β-NMF and sparsity promoting regularizations for complex mixture unmixing: Application to 2D HSQC NMR.

Afef CHERNI*, Sandrine ANTHOINE*, Caroline CHAUX*

*Aix-Marseille Univ, CNRS, Centrale Marseille, I2M, Marseille, France.

Overview

• **Introduction**

NMR: Nuclear Magnetic Resonance

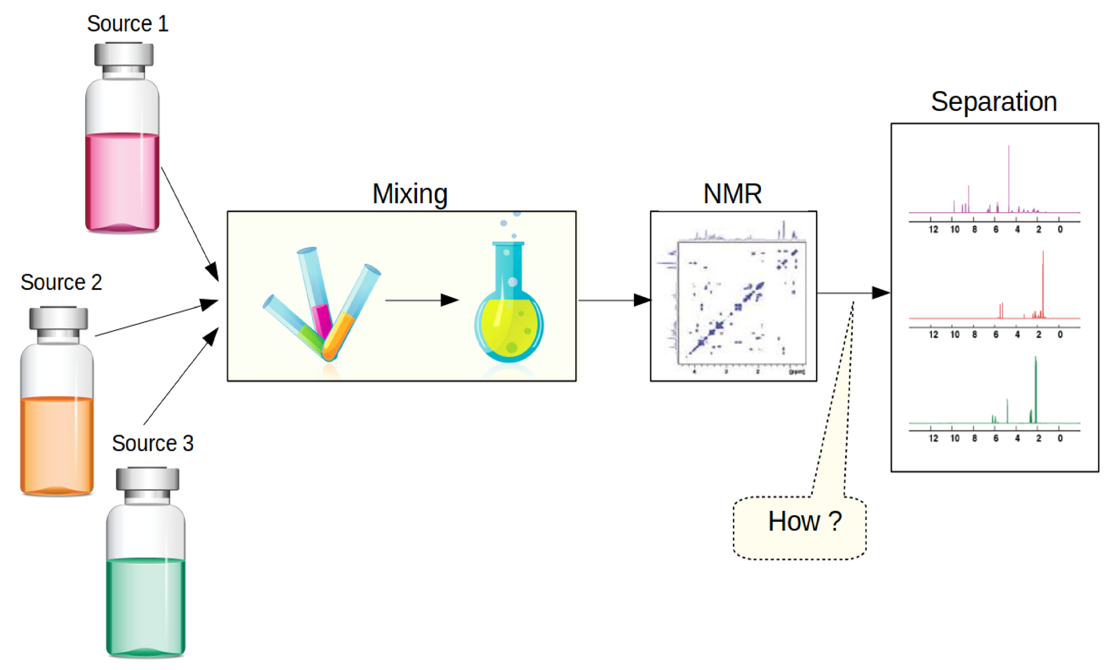
a spectroscopy technique used to identify molecules in a given chemical mixture.

2D HSQC: Heteronuclear Single Quantum Coherence

a NMR experience used to determinate the correlations between a carbon and its attached proteins.

BSS: Blind Source Separation

an efficient mathematical method used to analyze data which are modeled as the linear combination of elementary sources or components (see (1)).



• **Objective**

Given the measurements $\mathbf{X} \in \mathbb{R}^{M\times L}$, find the unknown sources $\mathbf{S} \in \mathbb{R}^{N\times L}$ and the unknown mixing matrix $\mathbf{A} \in \mathbb{R}^{M\times N}$ related to $\mathbf{X}$ through

$$\mathbf{X} = \mathbf{AS} + \mathbf{N} \approx \mathbf{AS} \tag{1}$$

• **Problem**

✗ Indeterminacies of solutions

$$(\exists \Lambda \in \mathbb{R}^{N\times N}) \quad \text{such that} \quad \mathbf{A}' = \mathbf{A}\Lambda \ \text{ et } \ \mathbf{S}' = \Lambda^{-1}\mathbf{S} \tag{2}$$

where Λ is a diagonal or a permutation matrix.

✗ 2D NMR spectra present a high level of sparsity with a spectral overlap and poor resolution.

Theory

• **Regularization approach**

$$\underset{\mathbf{A},\,\mathbf{S}}{\text{minimize}} \ \Theta(\mathbf{A},\mathbf{S}) := \underbrace{\Phi(\mathbf{A},\mathbf{S})}_{\text{Data fidelity}} + \underbrace{\Psi(\mathbf{A},\mathbf{S})}_{\text{Regularization term.}} \tag{3}$$

• **Standard choices**: **Fixing** $\Phi(\mathbf{A},\mathbf{S})$ as Frobenius norm and **adapting** $\Psi(\mathbf{A},\mathbf{S})$:

$$\underset{\mathbf{A},\,\mathbf{S}}{\text{minimize}} \ \Theta(\mathbf{A},\mathbf{S}) := \frac{1}{2}\|\mathbf{X}-\mathbf{AS}\|_F^2 + \lambda_{\mathbf{A}}\Psi_{\mathbf{A}}(\mathbf{A}) + \lambda_{\mathbf{S}}\Psi_{\mathbf{S}}(\mathbf{S}). \tag{4}$$

Previous approaches [1, 2]: solve (4) using different regularization functions defined for all $\mathbf{u} = (u_i)_{i=1\dots L} \in \mathbb{R}^L$ as:

$$\iota_+(\mathbf{u}) = \begin{cases} 0 & \text{if } u_i \geq 0 \ \forall i \\ +\infty & \text{otherwise.} \end{cases}$$

$$\ell_1(\mathbf{u}) = \left(\sum_{i=1}^{L} |u_i|\right)$$

$$\mathbf{Ent}(\mathbf{u}) = \sum_{i=1}^{L} \text{ent}(u_i)$$

$$\text{ent}(u) = \begin{cases} u\log(u) & \text{if } u > 0 \\ 0 & \text{if } u = 0 \\ +\infty & \text{otherwise.} \end{cases}$$

$\lambda_{\mathbf{A}}$ and $\lambda_{\mathbf{S}}$ are regularization parameters.

• **Generalization**: **Fixing** $\Phi(\mathbf{A},\mathbf{S})$ as β-divergence and **adapting** $\Psi(\mathbf{A},\mathbf{S})$

$$\underset{\mathbf{A},\,\mathbf{S}}{\text{minimize}} \ \Theta(\mathbf{A},\mathbf{S}) := \beta\text{-}\mathbf{div}(\mathbf{A},\mathbf{S}) + \lambda_{\mathbf{A}}\Psi_{\mathbf{A}}(\mathbf{A}) + \lambda_{\mathbf{S}}\Psi_{\mathbf{S}}(\mathbf{S}) \tag{5}$$

where

$$(\forall (\mathbf{u},\mathbf{v}) \in (\mathbb{R}_+^L)^2) \quad \beta\text{-}\mathbf{div}(\mathbf{u},\mathbf{v}) = \sum_{i=1}^{L} \beta\text{-div}(u_i|v_i) \tag{6}$$

and for all $(u,v) \in \mathbb{R}_+^2$ and $\beta \in \mathbb{R} \setminus \{0,1\}$

$$\beta\text{-div}(u|v) = \frac{1}{\beta(\beta-1)}\left(u^\beta + (\beta-1)v^\beta - \beta u v^{\beta-1}\right).$$

Practical implementation

• **Generic alternating minimization strategy**

For $k = 0, 1, \dots$

$$\mathbf{A}_{k+1} = \underset{\mathbf{A}}{\text{argmin}} \ \beta\text{-}\mathbf{div}(\mathbf{X},\mathbf{AS}_k) + \lambda_{\mathbf{A}}\Psi_{\mathbf{A}}(\mathbf{A}) \ \ (\mathbf{I})$$

$$\mathbf{S}_{k+1} = \underset{\mathbf{S}}{\text{argmin}} \ \beta\text{-}\mathbf{div}(\mathbf{X},\mathbf{A}_{k+1}\mathbf{S}) + \lambda_{\mathbf{S}}\Psi_{\mathbf{S}}(\mathbf{S}) \ \ (\mathbf{II})$$

• **Multiplicative algorithm based on a MM strategy for** $\beta > 2$

($\mathbf{I}$) $\Psi_{\mathbf{A}} = \iota_+$

$$\mathbf{A}_{k+1} = \left(\frac{\left(\mathbf{X} \odot (\mathbf{A}_k\mathbf{S})^{\odot(\beta-2)}\right)\mathbf{S}^T}{(\mathbf{A}_k\mathbf{S})^{\odot(\beta-1)}\mathbf{S}^T}\right)_+^{\odot\frac{1}{\beta-1}} \odot \mathbf{A}_k. \tag{7}$$

($\mathbf{II}$) $\Psi_{\mathbf{S}} =$

a) ι_+

$$\mathbf{S}_{k+1} = \left(\frac{\mathbf{A}^T(\mathbf{X} \odot (\mathbf{AS}_k)^{\odot(\beta-2)})}{\mathbf{A}^T(\mathbf{AS}_k)^{\odot(\beta-1)}}\right)_+^{\odot\frac{1}{\beta-1}} \odot \mathbf{S}_k \tag{8}$$

b) $\ell_1 + \iota_+$

$$\mathbf{S}_{k+1} = \left(\frac{\mathbf{A}^T(\mathbf{X} \odot (\mathbf{AS}_k)^{\odot(\beta-2)}) - \lambda_{\mathbf{S}}}{\mathbf{A}^T(\mathbf{AS}_k)^{\odot(\beta-1)}}\right)_+^{\odot\frac{1}{\beta-1}} \odot \mathbf{S}_k \tag{9}$$

c) $\mathbf{Ent} + \iota_+$

$$\mathbf{S}_{k+1} = \left(\frac{\gamma}{\alpha}\mathcal{W}\left(\frac{\alpha}{\gamma}\exp(-\frac{\delta}{\gamma})\right)\right)_+^{\odot\frac{1}{\beta-1}} \odot \mathbf{S}_k \tag{10}$$

where $\odot$ denotes the Hadamard product, $\mathcal{W}$ the Lambert function [3] and

$$\begin{cases} \alpha = \mathbf{A}^T(\mathbf{AS}_k)^{\odot(\beta-1)} \odot \mathbf{S}_k, \\ \gamma = \frac{\lambda_{\mathbf{S}}}{\beta-1}\mathbf{S}_k, \\ \delta = \lambda_{\mathbf{S}}(\mathbf{S}_k + \mathbf{S}_k \odot \log(\mathbf{S}_k)) - \mathbf{A}^T(\mathbf{X} \odot (\mathbf{AS}_k)^{\odot(\beta-2)}) \odot \mathbf{S}_k. \end{cases}$$

Application to 2D HSQC NMR

Real case

$\mathbf{X} \in \mathbb{R}^{5\times1024\times2048}$: 5 mixtures.

$\mathbf{A} \in \mathbb{R}^{5\times4}$: a mixture matrix.

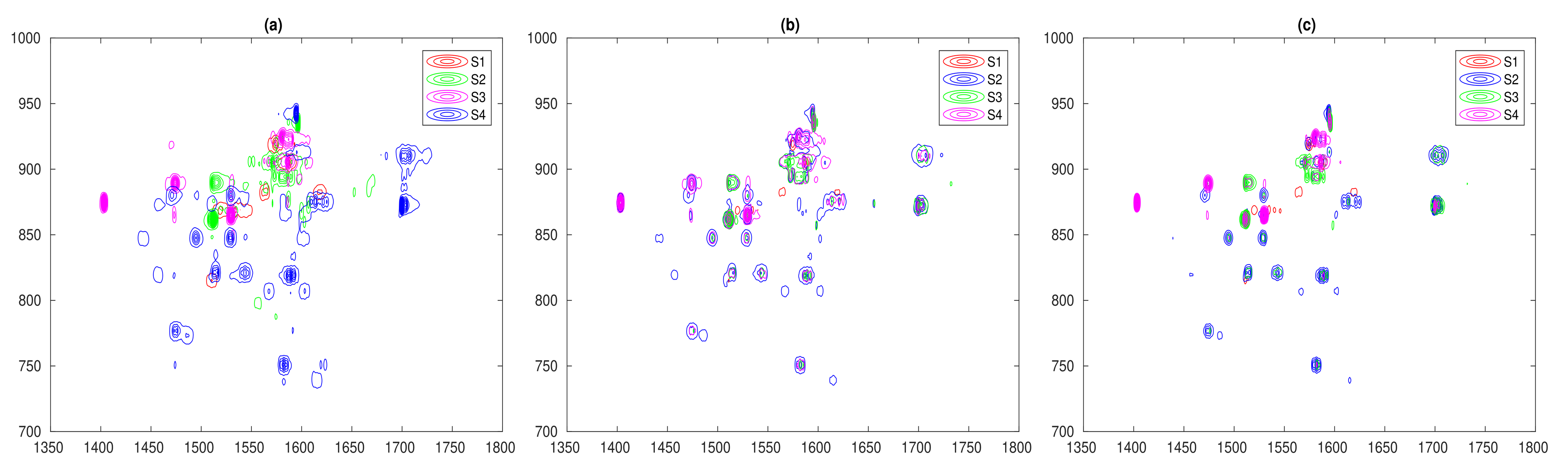
$\mathbf{S} \in \mathbb{R}^{4\times1024\times2048}$: 4 pure sources (Limonene, Nerol, α-Terpinolene, β-Caryophyllene).

Simulated case

$\mathbf{X}$ is simulated following model (1) with $\mathbf{N} \sim \mathcal{N}(0,\sigma^2)$ with $\sigma = 1.9713\times10^4$.

	Data fidelity term	$\lambda_{\mathbf{S}}$	$\Psi_{\mathbf{S}}$	SDR	SIR	SAR	Amari-index
Simulated case	Squared Frobenius		ι_+	18.073	28.854	18.514	0.0121
		0.1σ	$\ell_1 + \iota_+$	**30.299**	31.475	**39.462**	0.0272
			$\mathbf{Ent} + \iota_+$	18.287	36.859	18.354	0.0090
		σ	$\ell_1 + \iota_+$	21.140	21.788	29.872	0.0492
			$\mathbf{Ent} + \iota_+$	17.334	**36.909**	17.421	0.0198
		10σ	$\ell_1 + \iota_+$	17.041	25.581	22.104	0.0189
			$\mathbf{Ent} + \iota_+$	16.021	30.625	18.216	0.0861
	β-divergence		ι_+	**36.711**	40.854	**41.571**	**0.0054**
		0.1σ	$\ell_1 + \iota_+$	36.531	40.853	41.255	**0.0054**
			$\mathbf{Ent} + \iota_+$	**36.711**	40.854	41.570	**0.0054**
		σ	$\ell_1 + \iota_+$	32.041	40.868	34.135	**0.0054**
			$\mathbf{Ent} + \iota_+$	36.710	40.852	41.570	**0.0054**
		10σ	$\ell_1 + \iota_+$	22.906	**41.140**	23.102	**0.0054**
			$\mathbf{Ent} + \iota_+$	36.688	40.851	41.513	**0.0054**
Real case	Squared Frobenius	10σ	$\ell_1 + \iota_+$	04.984	13.956	07.951	0.1804
			$\mathbf{Ent} + \iota_+$	05.755	**14.434**	08.446	0.1793
	β-divergence	10σ	$\ell_1 + \iota_+$	**07.240**	11.487	10.574	**0.1610**
			$\mathbf{Ent} + \iota_+$	07.220	11.396	**10.632**	0.1657

Average criteria obtained in 2D NMR spectra with various $\lambda_{\mathbf{S}}$.



Pure 2D HSQC sources (a), estimated sources: using Eq.(4) with ℓ_1 norm (b), using Eq.(5) with **Ent** (c).

• **Conclusions**

✓ The β-divergence combined with ℓ_1 norm or **Ent** function ensures the BSS of the 2D HSQC NMR.

✓ In the real case, better SDR and SAR values are obtained using β-divergence. However, a slight deterioration on the SIR values is noticed.

• **Perspectives**

☞ Optimize the choice of $\lambda_{\mathbf{S}}$.

☞ Verify the linearity of the model (1) in the context of 2D NMR.

• **References**

[1] A. Cherni and C. Chaux. Régularisation mixte et parcimonie pour la séparation aveugle de sources en spectroscopie rmn 2d. 2019.

[2] A. Cherni, E. Piersanti, S. Anthoine, C. Chaux, L. Shintu, M. Yemloul, and B. Torrésani. Challenges in the decomposition of 2d nmr spectra of mixtures of small molecules. *Faraday discussions*, 218:459–480, 2019.

[3] R.-M. Corless, G.-H. Gonnet, D.-E. Hare, D.-J. Jeffrey, and D.-E. Knuth. On the lambert W function. *Advances in Applied Mathematics*, 5(1):329–359, 1996.

A*Midex Initiative d'excellence Aix-Marseille
CNRS
Institut de Mathématiques de Marseille
ICASSP2020 Barcelona