A Hybridization of Simulated Annealing and Local PCA for Automatic Component Assignment Within ICA

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Abstract. Independent component analysis (ICA) as well as blind source separation (BSS) often faces the problem of assigning the independent or uncorrelated components estimated with ICA or BSS techniques to underlying source signals, artifacts or noise contributions. In this work an automatic assignment tool is presented which uses *a priori* knowledge about the form of some of the signals to be extracted. The algorithm is applied to the problem of removing water artifacts from 2D NOESY NMR spectra. The algorithm uses local PCA to approximate the water artifact and defines a suitable cost function which is optimized using simulated annealing. The blind source separation of the water artifact from the remaining protein spectrum is done with the recently developed algorithm dAMUSE.

1 Introduction

Blind Source Separation (BSS) methods consider the separation of observed sensor signals into their underlying source signals knowing neither these source signals nor the mixing process. Considering biomedical applications, BSS methods are especially valuable to remove artifacts from the signals recorded. In many biomedical applications quite a number of independent components have to be determined with ICA algorithms and it is not *a priori* clear how many components should be assigned to the signals representing artifacts. This is especially obvious in 2D NOESY NMR proton spectra of proteins, where a prominent water artifact distorts the recorded spectra considerably. Recently artifact removal was considered using BSS techniques based on a generalized eigenvalue decomposition (GEVD) of a matrix pencil [11], [7]. Replacing the GEVD with the algorithm dAMUSE [12], [10], BSS and denoising can be achieved in one stroke. The method is very efficient and fast and outperformed FastICA and SOBI in

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all cases studied [9]. But, the estimated components related with the water artifacts had to be assigned by hand. With more than 100 estimated components this turns out to become a rather tedious undertaking prone to be biased by subjective judgements of the assignment criteria.

In this work we propose a local PCA approximation to the free induction decay (FID) related with the water artifact. Hereby we explicitly use knowledge about the form of the water FID and the fact that inevitably it will always dominate the total FID of these systems. We formulate a suitable cost function to be optimized by simulated annealing [3] to determine those underlying uncorrelated components, which are estimated with dAMUSE [12] and are related with the water artifact.

The following section introduces the new algorithm AutoAssign. To illustrate the proposed method, it is applied to experimental 2D NOESY NMR spectra of aqueous solutions of several protein fragments[1].

2 Theory

2.1 BSS – Model and Signal Separation with dAMUSE

Given N complex sensor signals $x(t_{1,n}, t_{2,l}) \equiv x_n[l]$ sampled at L discrete time instances, and arranged in a data matrix $\mathbf{X}_{N\times L}$ with N rows and L columns, where the rows of the data matrix correspond to 1D free induction decays (FIDs) of the 2D NOESY experiment taken at N discrete evolution times $t_{1,n} \equiv [n],\ n = 1, \ldots, N$. Note that FIDs represent superpositions of exponentially decaying sinusoids with different frequencies and decay constants, called interferograms. Blind source separation (BSS) then relies on the following linear mixing model $\mathbf{x}[l] = \mathbf{A}\mathbf{s}[l] + \boldsymbol{\epsilon}[l]$ where $l = 0, \ldots, L-1$ and $\mathbf{x}[l] = (x_1[l], \ldots, x_N[l])^T$ designates the observed signals (interferograms) sampled at time instance $[l]$, $\mathbf{s}[l]$ the underlying uncorrelated source signals (single FIDs) , $\mathbf{A}$ the stationary mixing matrix and $\boldsymbol{\epsilon}[l]$ an additional zero mean white Gaussian noise term which is independent of the source signals.

A generalized eigenvalue decomposition using congruent matrix pencils may be used to separate water artifacts, i.e. those FIDs originating from water proton magnetic moments, from 2D NOESY NMR spectra of proteins [8]. It provides the basis for the algorithm dAMUSE [12] used in this work. It solves the BSS problem relying only on second order GEVD techniques using congruent matrix pencils [13], [11]. The latter are formed with correlation matrices $(\mathbf{R}_{x1}, \mathbf{R}_{x2})$ of zero mean sensor signals $\mathbf{x}[l]$, i.e. the observed FIDs. The algorithm dAMUSE extends the GEVD using congruent matrix pencils to signals embedded in a high-dimensional feature space of delayed coordinates to provide a means to perform BSS and denoising simultaneously [10]. The method uses the concept of a trajectory matrix borrowed from singular spectral analysis (SSA)[2]. Consider N sensor signal components $x_n[l]$ comprising L samples, each row of the trajectory

[1] We are grateful to W. Gronwald and H. R. Kalbitzer to provide those spectra.

matrix [5] contains M delayed versions $x_n(l+(M-m)K), m=0,.....,M-1$, where K denotes the delay in number of sampling intervals between consecutive rows and M gives the dimension of the embedding space. The total trajectory matrix $\mathbf{X}^e$ of all N signals is formed by concatenating the component trajectory matrices $\mathbf{X}_n^e$ according to: $\mathbf{X}^e = [\mathbf{X}_1^e, \mathbf{X}_2^e, \ldots, \mathbf{X}_N^e]^T$. After embedding, the instantaneous mixing model can be written as $\mathbf{X}^e = \mathbf{A}^e\mathbf{S}^e$ where $\mathbf{S}^e$ represents the source signal trajectory matrix, $\mathbf{A}^e = \mathbf{A}_n \otimes \mathbf{I}_{M\times M}$ is a block matrix and $\mathbf{I}_{M\times M}$ denotes the identity matrix. The sensor pencil can be computed with $\mathbf{R}_{x1} = \langle \mathbf{X}^e(\mathbf{X}^e)^H \rangle$ and $\mathbf{R}_{x2} = \langle \mathbf{Z}\mathbf{Z}^H \rangle$ using the trajectory matrix $\mathbf{X}^e$ and a filtered version $\mathbf{Z} = \mathbf{X}^e\mathbf{C}^H$ with $\mathbf{C}$ a circular convolution matrix and ^{H} denoting the Hermitian conjugate [10].

The eigenvalues and eigenvectors of the congruent matrix pencil $(\mathbf{R}_{x1}, \mathbf{R}_{x2})$ can be obtained via standard eigenvalue decompositions (EVD) applied in two consecutive steps:

- Compute a standard EVD of the symmetric positive definite correlation matrix $\mathbf{R}_{x1} = \mathbf{V}\mathbf{\Lambda}\mathbf{V}^H$, i.e, the eigenvectors $(\mathbf{v}_i)$ and eigenvalues (λ_i) and organize the eigenvalues in descending order $(\lambda_1 > \lambda_2 > \ldots > \lambda_q \ldots > \lambda_{NM})$. For denoising purposes, among others a variance criterion can be established to retain only the largest eigenvalues exceeding a threshold parameter Θ [12].
- The transformation matrix can then be computed using the q largest eigenvalues and respective eigenvectors $\mathbf{Q} = \mathbf{\Lambda}^{-\frac{1}{2}}\mathbf{V}^H$ where $\mathbf{Q}$ is an $q \times NM$ matrix.
- Compute the matrix $\tilde{\mathbf{R}} = \mathbf{Q}\mathbf{R}_{x2}\mathbf{Q}^H$ and its standard eigenvalue decomposition: the eigenvector matrix $\mathbf{U}$ and eigenvalue matrix $\mathbf{D}_x$

The eigenvectors of the pencil $(\mathbf{R}_{x1}, \mathbf{R}_{x2})$ form the columns of the eigenvector matrix $\mathbf{E} = \mathbf{Q}^H\mathbf{U} = \mathbf{V}\mathbf{\Lambda}^{-\frac{1}{2}}\mathbf{U}$ which can be used to compute the output signals as described in [12].

2.2 The Algorithm AutoAssign

Applying the BSS algorithms above to 2D NOESY NMR spectra to separate the water artifact and other related artifacts from the protein spectra, the most tedious task is to assign the uncorrelated components estimated to the water signal. Because of erratic phase relations, up to 40 estimated components out of 128 or 256 need to be assigned to the water resonance. Hence an automated and objective assignment procedure deemed necessary.

The idea is to embed the signal in a high-dim feature space of delayed coordinates and to apply a cluster analysis to the columns of the corresponding trajectory matrix. Within each cluster a *local* PCA is then performed to obtain a low-dim approximation to the signals using only the most important principal components to approximate the signals. The latter are then fed into a suitable cost function which is optimized with simulated annealing.

Embedding and local PCA: Consider a signal $\mathbf{x}_n[l] = (x_n[l], x_n[l+1], \ldots, x_n[l+(M-1)])^T$ embedded in an M-dim feature space. Divide the space in k_c subspaces

$\mathcal{N}^{(k)}$ using *k-means* clustering and center the signals in each cluster locally by subtracting the cluster mean $\bar{\mathbf{x}}_n^{(i)} = (\mathcal{N}^{(i)})^{-1} \sum_{\mathbf{x}_n[l] \in \mathcal{N}^{(i)}} \mathbf{x}_n[l], \quad i = 1, \ldots, k_c$. Next a principal component analysis (PCA) is performed on each cluster separately. Then a local approximation $\tilde{\mathbf{x}}_n[l] = \sum_{j=1}^{p(i)} \alpha_j[l] \mathbf{w}_j^{(i)} + \bar{\mathbf{x}}_n^{(i)}$ to the time domain signal is computed, using only the eigenvectors $\mathbf{w}_j$ to the p largest eigenvalues and $\alpha_j[l] = \mathbf{x}_n[l] \cdot \mathbf{w}_j^{(i)}$ and $\mathbf{x}_n[l] \in \mathcal{N}^{(i)}$. This yields the new trajectory matrix $\tilde{\mathbf{X}}_n$, the entries of which represent local PCA approximations of the original signals

$$\tilde{\mathbf{X}}_n = \begin{bmatrix} \tilde{x}_n[M-1] & \tilde{x}_n[M] & \ldots & \tilde{x}_n[L-1] \\ \tilde{x}_n[M-2] & \tilde{x}_n[M-1] & \ldots & \tilde{x}_n[L-2] \\ \tilde{x}_n[M-3] & \tilde{x}_n[M-2] & \ldots & \tilde{x}_n[L-3] \\ \vdots & \vdots & \ddots & \vdots \\ \tilde{x}_n[0] & \tilde{x}_n[1] & \ldots & \tilde{x}_n[(L-1)-(M-1)] \end{bmatrix} \tag{1}$$

The final global approximation $\langle \tilde{\mathbf{x}}_n[l] \rangle_{[l]}, \quad l = M-1, ..., L-1$ is obtained by averaging all entries at the same time instance $[l]$ which lie along diagonals.

As the water FID provides the dominant contribution to each interferogram observed, the approximation can be simplified further by retaining only the principal component to the largest eigenvalue, i.e. $\mathbf{x}_{n,1}[l] = \alpha_1[l]\mathbf{w}_1$. The approximation thus contains the contribution from the water signal almost exclusively.

Simulated annealing: This approximation to the FID related with the water artifact is then used to define a cost function $\mathcal{E}(\boldsymbol{\beta}) = \sum_{l=0}^{L-1} (x_{n,\boldsymbol{\beta}}[l] - x_{n,1}[l])^2$ to be minimized with simulated annealing [3]. The BSS approximation to the water signal using the uncorrelated components estimated with the dAMUSE algorithm is obtained as $x_{n,\boldsymbol{\beta}}[l] = \sum_j \beta_j (\mathbf{A})_{nj} s_j[l]$ where a new configuration $\boldsymbol{\beta}$ is generated by changing any β_j randomly. A configuration is represented by a vector $\boldsymbol{\beta}$ which contains as many components β_j as there are sources $\mathbf{s}_j$. To each source one element of β is assigned which can take on the values $\beta_j \in \{0, 1\}$ only. The difference in the values of the cost function for the current and the new configuration $\Delta\mathcal{E} = \mathcal{E}(\boldsymbol{\beta}_{new}) - \mathcal{E}(\boldsymbol{\beta}_{old})$ determines the probability of acceptance of the new configuration in the simulated annealing algorithm according to

$$\frac{P[\beta_{new}]}{P[\beta_{old}]} = \min \left\{ 1, \exp \left(-\frac{\Delta\mathcal{E}}{k_B T} \right) \right\} \tag{2}$$

After convergence, the configuration which best fits to the local PCA approximation of the water signal is obtained. Nullifying these components deliberately, the water-artifact-free protein spectrum $\tilde{\mathbf{x}}_n$ can be reconstructed using the remaining estimated source signals $\tilde{\mathbf{s}}_n$ via $\tilde{\mathbf{x}}_n = \mathbf{A}\tilde{\mathbf{s}}_n$.

3 Results and Discussion

The algorithms discussed above have been applied to several experimental 2D NOESY proton NMR spectra of proteins dissolved in water. A simple pre-

saturation of the water resonance was applied to prevent saturation of the dynamic range of the analog-digital-converter (ADC). Every data set comprises 512 or 1024 FIDs $S(t_1, t_2) \equiv x_n[l]$ or their corresponding spectra $\hat{S}(1_1, \omega_2) \equiv \hat{x}_n[l]$, with $L = 2048$ samples each, which correspond to $N = 128$ or $N = 256$ FIDs evaluated at $t_1 \equiv [n]$. With each increment of the evolution period also the phase is incremented, hence only FIDs with equal phase modulations have been considered for analysis. A BSS analysis, using the algorithm dAMUSE [12] in combination with AutoAssign, was applied to all data sets.

3.1 Experimental Spectra

To test the performance of the algorithm AutoAssign in combination with the algorithm dAMUSE we applied it the following four sets of 2D NOESY proton NMR spectra of proteins dissolved in water:

- First we applied the algorithms to 2D NOESY proton NMR spectra of the cold-shock protein *Tm*CSP of the bacterium *Thermotoga maritima*. It represents a small globular protein with 66 amino acids [4].
- The spectra in Fig. 1 refer to the RAS-binding domain (RBD) of the protein RalGDS. The domain forms a 87 amino acids long C-terminus of the latter protein [1].
- The synthetic peptide P11 consists of 24 amino acids only and represents the helix H11 of the human Glutathion reductase [6].
- Finally the 2D NOESY NMR spectra of the *Histidine containing phosphocarrier protein* HPr of the bacterium *Staphylococcus carnosus* with 88 amino acids have been analyzed.

In each case a number $N_{IC} = N_{PC}$ of uncorrelated components has been estimated using dAMUSE and N_w components have been automatically assigned to the water artifact using the algorithm AutoAssign.

Table 1. Parameter values for the embedding dimension of the feature space of dAMUSE (M_{dAMUSE}) and localPCA ($M_{localPCA}$), the number (K) of sampling intervals used per delay in the trajectory matrix, the number of clusters (k_c) used with local PCA in AutoAssign, the number N_{pc} of principal components retained after the first step of the GEVD and the half-width (σ) of the Gaussian filter used in the algorithm dAMUSE

Parameter	TmCSP	RalGDS	P11	HPr
$M_{localPCA}$	40	50	30	50
M_{dAMUSE}	2	4	3	2
k_c	2	2	2	2
$N_{PC} = N_{IC}$	168	168	148	396
$N_w(dAMUSE)$	46	56	46	160
σ	0.3	0.1	0.3	0.03
K	1	1	1	1

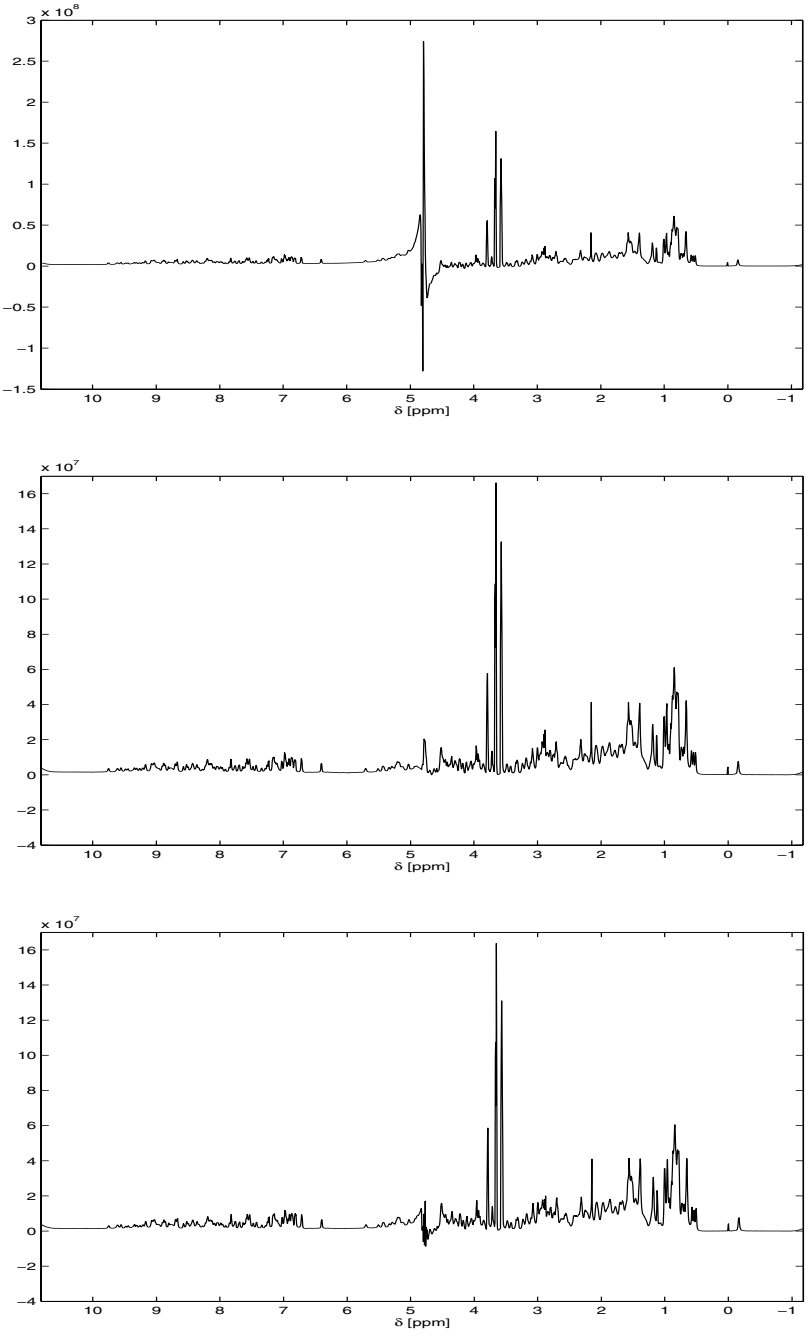

Fig. 1. RalGDS: a)- 1D slice of the original 2D NOESY spectrum corresponding to the shortest evolution period t_1, b)- corresponding protein spectrum obtained by subtracting the local PCA approximation to the FID of the water artifact from the total FID, c)- corresponding protein spectrum reconstructed with the dAMUSE and AutoAssign algorithms

Table 2. Signal-to-noise ratios of the reconstructed spectra of TmCSP, RalGDS, P11 and HPr obtained dAMUSE and AutoAssign

	SNR [dB]			
	TmCSP	RalGDS	P11	HPr
dAMUSE	19.3	21.9	21.9	19.8

To estimate a local PCA approximation of the water artifact, data have been projected into a $M_{localPCA}$-dimensional feature space and k_c clusters have been determined in feature space with a *k-means* algorithm. Also a Gaussian filter with width σ centered near the water resonance in the 1D proton NMR spectra has been used. The algorithm AutoAssign automatically identified a number N_w of uncorrelated components which have to be assigned to the water artifact. The algorithm dAMUSE was used to solve the corresponding BSS problem. Remember that the automatic assignment has been done with the FIDs corresponding to the shortest evolution period only and it is assumed that this assignment also holds for all other evolution periods as well. Note that all parameters have been varied and optimal parameters have been selected according to the best minimum of the cost function of the SA-algorithm. The parameters yielding the best minimum of the cost function with the simulated annealing algorithm are collected in Table 1.

With all experimental spectra the SNR has been determined relative to the *approximated* protein spectra, which were obtained by subtracting a local PCA approximation of the FID of the water artifact from the total FID as explained in the theory section. Hence with all experimental spectra the corresponding *approximated* spectra formed the reference against which the *reconstructed* spectra have been compared. The SNRs of the reconstructed spectra obtained with dAMUSE plus AutoAssign are summarized in Table 2. Fig. 1 shows a 1D slice of the 2D NOESY NMR spectrum together with the *approximated* spectrum. The local PCA yields a very good approximation of the contribution of the water artifact to the total FID. After subtraction and Fourier transformation only a small water peak remains in the resulting protein spectrum. The *reconstructed* spectrum obtained with the algorithms dAMUSE and AutoAssign is also shown in Fig. 1. Excellent results are also obtained with no intensity distortions of the protein peaks of the spectra. Also all baseline distortions are perfectly straightened out and even peaks very close to the water artifact are well recovered. Comparable results are obtained with the other proteins as well but are not shown because of space limitations.

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