AutoAssign – An Automatic Assignment Tool for Independent Components

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Abstract. In this work an automatic assignment tool for estimated independent components within an independent component analysis is presented. The algorithm is applied to the problem of removing the water artifact 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 the 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 [5, 10]. Replacing the GEVD with the algorithm dAMUSE [8, 9], BSS and denoising can be achieved in one stroke. The method is very efficient and fast and outperformed FastICA and SOBI in all cases studied [7]. 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 and to use simulated annealing [3] to

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determine those underlying uncorrelated components, estimated with dAMUSE, which have to be assigned to the water artifact.

The following section will provide a short summary of the algorithm dAMUSE [9] and introduces the new algorithm AutoAssign. To illustrate the proposed method, an application is discussed comprising theoretical 2D NOESY NMR spectra with added noise and an experimental water resonance added as well.

2 Theory

2.1 BSS Model

Given N complex sensor signals $x(t_{1,n}, t_{2,l}) \equiv x_n[l]$ sampled at L discrete time instances, they can be 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 $t_{1,n} \equiv [n],\ n = 1, \ldots, N$. 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 sampled at time instance l, $\mathbf{s}[l]$ the underlying uncorrelated source signals, $\mathbf{A}$ the stationary mixing matrix and $\boldsymbol{\epsilon}[l]$ an additional zero mean white Gaussian noise term which is independent of the source signals.

2.2 The Algorithm dAMUSE

A generalized eigenvalue decomposition using congruent matrix pencils may be used to separate water artifacts from 2D NOESY NMR spectra of proteins [6]. It provides the basis for the algorithm dAMUSE [9] used in the following, hence a short summary of the algorithm will be given.

Matrix Pencils: To solve the BSS problem we rely on second order GEVD techniques using congruent matrix pencils [10, 11]. First a matrix pencil $(\mathbf{R}_{x1}, \mathbf{R}_{x2})$ is computed with the sensor signals $\mathbf{x}[l]$, i.e. the observed FIDs. The $\mathbf{R}_{xj},\ j = 1, 2$ denote corresponding correlation matrices of zero mean data. A GEVD of the sensor pencil then provides a solution for the BSS problem [10] and is given by $\mathbf{R}_{x1}\mathbf{E} = \mathbf{R}_{x2}\mathbf{E}\boldsymbol{\Lambda}$ where $\mathbf{E}$ represents a *unique* eigenvector matrix if the diagonal matrix $\boldsymbol{\Lambda}$ has *distinct* eigenvalues λ_i.

Embedding the Signals in Feature Space: Recently the GEVD using congruent matrix pencils has been extended to data embedded in a high-dimensional feature space of delayed coordinates to provide a means to perform BSS and denoising simultaneously [8, 9]. The method uses the concept of a trajectory matrix borrowed from singular spectral analysis (SSA) [1]. Consider a sensor signal component $x_n[l]$, each row of the trajectory matrix [4] contains delayed versions $x_n(l + (M - m)K)$, where K denotes the delay in number of sampling intervals between consecutive rows and M gives the dimension of the embedding space. Using a set of L samples and M delayed versions of the signal

$x_n[l+(M-m)K]$, $l=0,\ldots,L-1$, $m=0,\ldots,M-1$, the trajectory matrix is given by

$$(\mathbf{X}_n^e) = \begin{bmatrix} x_n[(M-1)K] & x_n[1+(M-1)K] & \cdots & x_n[L-1] \\ x_n[(M-2)K] & x_n[1+(M-2)K] & \cdots & x_n[L-1-K] \\ \vdots & \vdots & \ddots & \vdots \\ x_n[0] & x_n[1] & \cdots & x_n[L-1-(M-1)K] \end{bmatrix} \quad (1)$$

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 $\mathbf{S}^e$ also 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. Then if $\mathbf{A}_n$ is an invertible matrix, $\mathbf{A}^e$ is also invertible as it is the Kronecker product of two invertible matrices. The sensor pencil can be computed with $\mathbf{R}_{x1} = L^{-1}\mathbf{X}\mathbf{X}^H$ and $\mathbf{R}_{x2} = L^{-1}\mathbf{Z}\mathbf{Z}^H$ using the trajectory matrix $\mathbf{X}^e$ and a filtered version $\mathbf{Z}^e = \mathbf{X}\mathbf{C}^H$ with $\mathbf{C}$ a circular convolution matrix and H denoting the Hermitian conjugate [8]. The sensor pencil is again congruent with a corresponding source pencil, hence the respective eigenvectors are related by $\mathbf{E}_s^H = \mathbf{E}^H \mathbf{A}^e$. The linear transformation of the trajectory matrices then reads $\mathbf{Z}^e = \mathbf{E}^H \mathbf{X}^e = \mathbf{E}^H \mathbf{A}^e \mathbf{S}^e = \mathbf{E}_s^H \mathbf{S}^e$ Assuming that the source signals and their filtered versions are uncorrelated, the matrix $\mathbf{E}_s$ is block-diagonal, with block size $(M \times M)$.

Denoising Using the Algorithm dAMUSE: The eigenvalues and eigenvectors of a matrix pencil can be obtained via standard eigenvalue decompositions (EVD) applied in two consecutive steps. Considering the pencil $(\mathbf{R}_{x1}, \mathbf{R}_{x2})$ the following steps are performed:

- Compute a standard eigenvalue decomposition 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, a variance criterion has been established to retain only the largest eigenvalues exceeding a threshold parameter Θ [9].
- The transformation matrix can then be computed using the q largest eigenvalues and respective eigenvectors $Q = \mathbf{\Lambda}^{-\frac{1}{2}}\mathbf{V}^H$ 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 above.

2.3 The Algorithm AutoAssign

Applying the BSS algorithms above to 2D NOESY NMR spectra to separate the water artifact and 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 feed 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 subspaces $\mathcal{N}^{(k)}$ using *k-means* clustering and center the signals in each cluster locally by subtracting the cluster mean $\bar{\mathbf{x}}_n^{(k)} = (\mathcal{N}^k)^{-1} \sum_{\mathbf{x}_n[l] \in \mathcal{N}^k} \mathbf{x}_n[l]$. Next a principal component analysis (PCA) is performed on each cluster separately. Then a local approximation $\mathbf{x}_{n,p}^{(k)}[l] = \sum_{j=1}^{p} \alpha_j[l]\mathbf{w}_j + \bar{\mathbf{x}}_n^{(k)}$ to the time domain signal is computed, using only the eigenvectors $\mathbf{w}_j$ to the p largest eigenvalues and $\alpha_j = \langle \mathbf{x}_{n,p}^{(k)}[l]\mathbf{w}_j \rangle$. This yields the new trajectory matrix $\mathbf{X}_{n,p}^{(k)}$ with entries $\mathbf{x}_{n,p}^{(k)}[l]$ and M delayed version thereof. The final local approximation $\langle \mathbf{x}_{n,p}^{(k)}[l] \rangle_{[l]}$ is obtained by averaging all entries at the same time instance (which lie along diagonals). Putting together all these local approximations yields the final approximation to the original signal observed.

As the water signal provides the dominant contribution to each FID 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 $\Delta\mathcal{E} = \mathcal{E}(\boldsymbol{\beta}_n) - \mathcal{E}(\boldsymbol{\beta}_{n+1})$ determines the probability of acceptance of the new configuration in the simulated annealing algorithm according to

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

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 were applied to an artificial 2D NOESY proton NMR spectra of proteins dissolved in water. Every data set comprises 512 or 1024 FIDs $S(t_1, t_2) \equiv x_n[l]$, with $L = 2048$ samples each, which correspond to $N = 128$ or $N = 256$ evolution periods $t_1 \equiv [n]$. To each evolution period belong four FIDs with different phase modulations, hence only FIDs with equal phase modulations have been considered for analysis. A BSS analysis, using the algorithm dAMUSE, was applied to the FIDs collected in the data matrix $\mathbf{X}$. Filtering was done in the frequency domain for convenience. Hence, all FIDs have been Fourier transformed with respect to the sampling time t_2 to obtain 1D spectra $\hat{S}(t_1, \omega_2) \equiv \hat{\mathbf{x}}_n(\omega)$, $0 < n \leq 128$ or $0 < n \leq 256$. The filtered versions of the data were obtained by applying a Gaussian filter $\hat{h}(\omega)$ with width $\sigma = 1$, centered near the water resonance, to each row of the data matrix $\hat{\mathbf{X}}$. After filtering the data have been back-transformed to the time domain to calculate the corresponding correlation matrices of the pencils. The automatic assignment of the uncorrelated components, estimated with dAMUSE, which belong to the water resonance was achieved using the proposed algorithm AutoAssign which is based on a local PCA and a simulated annealing optimization.

For test purposes, a theoretical 2D NOESY proton NMR spectrum of the cold-shock protein of the bacterium *Thematoga maritima*, containing only protein resonances, was used. The spectrum was obtained through reverse calculation using the algorithm RELAX [2]. Gaussian white noise with realistic amplitude as well as an experimentally recorded water resonance were added to the theoretical spectrum (see Fig. 1).

The BSS was done with the algorithm dAMUSE [9] using $K = 1$. The second correlation matrix $\mathbf{R}_{x2}$ of the pencil was computed with the theoretical spectrum with added noise taken as the filtered version of the original spectrum. An approximation of the water artifact dominating the time domain FIDs was obtained with the local PCA algorithm. As the experimental pure water FID was available also, both could be compared to access the quality of the approximation. To perform local PCA, each sample of the data was projected into a $M = 40$ dimensional feature space and *k-means* clustering was used to divide the projected data into $k = 2$ cluster. Only the largest principal component was considered to approximate the water signal.

Fig. 2-a) compares the total FID corresponding to the shortest evolution period with the local PCA approximation (Fig. 2-b)) of the latter. It is immediately obvious that the water artifact dominates the total FID. It is seen that local PCA provides a very good approximation to the water artifact. This can be corroborated by subtracting the approximate water FID from the total FID and transforming the resulting FID into the frequency domain. The resulting protein spectrum contains only small remnants of the huge water artifact as can be seen in Fig. 3. The spectra thus obtained will henceforth be called *approximated spectra*.

This indicates that it should be possible to use the local PCA approximation of the water artifact as a reference signal in a cost function to be min-

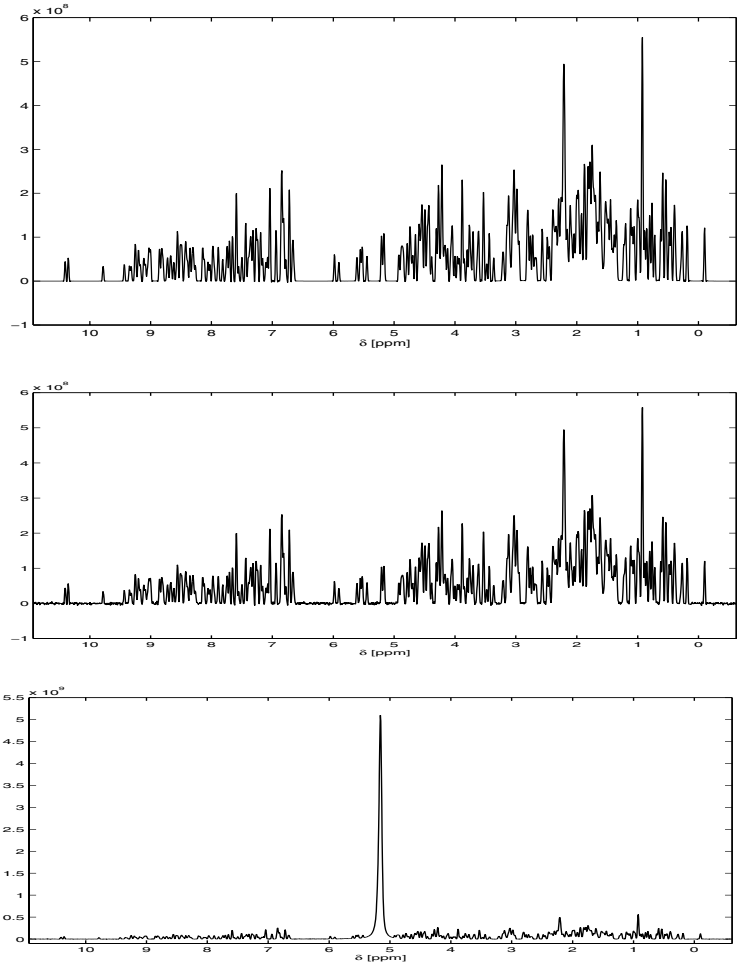

Fig. 1. (a) – Theoretical protein spectrum, (b) – Theoretical protein spectrum with Gaussian noise, (c) – Theoretical spectrum with Gaussian noise and an experimentally recorded water resonance.

imized with a simulated annealing algorithm. This is confirmed by analyzing the theoretical protein spectra plus noise plus water artifact (see Fig. 1-c)) with the dAMUSE algorithm to extract the uncorrelated components and using simulated annealing (SA) to automatically assign those components related with the water artifact. The SA-algorithm identifies the same 9 components irrespective whether the experimental water FID or its local PCA approximation has been used in the cost function. Without denoising, the reconstructed protein spectrum resembles the original noisy spectrum (Fig. 1-b)) except for a much enhanced noise level. Calculating the signal-to-noise ratio (SNR) via $SNR(\mathbf{x}, \mathbf{x}_{noise})[dB] = 20 \log_{10} \frac{\|\mathbf{x}\|}{\|\mathbf{x}-\mathbf{x}_{noise}\|}$ where $\mathbf{x}$ denotes the theoretical spec-

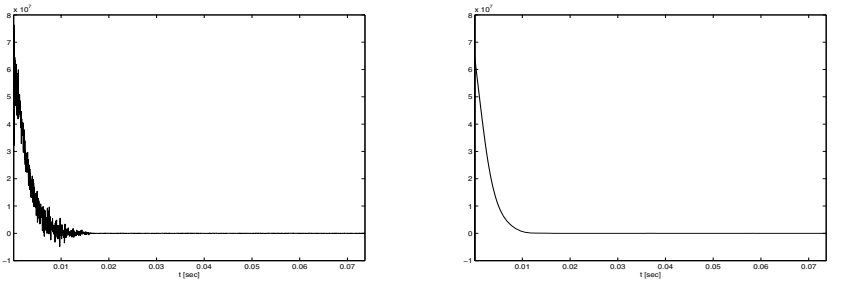

Fig. 2. Free Induction Decays (FID) of a) – the total FID of the protein signal plus additive noise plus an experimental water FID, b) – local PCA approximation of the total FID.

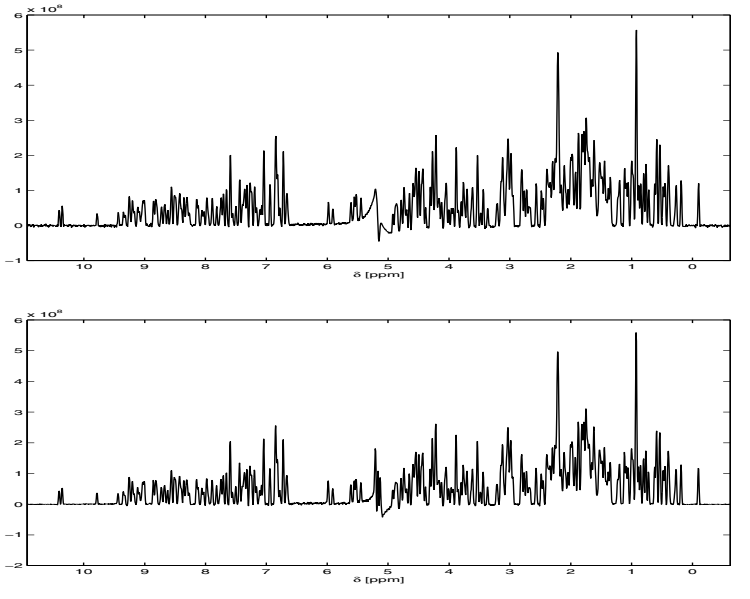

Fig. 3. a) – Protein spectrum obtained after subtracting the approximated water FID from the total FID and Fourier transformation of the difference FID, b) – Reconstructed protein spectrum obtained with dAMUSE.

trum, $\mathbf{x}_{noise}$ its noisy counterpart, the theoretical spectrum plus gaussian noise shows a SNR of $24.5dB$, whereas the reconstructed protein spectrum only yields a SNR of $10.1dB$. Denoising can be accomplished elegantly with the dAMUSE algorithm which achieves blind source separation and denoising simultaneously. The water related components extracted are automatically assigned with the algorithm AutoAssign using a local PCA approximation to the water artifact. The optimal number M of delays as well as the optimal size of the time lag have been determined by the best minimum to the cost function obtained with

the SA algorithm. A minimum of the cost function has been obtained with using one time-delayed FID, a lag of one sampling interval and by retaining 158 eigenvectors (out of $2 \cdot 128$) after the first step of the algorithm dAMUSE. The result of the dAMUSE denoising is shown in Fig. 3, the SNR achieved amounts to $SNR = 22.1\ dB$.

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