A Sparse Component Analysis Approach to EPR Spectra Decomposition

Chunqi Chang[†], Jiyun Ren[†], Peter C. W. Fung[‡], and Francis H. Y. Chan[†]

†Department of Electrical and Electronic Engineering, The University of Hong Kong
Pokfulam Road, Hong Kong
‡Department of Medicine, The University of Hong Kong, Pokfulam Road, Hong Kong
Email: {cqchang, jyren, fhychan}@eee.hku.hk, hrspfcw@hkucc.hku.hk

Abstract—Organic free radicals play important roles in many physiological and pathological pathways in biological systems. These radicals can be detected and quantified by their EPR spectra. The measured EPR spectra are often mixtures of pure spectra of several different free radicals and other chemicals. Blind source separation can be applied to estimate the pure spectra of interested free radicals. Because the pure EPR spectra are often not independent of each other, the ICA based approach cannot accurately get the wanted spectra. In this paper we present a sparse component analysis method, which exploiting the sparsity of the EPR spectra, to reliably extract the pure source spectra from their mixtures with high accuracy. The proposed method can also be used in other similar applications, or be utilized in the sparse decomposition approach to blind source separation.

1. Introduction

Independent component analysis (ICA) and blind source separation (BSS) have many applications in various areas including communication, acoustics, radar, and biomedical engineering. Recently they have found their applications in spectral analysis of Electron Paramagnetic Resonance (EPR) spectroscopy [1]. EPR spectroscopy is similar to the more widely known MR spectroscopy, while the former using paramagnetic resonance.

EPR spectroscopy is a standard way to detect and quantitatively measure organic free radicals generated in biological systems. Because of the lack of sensitivity of a specific free radical in the current EPR technique, the signals (called EPR spectra) measured may be a superimposition of the spectra of all existing free radicals and, maybe, other chemicals. The superimposed spectra can be called as multi-component mixtures, while each individual spectrum that constitutes the mixtures is called a component spectrum. Such superposition leads a difficulty in quantitative analysis of the EPR spectra, especially when the component spectra are overlapping.

There has been much interest in numerically decomposing multi-component mixtures of EPR spectra into pure component spectra. Traditional approach to determine the component spectra is by matching the mixtures manually to the spectra of all known and possible pure components [2]. This approach is not very effective and highly dependent on the contents of the component spectra. Svistunenko et al [3] proposed a simplified method that utilizes a set of mixtures of varying compositions, but the method still requires a priori information concerning the shapes of the component spectra. Since the component spectra may be very difficult to be acquired as a priori, generic species free methods not relying on a priori knowledge of the shapes of the pure component spectra will be of great advantage. Generally, as in [3], such methods also depend on multiple mixtures with distinct compositions. A representative approach was proposed in [4] where a self modeling procedure and a procedure utilizing the symmetric property of the spectra were applied with a preprocessing by principle component analysis (PCA). PCA has been widely used in analytical spectroscopy, and it can decompose the mixtures into pure components when the peaks in each component are well separated from those of every others [5]. If peaks of different component spectra are overlapped, they must be linear combinations of the principle components of the PCA analysis, and some post-processing, as used in [4], is required to get the pure spectra. Another post-processing approach used in [5] assumes that each component spectrum has only one peak.

Realizing that the problem that the above species-free methods aims to solve is exactly the blind source separation problem familiar to the signal processing community, the authors of this paper, for the first time, proposed an ICA-based BSS approach in [1] with promising results. Assuming the sources, i.e. the component spectra in this study, are statistically non-Gaussian and independent, the BSS problem can be solved by ICA, which is inherently based on higher order statistics. Representative ICA methods are JADE [6], InfoMax [7], and FastICA [8]. Alternatively, second order statistics based methods can also be applied to solve the BSS problem if the sources are statistically uncorrelated over a set of time lags [9, 10]. However, since in fact the component EPR spectra are neither completely independent nor completely uncorrelated, the decomposition result of the BSS approach to mixed EPR spectra analysis is not perfect, as shown in our previous studies in [1].

In this study we propose a novel method to perfectly decompose multi-component EPR spectra mixtures into pure component spectra that employs the sparsity of the component spectra.

2. The Problem

In biological systems, organic free radicals play important roles in many physiological and pathological pathways. Such free radicals can be routinely measured by the technique of Electron Paramagnetic Resonance (EPR) spectroscopy. Organic free radicals are too highly reactive to be detected without using spin trap agents to extend their half-life [11]. However, spin trap agents are not that ideally species specific. For example, the widely used agents 5-(diethoxyphosphoryl)-5-methyl-1-pyrroline-N-oxide (DEPMPO) for superoxide ($O_2^{\bullet-}$) radical will also simultaneously trap hydroxyl radical ($OH^{\bullet}$) in in vivo systems [12]. Consequently, the measured EPR spectrum using the spin trap agent DEPMPO will be a linear superposition of the spectra of DEPMPO adducts of the above two free radicals if both radicals present, which is common in biological systems. Figure 1 shows typical EPR spectra of DEPMPO adduct of hydroxyl and that of superoxide, while Figure 2 shows two actually measured EPR spectra of mixtures of hydroxyl and superoxide.
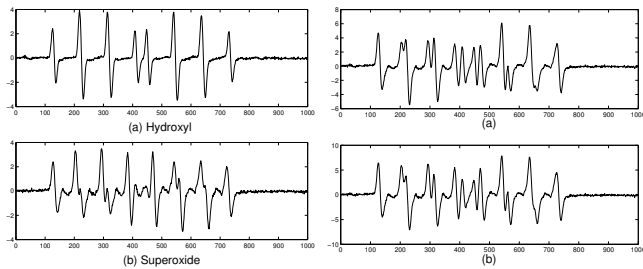

Figure 1: EPR spectra of free radical adducts (a) hydroxyl; (b) superoxide

Figure 2: Mixtures of EPR spectra shown in Fig. 1

Since the hydroxyl spectrum and the superoxide spectrum are overlapping, without the help of signal separation, one cannot tell out from the measured multi-component mixtures the exact quantity of each of the two free radicals. Traditional spectroscopy analysis method such as self-modeling does not work well in our case. In fact, the multi-component mixture spectra are linear superpositions of pure component spectra, and thus the problem falls into a standard blind source separation framework. Exploiting the model of blind source separation, in our previous study we proposed a FastICA approach to solve the problem and got improved results [1]. In that study we assume that two pure EPR spectra are statistically non-Gaussian and independent of each other. However, our assumption of independence is not well satisfied. This can be clearly shown by a close examination of the two spectrum shown in Figure 1. In fact, the violation of this assumption makes that the ICA method cannot perfectly separate the two overlapping pure spectra, as shown in Figure 7 and discussed in Section 4. In order to improve the performance of spectra separation, in the next section we propose an approach of

sparse component analysis.

3. Sparse Component Analysis

A signal is called sparse if it has some peaks and relatively flat area in between the peaks, as shown in Figure 3 (a,b). Denote the two sparse signals as $s_1(n)$ and $s_2(n)$, and we have the following two linear mixtures

$$
\begin{aligned}
x_1(n) &= s_1(n) + c_2 s_2(n) \\
x_2(n) &= c_1 s_1(n) + s_2(n),
\end{aligned} \tag{1}
$$

which are shown in Figure 3 (c,d). We can see that there are two distinct lines in the scatter plot of $x_1(n)$ and $x_2(n)$, with their slopes as $\frac{1}{c_1}$ and c_2. It suggests that we can separate the two sparse sources from the two mixtures by determining the slopes of the lines in the scatter-plot. The slopes can be determined by either a C-means clustering based approach [13] or a potential function based approach [14]. Both approaches work well when the sources are sparse enough.
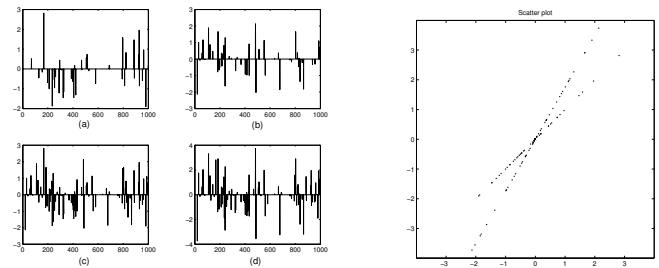

Figure 3: (a,b) Two sparse signals; (c,d) Two mixtures of the above two signals
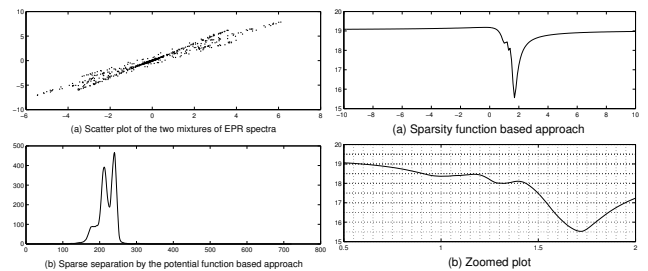

Figure 4: Scatter plot of the two mixtures of sparse sources

Figure 5: Scatter plot of the two mixtures shown in Fig.2

Figure 6: (a) $J(c)$ for Fig.2; (b) Zoomed plot of (a)

However, if the sources are not too sparse, as the case of EPR spectra of free radicals, it is hard to find the distinct lines and determine their scopes from the scatter plot of the mixtures, as shown in Figure 5 (a). In fact, the potential function based approach in [14], where the potential function of this case is shown in Figure 5 (b), cannot reliably separate the two source EPR spectra. So we need to develop more reliable methods to separate sparse sources from their linear mixtures.

3.1. Sparsity function

There may be many ways to quantify the degree of sparse of a signal. A sparse signal has its energy concentrated in some narrow segments of the signal. Notice that the function $a^2 + b^2$, subject to $|a| + |b| = 1$, has its maximum of 1 when either a or b is zero and its minimum of $\frac{1}{2}$ when $a = b = \frac{1}{2}$, so we can define the sparsity of a signal as its total energy normalized to the sum of the absolute values of the signal. Mathematically the sparsity function of signal $x(n)$ can be defined as

$$ S_x = \frac{\sum_n x^2(n)}{(\sum_n |x(n)|)^2}. \qquad (2) $$

Note that S_x has a maximum of 1 when $x(n) = 0$ for all $n \neq n_0$ where n_0 is arbitrary, i.e., $x(n)$ is most sparse, and a minimum of $\frac{1}{N}$, where N is the length of $x(n)$, when $x(n) = constant$ for all n. Thus, S_x indeed defines the degree of sparse of a signal $x(n)$.

3.2. Principle of sparse separation

If the peaks of two sparse signals, $s_1(n)$ and $s_2(n)$, are not all severely overlapped, then it can be shown that the sparsity of the mixture $x(n) = c_1 s_1(n) + c_2 s_2(n)$ will be less than the maximum of the sparsities of the two source signals. That is to say $S_x \leq \max(S_{s_1}, S_{s_2})$. Define $f_1(c)$ be the sparsity of $s_1(n) + c s_2(n)$ and $f_2(c)$ be the sparsity of $s_2(n) + c s_1(n)$, it can also be shown that $f_1(c)$ and $f_2(c)$ both have local maximum at $c = 0$. This means that the sparsity of a sparse signal will go down if slightly superimposed by another sparse signal. This property can be utilized to separate the sparse sources from their mixtures. Based on Equation 1, the de-mixing process can be described by

$$ s_c(n) = x_2(n) - c x_1(n), \qquad (3) $$

where c is determined by finding the minima of the objective function

$$ J(c) = 1/S_{s_c}, \qquad (4) $$

where S_{s_c} is the sparsity of $s_c(n)$.

Applied to the mixtures of free radical EPR spectra as shown in Figures 1 and 2, $J(c)$ has the form shown in Figure 6. It can be seen that $J(c)$ has three local minima rather than two. From the principle above we can conclude that the minimum with the lowest value is corresponding to the most sparse source signal, while that with the highest value corresponding to the other.

4. Results and Discussions

Using the pure EPR spectra of the two free radicals hydroxyl and superoxide, as shown in Figure 1, we simulate the spectra mixing effect numerically, for two cases where one is noise free and the other has a SNR of 20dB. We apply our sparsity based approach to the simulated EPR mixing spectra. The results are shown in Figures 8 and 10. For the purpose of comparison, we also apply the FastICA method to the same simulated spectra, and the results are shown in Figures 7 and 9.
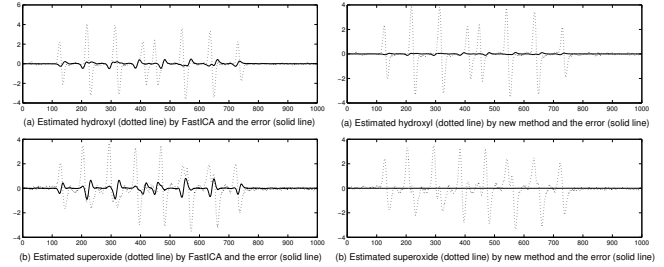

Figure 7: FastICA approach, noise free, (a) hydroxyl; (b) superoxide

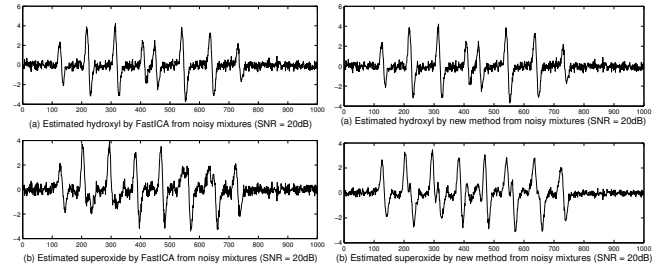Figure 8: Sparsity based approach, noise free, (a) hydroxyl; (b) superoxide

Figure 9: FastICA approach, SNR=20dB, (a) hydroxyl; (b) superoxide

Figure 10: Sparsity based approach, SNR=20dB, (a) hydroxyl; (b) superoxide

The results for the noise-free case are shown in Figures 7 and 8, where the dotted lines represent the estimated EPR spectra and the solid lines represent the errors comparing to the true sources. From Figure 8 we can see that our sparsity based approach can almost perfectly get the two pure EPR spectra. While on the other hand, the spectra estimated by the FastICA approach are severely distorted and the estimation error is very notable, as shown in Figure 7. The lower trace of Figure 7 shows that the distortion of several peaks in the superoxide spectrum estimated by FastICA are very severely distorted, and this makes FastICA not very suitable for EPR spectra decomposition since it is unfortunately these peaks who contain useful information of the EPR spectra.

Figures 9 and 10 are the results for the case of SNR=20dB. In these two figures we only give the estimated EPR spectra for a better view, while one can compare them to the true spectra shown in Figure 8 to obtain a sense of their distortion and estimation error. As shown in Figure 10, the peaks of the EPR spectra estimated by our new method are all perfectly reserved though the background of the spectra are noisy than the true ones. However, the background does not contain any useful information. Therefore our new method can work almost equally

well in the case of SNR=20dB to the noise free case. and even more severe in the noisy case. While the EPR spectra estimated by FastICA are even more severely distorted than in the noise free case, as shown in Figure 9.

If we have more than two mixtures available, which are all composed by the same two source spectra, a PCA preprocessing can reduce the number of mixtures to two, with improved signal to noise ratio and without loss of useful information.

It seems to be very surprising that the optimization of a very simple sparsity function, shown as Equation 2, is able to separate sources not independent, since the numerator of Equation 2 is only an estimation of second order statistics, while it is well known that it is impossible to separate linear mixtures using only second order statistics (without exploiting the temporal information) even for independent sources. However, one should note that the denominator of Equation 2 is a highly nonlinear function and it contains up to infinity higher order statistics.

5. Conclusions

There is a need to get pure EPR spectra from their mixtures, and this task can be done through blind source separation. However, the ICA based approach does not work well since the assumption of statistically independence cannot be satisfied. By exploiting the sparsity of the EPR spectra, we proposed a new sparse component analysis method that can perfectly separate the pure spectra from the mixtures in the noise free case and still works well when the signal is noisy. The new sparse component analysis method may also apply to any other situations where the sources have a reasonable degree of sparsity. It can also play a helpful role in the research of general independent component analysis or blind source separation using sparse representation, as studied in [13, 14].

References

[1] J. Y. Ren, C. Q. Chang, P. C. W. Fung, J. G. Shen, and F. H. Y. Chan, "Free radical EPR spectroscopy analysis using blind source separation," *Journal of Magnetic Resonance*, vol.166, pp.82–91, 2004.

[2] B. Kirste, "Methods for automated analysis and simulation of electron paramagnetic resonance spectra," *Anal. Chim. Acta.*, vol.265, pp.191–200, 1992.

[3] D. A. Svistunenko, M. A. Sharpe, P. Nicholls, M. T. Wilson, and C. E. Cooper, "A new method for quantization of spin concentration by EPR spectroscopy: Application to methemoglobin and metmyoglobin," *Journal of Magnetic Resonance*, vol.142, pp.266–275, 2000.

[4] O. Steinbock, B. Neumann, B. Cage, J. Saltiel, S. C. Muller, and N. S. Dalal, "A demonstration of principal component analysis for EPR spectroscopy: Identifying pure component spectra from complex spectra," *Analytical Chemistry*, vol.69, pp.3708–3713, 1997.

[5] R. Stoyanova, A. C. Kuesel, and T. R. Brown, "Application of principal-component analysis for NMR spectral quantization," *Journal of Magnetic Resonance, Series A*, vol.115 pp.265–269, 1995.

[6] A. Prieto, B. Prieto, C. Puntonet, A. Canas, and P. MartinSmith, "Geometric separation of linear mixtures of sources: Application to speech signals," In J. Cardoso, C. Jutten, and P. Loubaton, eds.: *Independent Component Analysis and Signal Separation (Proc. ICA'99)*, pp.295–300, 1999.

[7] A. J. Bell and T. J. Sejnowski, "An information-maximization approach to blind separation and blind deconvolution," *Neural Computation* vol.7, pp.1129–1159, 1995.

[8] A. Hyvrinen, "Fast and robust fixed-point algorithms for independent component analysis," *IEEE Trans. Neural Netw*, vol.10, pp.626–634, 1999.

[9] L. Tong, R. W. Liu, V. Soon, and Y. F. Huang, "Indeterminacy and identifiability of blind identification," *IEEE Transactions on Circuits and Systems*, vol.38, pp.499–509, 1991.

[10] C. Q. Chang, Z. Ding, S. F. Yau, and F. H. Y. Chan, "A matrix-pencil approach to blind separation of colored nonstationary signals," *IEEE Transactions on Signal Processing*, vol.48, pp.900–907, 2000.

[11] L. J. Berliner, V. Khramtsov, H. Fujii, and T. L. Clanton, "Unique in vivo applications of spin traps," *Free Radic. Biol. Med.*, vol.30, pp.489–99, 2001.

[12] K. J. Liu, M. Miyake, T. Panz, and H. Swartz, "Evaluation of DEPMPO as a spin trapping agent in biological systems," *Free. Radic. Biol. Med.*, vol.26, pp.714–21, 1999.

[13] M. Zibulevsky, and B. A. Pearlmutter, "Blind source separation by sparse decomposition in a signal dictionary," *Neural Computation*, vol.13, pp.863–882, 2001.

[14] P. Bofill, and M. Zibulevsky, "Undetermined blind source separation using sparse representations," *Signal Processing*, vol.81, pp.2353–2362, 2001.