate of Δ in the estimation of the remaining parameters. This provides more accurate parameter estimates at a nominal increase in computational cost. We develop the proposed algorithm in Section 2 and investigate its performance numerically in Section 3.

A word on notation: $(\cdot)^T$, $(\cdot)^*$ and $\|\cdot\|$ are used to represent the transpose, the conjugate transpose and the norm, respectively, while $\mathrm{diag}\{\mathbf{x}\}$ represents a diagonal matrix, formed with the vector $\mathbf{x}$ along its diagonal.

2. THE PROPOSED ALGORITHM

To demonstrate the proposed robust algorithm, we consider the problem of doublet parameter estimation often encountered in MRS applications (the same approach can be easily extended for a triplet). We assume that the measured data consists of N time-domain samples being modelled as a sum of M exponentially damped complex sinusoids (see, e.g., [3])

$$y(t) = \sum_{k=1}^{M} \rho_k \gamma_k^t + e(t) \tag{1}$$

$$\gamma_k = e^{-\alpha_k + i\omega_k}, \tag{2}$$

THIS WORK WAS SUPPORTED IN PART BY THE SWEDISH RESEARCH COUNCIL, CARL TRYGGER'S FOUNDATION, SWEDEN, AND THE SWEDISH FOUNDATION FOR INTERNATIONAL COOPERATION IN RESEARCH AND HIGHER EDUCATION (STINT).

where $t = 0, 1, \ldots, N-1$, $e(t)$ is the noise term, γ_k represent the signal modes, and ρ_k, α_k and ω_k are the (unknown) complex amplitude, damping constant and angular frequency of the kth damped sinusoid, respectively (with sampling period absorbed in α_k and ω_k for notational convenience). Here, the problem of interest is to use the data, $\{y(t)\}_{t=0}^{N-1}$, to estimate the parameters $(\rho,\ \alpha, \omega)$ of a pair of modes while incorporating the (approximate) prior knowledge

$$\begin{aligned} \alpha_2 &= \alpha_1 & (3) \\ \omega_2 &= \omega_1 + \Delta_I, \qquad \Delta_I \in [\underline{\Delta} \quad \overline{\Delta}] & (4) \end{aligned}$$

where $\underline{\Delta}$ and $\overline{\Delta}$ represent lower and upper limits of the known range of frequency spacing between the two peaks. We may rewrite (4) in terms of a known and an uncertain offset as

$$\begin{aligned} \omega_2 &= \omega_1 + \Delta + u, \quad |u| \leqslant \frac{\overline{\Delta} - \underline{\Delta}}{2} \triangleq \epsilon & (5) \\ \Delta &\triangleq \frac{\overline{\Delta} + \underline{\Delta}}{2}. & (6) \end{aligned}$$

As noted in the introduction, frequency-selective Fourier transform can be applied to the measured data to allow for maximal out-of-band interference rejection and computational efficiency. This is achieved by defining a set of L frequency points

$$\left\{ \frac{2\pi l_1}{N}, \frac{2\pi l_2}{N}, \ldots, \frac{2\pi l_L}{N} \right\}, \tag{7}$$

with $l_1, \ldots, l_L$, being given, not necessarily consecutive, integers selected such that (7) covers the band containing only the doublet of interest. The frequency-selected Fourier transformed data vector, here denoted $\mathbf{Y}$, can then be written as

$$\begin{aligned} \mathbf{Y} &= \mathbf{V}_L^* \mathbf{y} & (8) \\ \mathbf{y} &= \begin{bmatrix} y(0) & \ldots & y(N-1) \end{bmatrix}^T & (9) \\ \mathbf{V}_L &= \begin{bmatrix} \mathbf{v}_{l_1} & \cdots & \mathbf{v}_{l_L} \end{bmatrix} & (10) \\ \mathbf{v}_{l_j} &= \begin{bmatrix} 1 & e^{i2\pi l_j/N} & \ldots & e^{i2\pi l_j(N-1)/N} \end{bmatrix}^T & (11) \end{aligned}$$

Using SELF-SVD [16], we may form a matrix $\mathbf{W}$ that has the same range space as the $S \times 2$ matrix $\mathbf{A}$, where

$$\begin{aligned} \mathbf{A} &= \begin{bmatrix} \mathbf{a}_S(\gamma_1) & \mathbf{a}_S(\gamma_2) \end{bmatrix} & (12) \\ \mathbf{a}_S(\gamma_k) &= \begin{bmatrix} 1 & \gamma_k & \ldots & \gamma_k^{S-1} \end{bmatrix}^T. & (13) \end{aligned}$$

In the interest of brevity, we refer the reader to [16] for details on computing $\mathbf{W}$ and on selection of the user parameter S. Using (3) and (5), we may rewrite (12) as

$$\mathbf{A} = \begin{bmatrix} \mathbf{a}_S(\gamma_1) & \mathbf{a}_S\left(\gamma_1 e^{i(\Delta+u)}\right) \end{bmatrix}. \tag{14}$$

Following the MUSIC-like approach presented in [14] (see also [17]), we define a $S \times (S-2)$ matrix, $\mathbf{H}$, that forms an orthonormal basis of the null space of $\mathbf{W}^*$. Thus, orthogonality between $\mathbf{A}$ and $\mathbf{H}$ implies that

$$\mathbf{H}^* \mathbf{a}_S(\gamma) = 0, \tag{15}$$

iff $\alpha = \alpha_1$ and $\omega = \omega_1$ or $\omega = \omega_1 + \Delta + u$. Combining (15) with the observation that

$$\mathbf{a}_S\left(\gamma_1 e^{i(\Delta+u)}\right) = \mathbf{U}^* \mathbf{D}^* \mathbf{a}_S(\gamma_1), \tag{16}$$

where

$$\begin{aligned} \mathbf{D} &= \operatorname{diag}\left\{ \begin{bmatrix} 1 & e^{-i\Delta} & \ldots & e^{-i(S-1)\Delta} \end{bmatrix} \right\} & (17) \\ \mathbf{U} &= \operatorname{diag}\left\{ \begin{bmatrix} 1 & e^{-iu} & \ldots & e^{-i(S-1)u} \end{bmatrix} \right\}, & (18) \end{aligned}$$

leads to the following constrained minimization for estimating u, α and ω

$$\begin{aligned} &\min_{\alpha_1, \omega_1, u} \mathbf{a}_S^*(\gamma_1) \left[\mathbf{H}\mathbf{H}^* + \mathbf{U}\mathbf{D}\mathbf{H}\mathbf{H}^*\mathbf{D}^*\mathbf{U}^* \right] \mathbf{a}_S(\gamma_1) \\ &\qquad \text{subject to } |u| \leqslant \epsilon \end{aligned} \tag{19}$$

Further, reminiscent of [15], it can be shown that

$$\operatorname{rank}\left(\mathbf{H}\mathbf{H}^* + \mathbf{U}\mathbf{D}\mathbf{H}\mathbf{H}^*\mathbf{D}^*\mathbf{U}^* \right) = S - 1. \tag{20}$$

Thus, the minimization in (19) can be seen as a problem of finding the eigenvector associated with the smallest unique eigenvalue of

$$\mathbf{G}_u \triangleq \mathbf{H}\mathbf{H}^* + \mathbf{U}\mathbf{D}\mathbf{H}\mathbf{H}^*\mathbf{D}^*\mathbf{U}^*. \tag{21}$$

Further, for a small ϵ, the uncertain offset u, defined in (5), may be estimated as the argument in the range

$$r = [-\epsilon \quad \epsilon], \tag{22}$$

where this smallest eigenvalue occurs, i.e.,

$$\hat{u} = \arg\min_{u \in r} \lambda_{min}\{\mathbf{G}_u\}, \tag{23}$$

where $\lambda_{min}\{\mathbf{G}_u\}$ denotes the smallest eigenvalue of $\mathbf{G}_u$. Using (23), we can now find the eigenvector $\mathbf{b}$ associated with the smallest eigenvalue of $\mathbf{G}_{\hat{u}}$. From (19), we have

$$\mathbf{a}_S(\gamma_1) \sim \mathbf{b}. \tag{24}$$

Noting that

$$\overline{\mathbf{a}}_S \gamma_1 = \underline{\mathbf{a}}_S, \tag{25}$$

where

$$\begin{aligned} \overline{\mathbf{a}}_S &\triangleq [\mathbf{I}_{S-1} \quad 0] \mathbf{a}_S & (26) \\ \underline{\mathbf{a}}_S &\triangleq [0 \quad \mathbf{I}_{S-1}] \mathbf{a}_S, & (27) \end{aligned}$$

gives

$$\overline{\mathbf{b}} \gamma_1 = \underline{\mathbf{b}}, \tag{28}$$

where $\overline{\mathbf{b}}$ and $\underline{\mathbf{b}}$ are defined similar to $\overline{\mathbf{a}}_S$ and $\underline{\mathbf{a}}_S$, respectively. From (28), the least squares estimate of γ_1 is simply

$$\hat{\gamma}_1 = \frac{\overline{\mathbf{b}}^* \underline{\mathbf{b}}}{\| \overline{\mathbf{b}} \|^2}. \tag{29}$$

The estimate, $\hat{\gamma}_1$, can then be used to extract estimates of damping and frequency parameters as

$$\hat{\alpha}_1 = -\Re\left\{\log\{\hat{\gamma}_1\}\right\} \tag{30}$$

$$\hat{\omega}_1 = \Im\left\{\log\{\hat{\gamma}_1\}\right\}, \tag{31}$$

where $\Re\{z\}$, $\Im\{z\}$ and $\log\{z\}$ represent the real part, the imaginary part and the complex natural log of the complex number z, respectively. Finally, defining

$$\boldsymbol{\theta} = [\rho_1 \quad \rho_2]^T, \tag{32}$$

we note that the noise-free part of $\mathbf{Y}$ can be written as

$$\mathbf{V}_L^* \left[\mathbf{a}_N(\hat{\gamma}_1) \quad \mathbf{a}_N(\hat{\gamma}_2)\right] \boldsymbol{\theta} \triangleq \boldsymbol{\Sigma}\boldsymbol{\theta}, \tag{33}$$

where

$$\hat{\gamma}_2 = \hat{\gamma}_1 e^{i(\Delta + \hat{u})}. \tag{34}$$

Hence, the least squares estimate of $\boldsymbol{\theta}$ is given by

$$\hat{\boldsymbol{\theta}} = (\boldsymbol{\Sigma}^* \boldsymbol{\Sigma})^{-1} \boldsymbol{\Sigma}^* \mathbf{Y}. \tag{35}$$

We note that (23) involves a 1D search over the (typically small) range of u. For a small enough range, we may make use of matrix perturbation theory to avoid computing the eigenvalues of $\mathbf{G}_u$ at each grid point. This can be achieved by first computing the eigenvalue decomposition of $\mathbf{G}_{j_0}$ (where j_0 is some central point in the grid) and then using the approximation [18, 19]

$$\lambda_j \approx \lambda_{j_0} + \mathbf{x}_{j_0}^* (\mathbf{G}_j - \mathbf{G}_{j_0}) \mathbf{x}_{j_0}, \tag{36}$$

where $(\lambda_{j_0}, \mathbf{x}_{j_0})$ represent the smallest eigenvalue and the associated eigenvector of $\mathbf{G}_{j_0}$, while the approximation error is of the order

$$\|\mathbf{G}_j - \mathbf{G}_{j_0}\|^2. \tag{37}$$

For cases with large ranges involved, we can divide the search into smaller intervals and apply the perturbation formula separately within each interval. This approximation approach has empirically been found to work well. Finally, we remark that the matrix $\mathbf{H}$ is only introduced for algorithm development. In actual computations, $\mathbf{H}\mathbf{H}^*$ can be replaced by $\mathbf{I} - \mathbf{W}\mathbf{W}^*$.

3. NUMERICAL EXAMPLES

In this section, we apply the proposed robust algorithm to simulated data mimicking a typical MRS signal. The

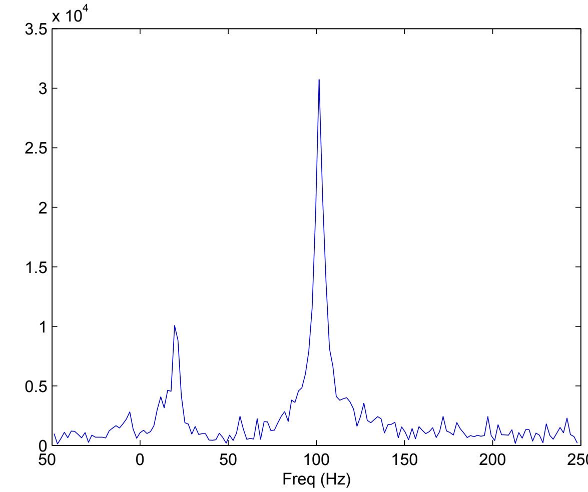

Figure 1: Part of the FFT spectrum of the simulated signal showing the doublet of interest, at $\sigma = 30$.

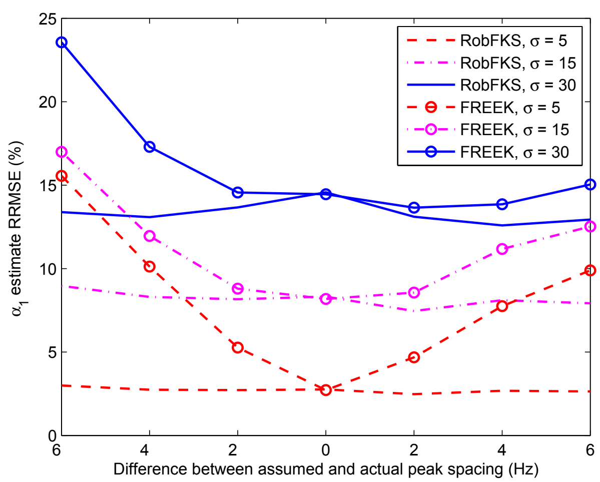

Figure 2: Damping constant estimate RRMSE versus the difference between assumed and actual peak spacing, at $\sigma = 5$, 15 and 30.

simulated data follows (1), and consists of a doublet with the following parameters

$$\rho_1 = 100 \text{ units}, \ \alpha_1 = 10 \text{ Hz}, \ \omega_1 = 20 \text{ Hz}$$

$$\rho_2 = 320 \text{ units}, \ \alpha_2 = 10 \text{ Hz}.$$

The frequency ω_2 is varied in the range [94,106] Hz to show the effects of error in prior knowledge. We assume that $N = 512$ time-domain samples are collected at a sampling frequency of 1 KHz. The noise added is complex white Gaussian with standard deviation σ. Figure 1 shows part of the FFT spectrum of the simulated signal covering the doublet of interest. In all the simulations, RobFKS uses $\Delta = 80$ Hz with $\epsilon = 6$ Hz, i.e., it allows for an uncertainty of ± 6 Hz in the assumed spacing between the two peaks. We compare the results with the FREEK algorithm that uses the prior knowledge $\Delta = 80$ Hz without allowing for any uncertainty. For each

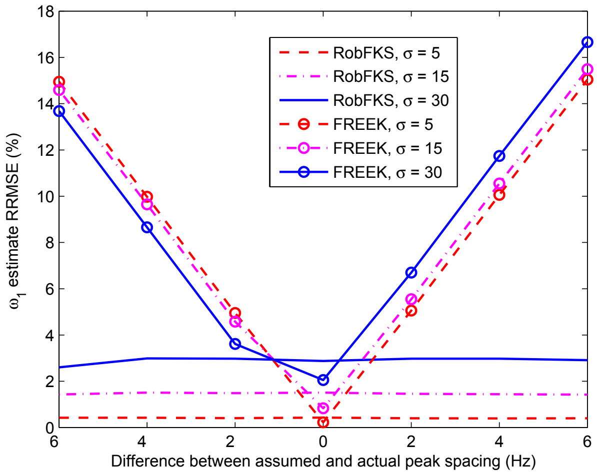

Figure 3: Frequency estimate RRMSE versus the difference between assumed and actual peak spacing, at $\sigma = 5$, 15 and 30.

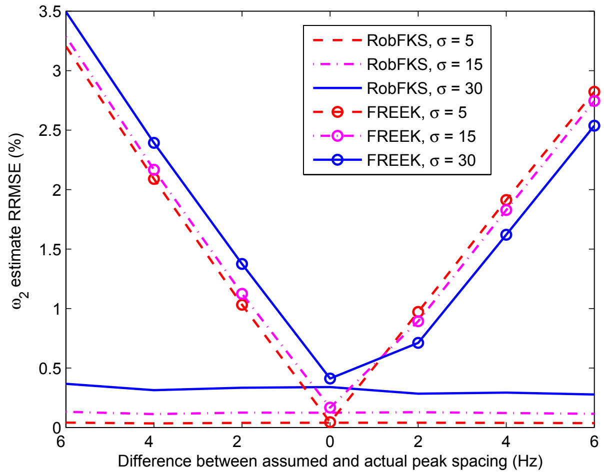

Figure 4: Frequency estimate RRMSE versus the difference between assumed and actual peak spacing, at $\sigma = 5$, 15 and 30.

parameter, results of $C = 500$ Monte Carlo simulations are used to calculate the relative root mean square error (RRMSE)

$$\text{RRMSE (\%)} \triangleq 100\sqrt{\frac{1}{C}\sum_{q=1}^{C}\frac{(\theta-\hat{\theta}_q)^2}{\theta^2}}, \tag{38}$$

where θ represents the true value of the parameter and $\hat{\theta}_q$ is the estimate from the qth Monte Carlo run. The search region used for u was [-6,6] Hz (in 200 steps). In order to avoid evaluating the eigenvalue decomposition of $\mathbf{G}_u$ at each grid point, the search region was divided into 20 equal intervals and the perturbation formula given in (36) was applied to each interval separately.

Figures 2-6 show the RRMSE results for amplitudes (absolute), damping constants and frequencies of the two peaks versus the difference between the actual and assumed spacing. Each figure shows results at noise standard deviation of 5, 15 and 30. As expected, RobFKS shows robustness to the error in the prior knowledge at all noise levels. The performance of the FREEK algorithm declines as the deviation of the actual spacing from the assumed spacing increases. The figures also show that the error in the assumed knowledge affects the estimates of all the parameters in case of FREEK. However, RobFKS does not suffer from this limitation as it uses a robust estimate of the spacing in the estimation of the remaining parameters. Finally, we compare the computation time of RobFKS with FREEK and KNOB-SVD. The CPU times for the three knowledge-based estimators are shown in Table 1. As is clear from these results, RobFKS provides robustness at a nominally higher computation cost than it's non-robust counterpart, FREEK.

FREEK	RobFKS	KNOB-SVD
0.062	0.421	10.6

Table 1: CPU times (seconds) for estimation of the doublet parameters.

4. CONCLUSIONS

In this work, we extended a recently proposed knowledge-based parameter estimation method to make it robust to errors in the a priori information. The proposed robust frequency-selective knowledge-based parameter estimation method, herein termed RobFKS, incorporates prior information typically available in MRS applications, while allowing for uncertainty in this information. Numerical investigations show that the proposed approach provides significant performance gains as compared to the existing non-robust version, when mismatch between the actual and the assumed parameter relations exists.

REFERENCES

[1] J. W. Akitt and B. E. Mann, *NMR and Chemistry*. Cheltenham, UK: Stanley Thornes, 2000.

[2] J. M. Tyszka, S. E. Fraser, and R. E. Jacobs, "Magnetic resonance microscopy: recent advances and applications," *Current Opinion in Biotechnology*, vol. 16, no. 1, pp. 93–99, February 2005.

[3] L. Vanhamme, T. Sundin, P. Van Hecke, S. Van Huffel, and R. Pintelon, "Frequency-selective quantification of biomedical magnetic resonance spec-

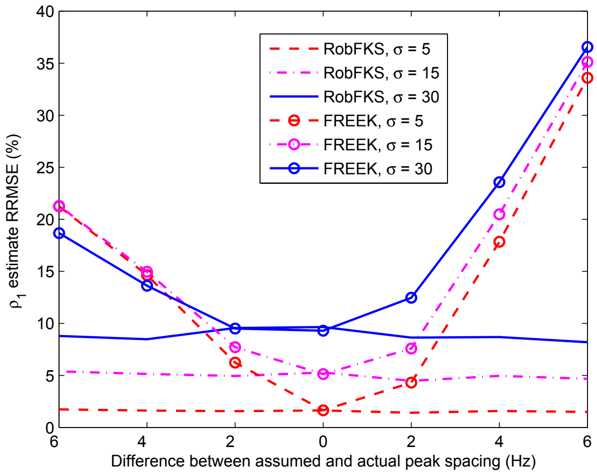

Figure 5: Amplitude estimate RRMSE versus the difference between assumed and actual peak spacing, at $\sigma = 5$, 15 and 30.

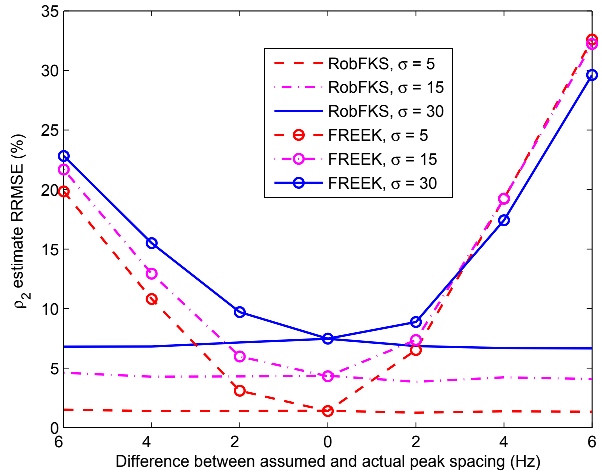

Figure 6: Amplitude estimate RRMSE versus the difference between assumed and actual peak spacing, at $\sigma = 5$, 15 and 30.

troscopy data," *Journal of Magnetic Resonance*, vol. 143, no. 1, pp. 1–16, 2000.

[4] H. Barkhuysen, R. de Beer, and D. van Ormondt, "Improved algorithm for noniterative time-domain model fitting to exponentially damped magnetic resonance signals," *Journal of Magnetic Resonance*, vol. 75, pp. 553–557, 1987.

[5] S. Y. Kung, K. S. Arun, and D. V. B. Rao, "State-space and singular-value decomposition-based approximation methods for the harmonic retrieval problem," *J. Opt. Soc. Am.*, vol. 73, no. 12, pp. 1799–1811, 1983.

[6] S. V. Huffel, H. Chen, C. Decanniere, and P. V. Hecke, "Algorithm for time-domain NMR data fitting based on total least squares," *Journal of Magnetic Resonance*, vol. 110, pp. 228–237, 1994.

[7] Y. Y. Lin, P. Hodgkinson, M. Ernst, and A. Pines, "A novel detection-estimation scheme for noisy NMR signals: Applications to delayed acquisition data," *Journal of Magnetic Resonance*, vol. 128, pp. 30–41, 1997.

[8] F. DiGennaro and D. Cowburn, "Parametric estimation of time-domain NMR signals using simulated annealing," *Journal of Magnetic Resonance*, vol. 96, pp. 582–588, 1992.

[9] O. M. Weber, C. O. Duc, D. Meier, and P. Boesiger, "Heuristic optimization algorithms applied to the quantification of spectroscopic data ," *Magn. Reson. Med.*, vol. 39, pp. 723–730, 1998.

[10] G. J. Metzger, M. Patel, and X. Hu, "Application of genetic algorithms to spectral quantification ," *Journal of Magnetic Resonance*, vol. 110, pp. 316–320, 1996.

[11] P. Stoica, Y. Selén, N. Sandgren, and S. V. Huffel, "Using prior knowledge in SVD-based parameter estimation for magnetic resonance spectroscopy - the ATP example," *IEEE Transactions on Biomedical Engineering*, vol. 51, pp. 1568–1578, 2004.

[12] ——, "Using prior knowledge in SVD-based nmr spectroscopy - the ATP example," in *Proc. of the 7th International Symposium on Signal Processing and its Applications ISSPA*, Paris, France, 2003, pp. 33–36.

[13] T. Laudadio, Y. Selén, L. Vanhamme, P. Stoica, P. V. Hecke, and S. V. Huffel, "Subspace-based MRS data quantitation of multiplets using prior knowledge," *Journal of Magnetic Resonance*, vol. 168, pp. 53–65, 2004.

[14] N. Sandgren, P. Stoica, and Y. Selén, "Frequency-selective magnetic resonance spectroscopy using prior information for data with low signal to noise ratio," in *Proc. of the 18th International BIOSIGNAL conference*, Brno, Czech Republic, 2006, pp. 21–23.

[15] ——, "Frequency-selective SVD-based magnetic resonance spectroscopy with prior knowledge," in *Proc. of the 38th Asilomar Conference on Signals, Systems and Computers*, Pacific Grove, USA, 2004, pp. 1605–1608.

[16] P. Stoica, N. Sandgren, Y. Selén, L. Vanhamme, and S. V. Huffel, "Frequency-domain method based on the singular value decomposition for frequency-selective NMR spectroscopy," *Journal of Magnetic Resonance*, vol. 165, pp. 80–88, 2003.

[17] P. Stoica and R. Moses, *Spectral Analysis of Signals*. Upper Saddle River, NJ: Pearson Prentice Hall, 2005.

[18] S. H. Chen and J. Wu, "Interval optimization of dynamic response for uncertain structures with natural frequency constraints," *Engineering Structures*, vol. 26, pp. 221–232, 2004.

[19] G. W. Stewart and J. Sun, *Matrix Perturbation Theory*. New York: Academic Press, 1990.