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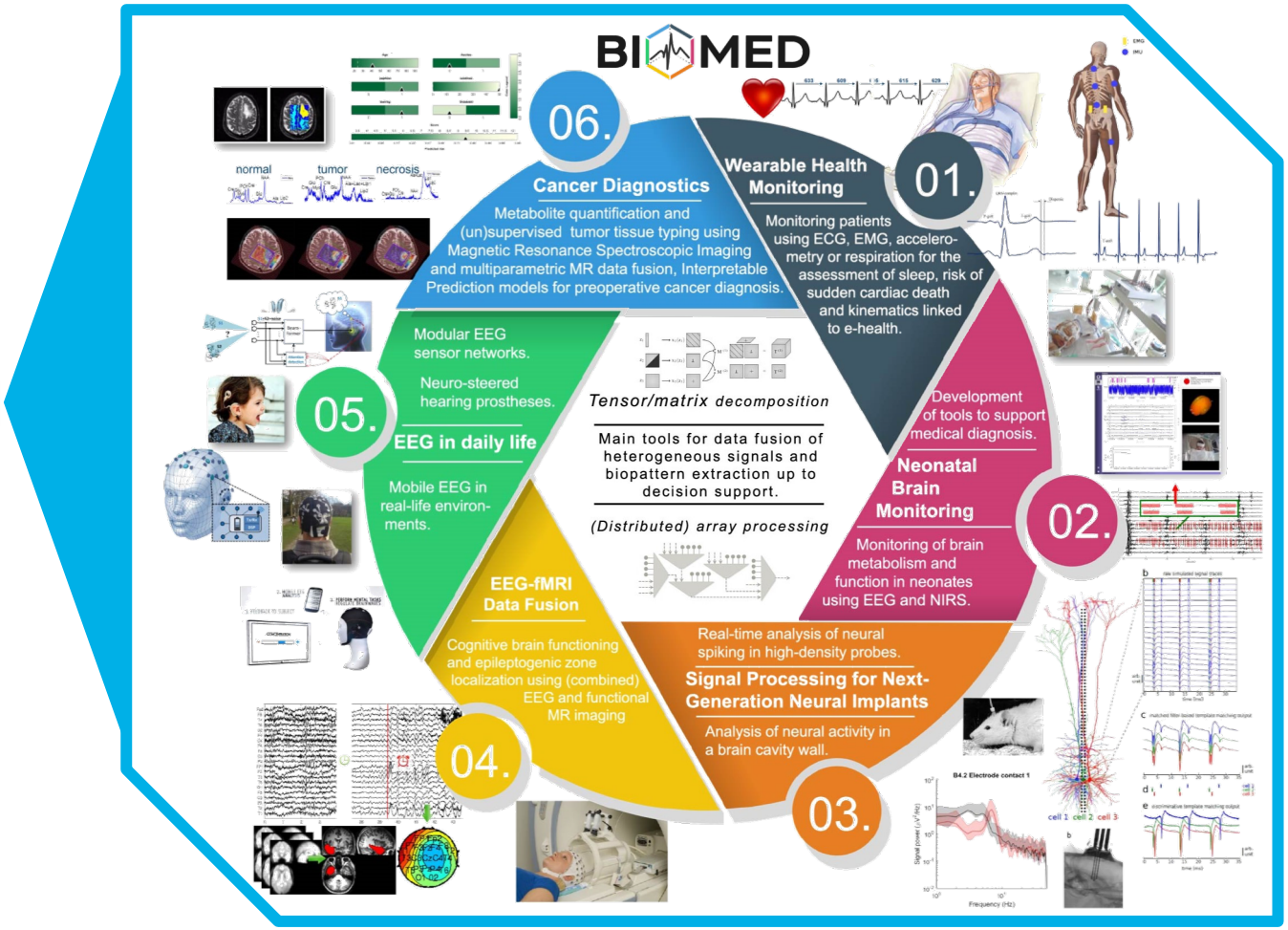
Established by the European Commission

Tensor-based blind source separation of (simultaneous) EEG and fMRI

Borbála Hunyadi

Research in close collaboration with

UZ LEUVEN



BIOMED

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EEG-fMRI data fusion

UZ Leuven Departments:

Radiology

Neurology

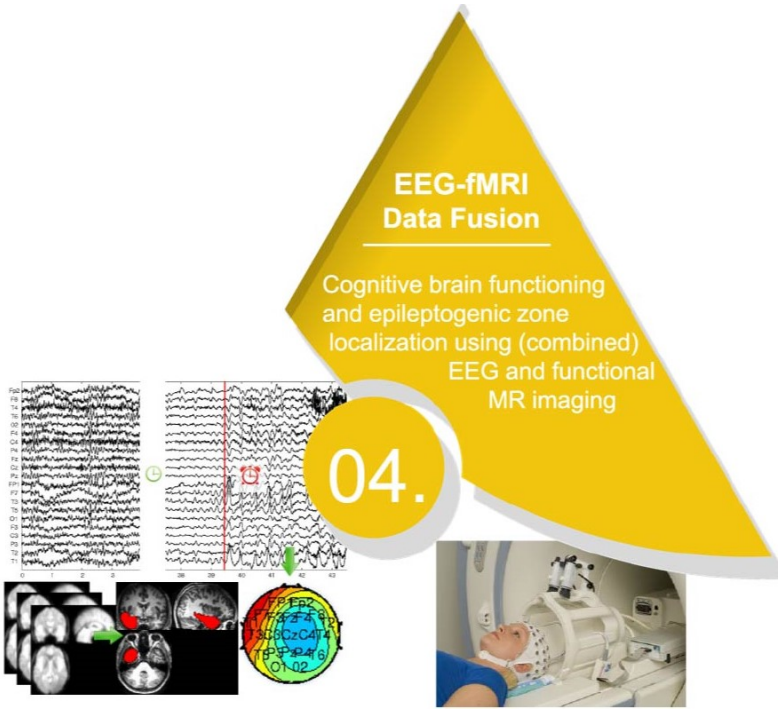
KU Leuven:

Dept. of Psychology

Dept. of Kinesiology and Rehabilitation Sciences

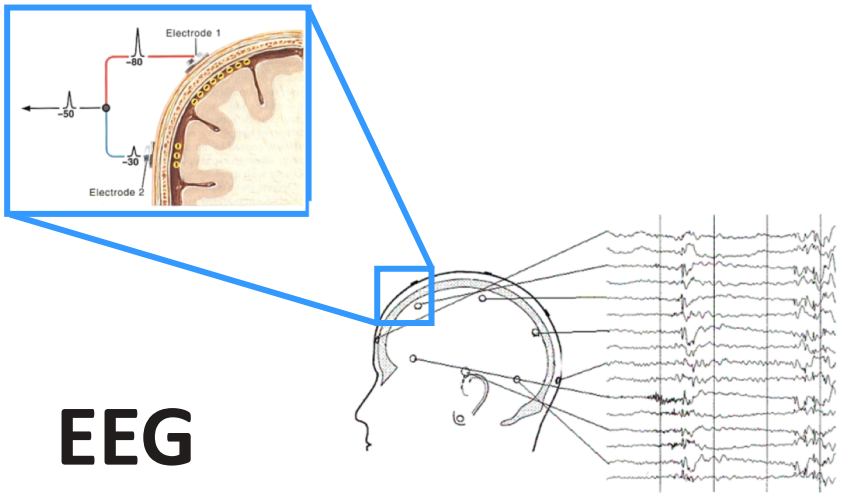
Oxford University:

Dept. of Engineering Science



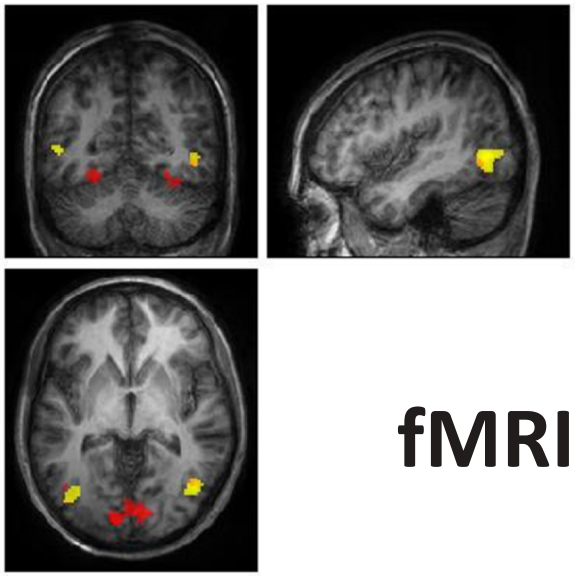
Recording brain activity with EEG and fMRI

EEG measures electrical potentials on the scalp



EEG

fMRI localizes active brain regions



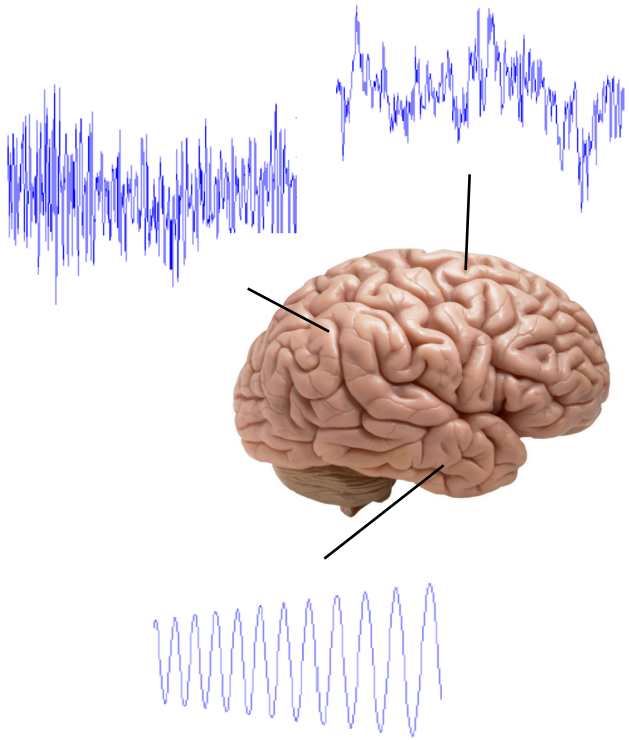
fMRI

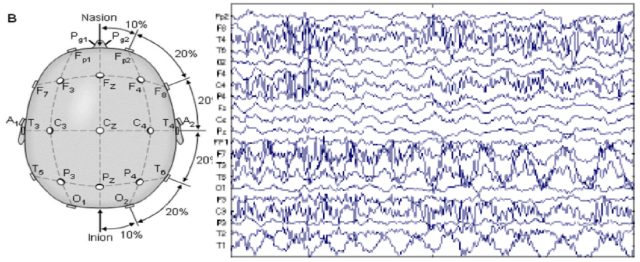
Combining EEG and fMRI:

EEG *good* ***temporal resolution*** *(~ ms)*

fMRI *good* ***spatial resolution*** *(~ mm)*

Recording brain activity with EEG and fMRI





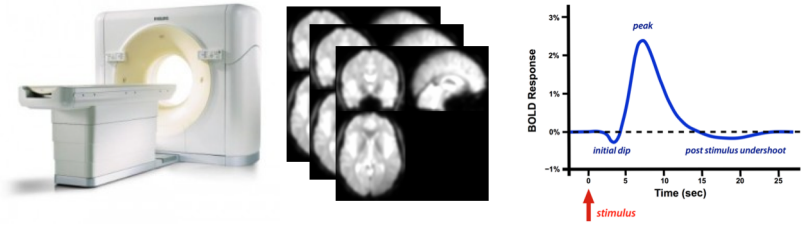
EEG

Mixture and

indirect

measurement

fMRI



Blood **O**xygen **L**evel **D**ependent Signal

Motivation for tensor-based BSS and fusion

- Both EEG and fMRI record a mixture of brain and non-brain signals
- Low SNR → the more information the better
- Complementary in terms of
  - Temporal and spatial resolution
  - Origin of the signal (electrical vs metabolic)

KEYTOOL : Blind source separation

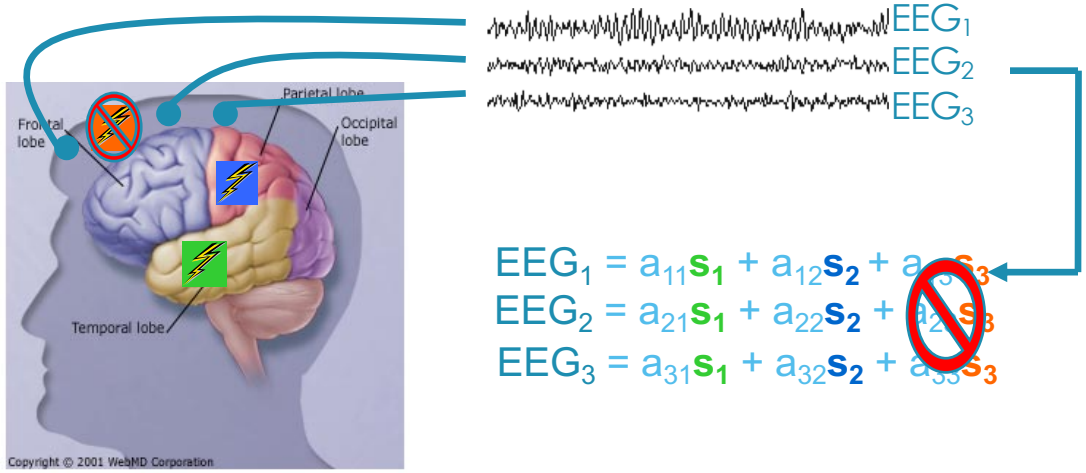
Signal analysis difficult because of artefacts → **REMOVE**

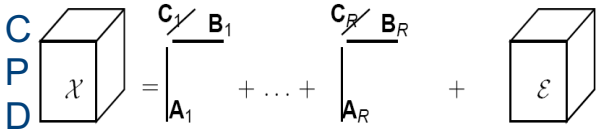
Matrix based Blind Source Separation (BSS)

- ***Non-unique*** →*Constraints are needed (orthogonal, independency)*

TENSOR based BSS: unique under mild conditions

ADD extra problem-specific constraints (nonnegative, sparse)





Applications

- **Epilepsy**
- Other neurological diseases
  - Sleep disorders
  - Schizophrenia
  - Alzheimer's disease
  - Stroke
- Cognitive science
  - **Task – information processing in the brain**
  - Resting state
- Assistive technologies
  - Consciousness detection
  - **BCI**, BMI
- Commercial
  - Gaming
  - neuroeconomics

Epilepsy surgery

Refractory epilepsy

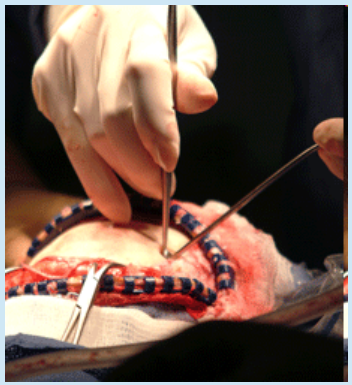
- ~30% of all epilepsies
- The occurrence of seizures cannot be controlled by medication

Focal epilepsy

- Seizure originates within a certain network in the brain

Surgery

- Key to success: precise **localization** of the epileptogenic zone

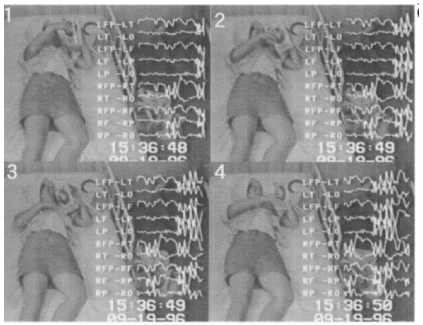


Presurgical evaluation

Epileptogenic zone

- Hypothetical region
- Use of complementary techniques

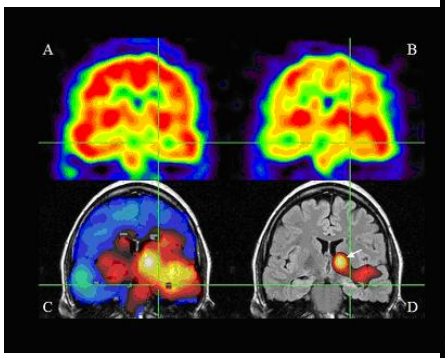
Ictal Video-EEG monitoring



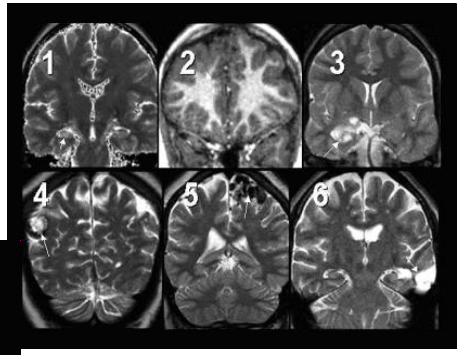
[Y. Shirasaka, I. Mitsuyoshi Brain and Development 1999]

Interictal EEG-fMRI

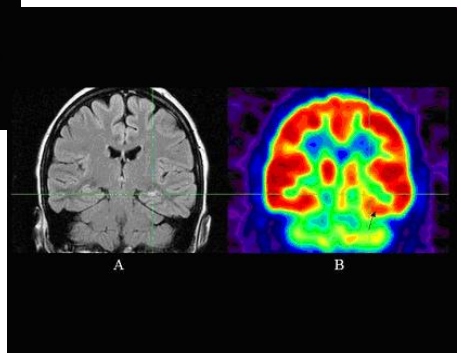
http://fmri.uib.no/



SISCOM



Structural MRI



PET

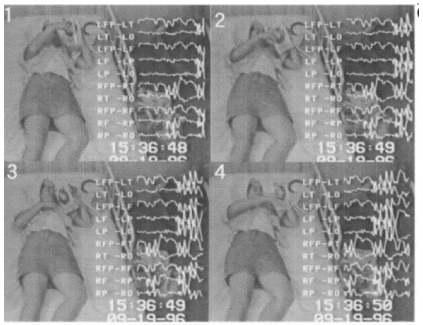
+ Psychological and psychiatric evaluation

Presurgical evaluation

Epileptogenic zone

- Hypothetical region
- Use of complementary techniques

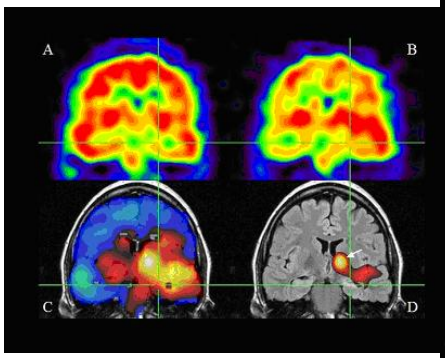
Ictal Video-EEG monitoring



[Y. Shirasaka, I. Mitsuyoshi Brain and Development 1999]

Interictal EEG-fMRI

http://fmri.uib.no/



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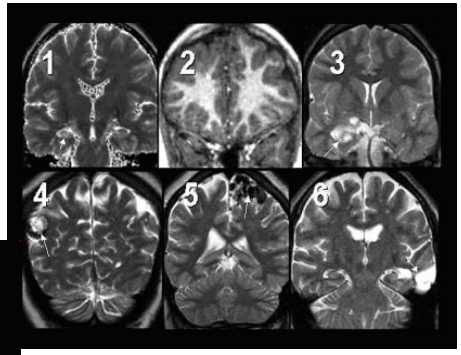
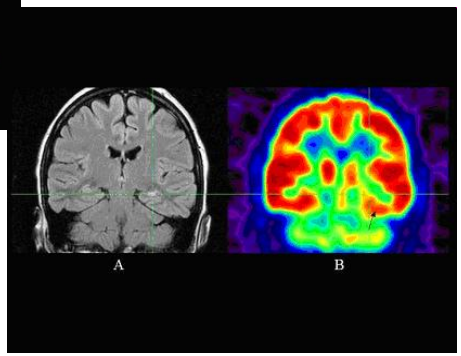


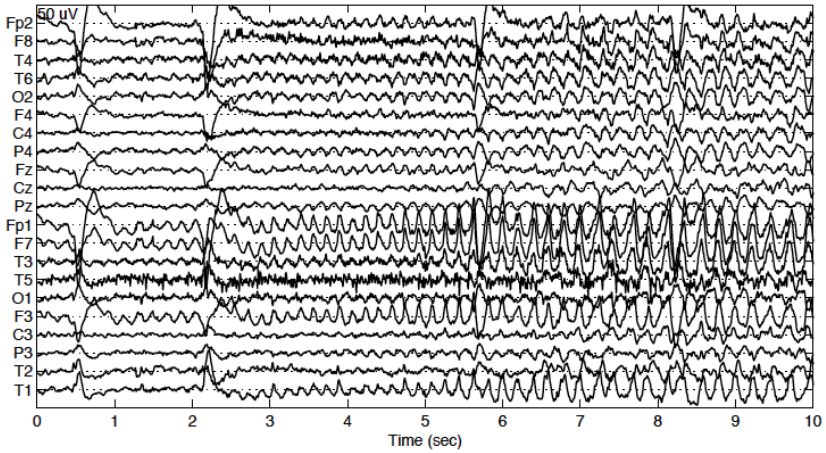
Structural MRI



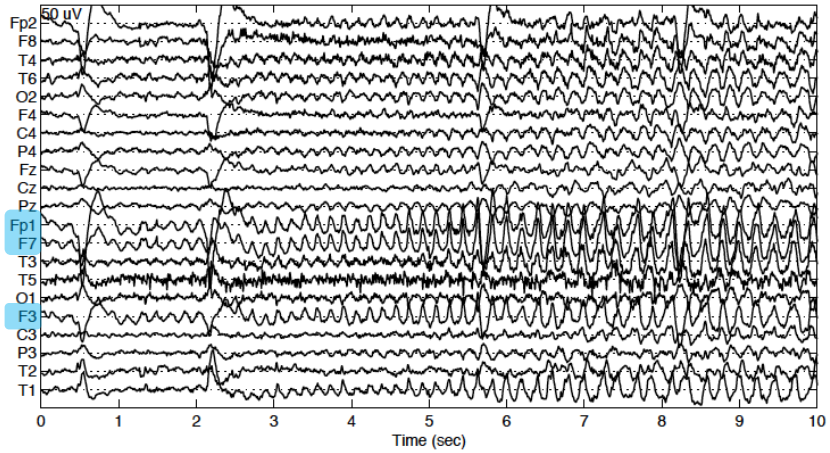
PET

+ Psychological and psychiatric evaluation

EEG analysis



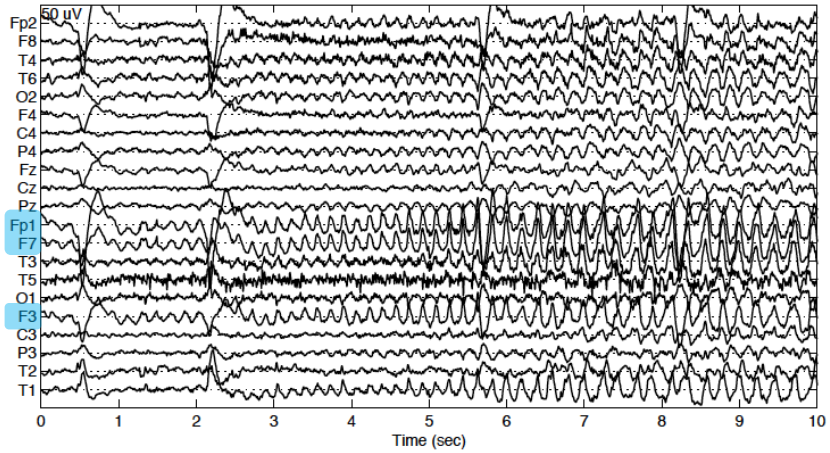
Automated EEG analysis

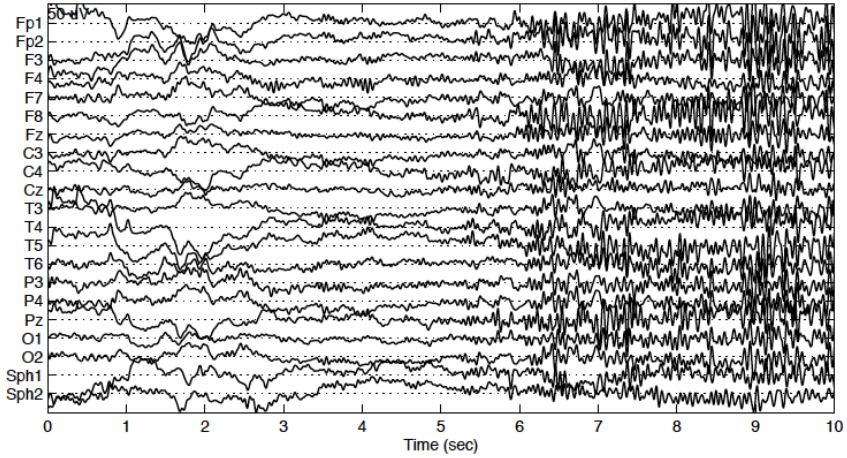


Goal (clinic):

- identify the channels where the seizure originates

Automated EEG analysis





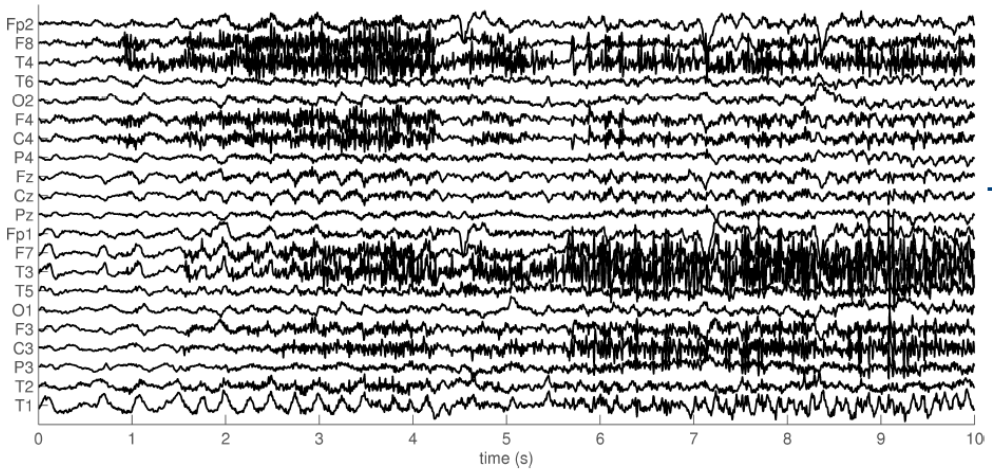
Goal (clinic):

- identify the channels where the seizure originates

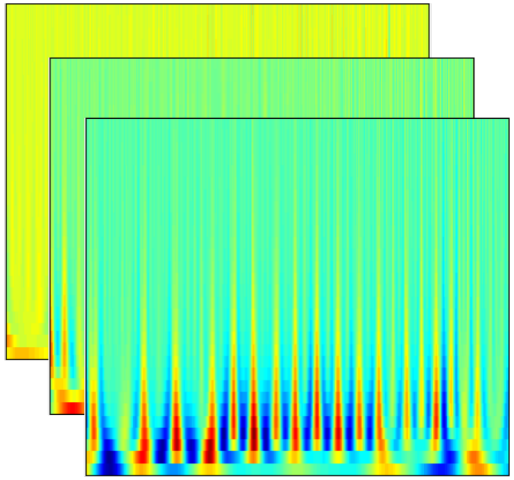
Goal (signal processing):

- Automate visual analysis
- Artifact removal

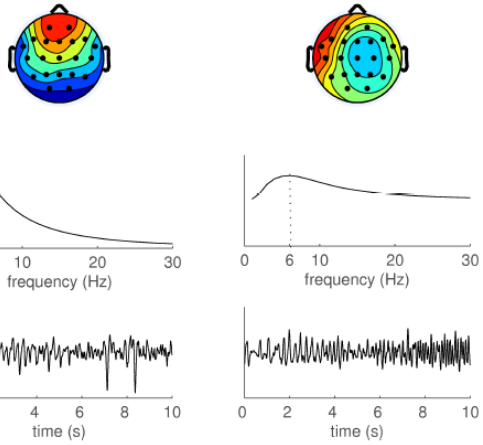
Automated tensor-based EEG analysis



Tensorization



Tensor model



Interpretation

$$\mathcal{T} = \frac{\mathbf{c}_1}{\mathbf{a}_1 \quad \mathbf{b}_1} + \frac{\mathbf{c}_2}{\mathbf{a}_2 \quad \mathbf{b}_2} + \ldots + \frac{\mathbf{c}_R}{\mathbf{a}_R \quad \mathbf{b}_R}$$

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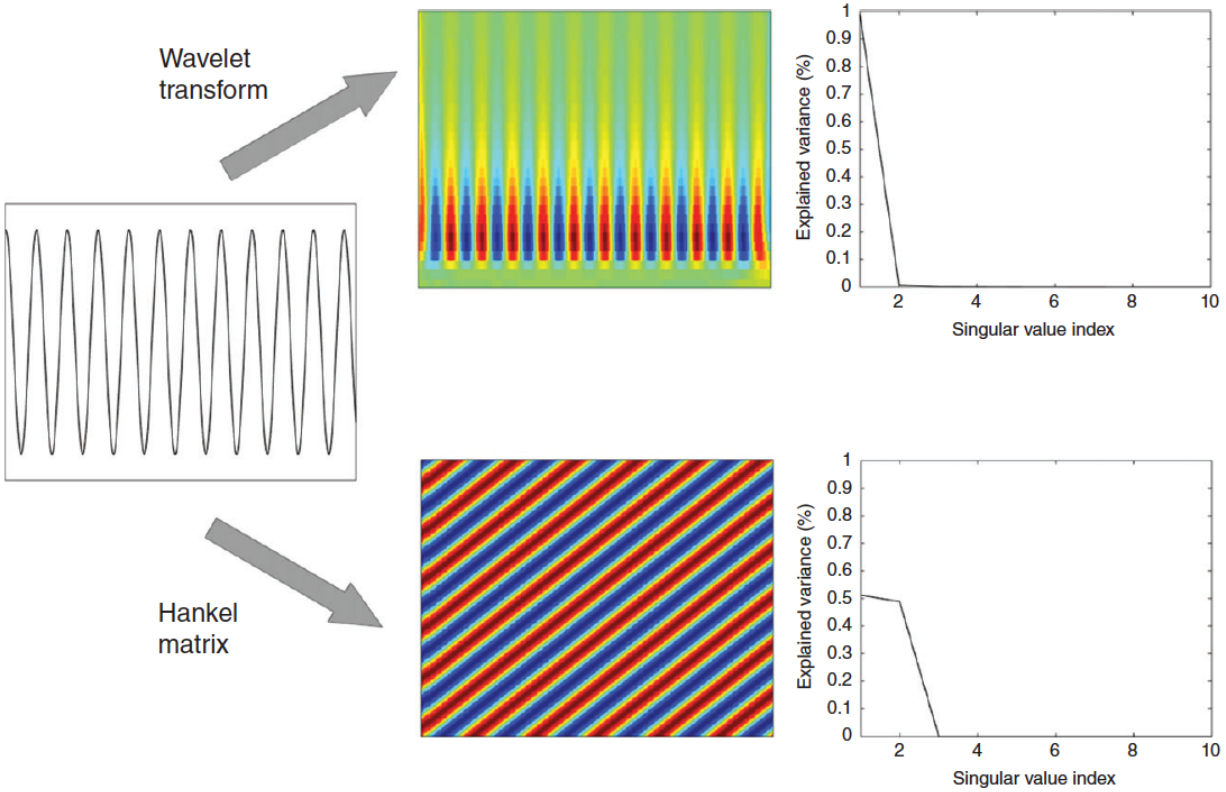
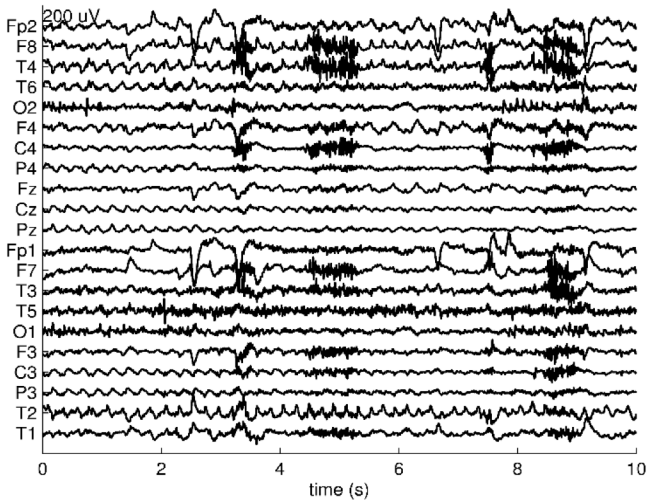
Tensorization and signal model

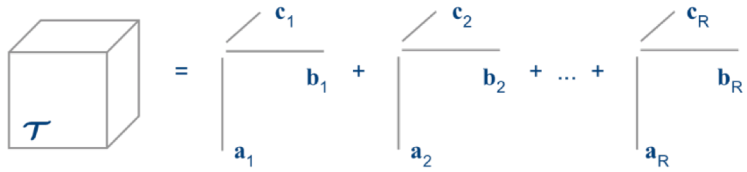
- Time-frequency transformation (oscillatory patterns)
  - Short-time Fourier
  - Wavelet transform
  - Hilbert-Huang
- Hankelization (sums of exponentials)
- Löwnerization (rational functions)
- Etc.



Tensor model selection



CPD:

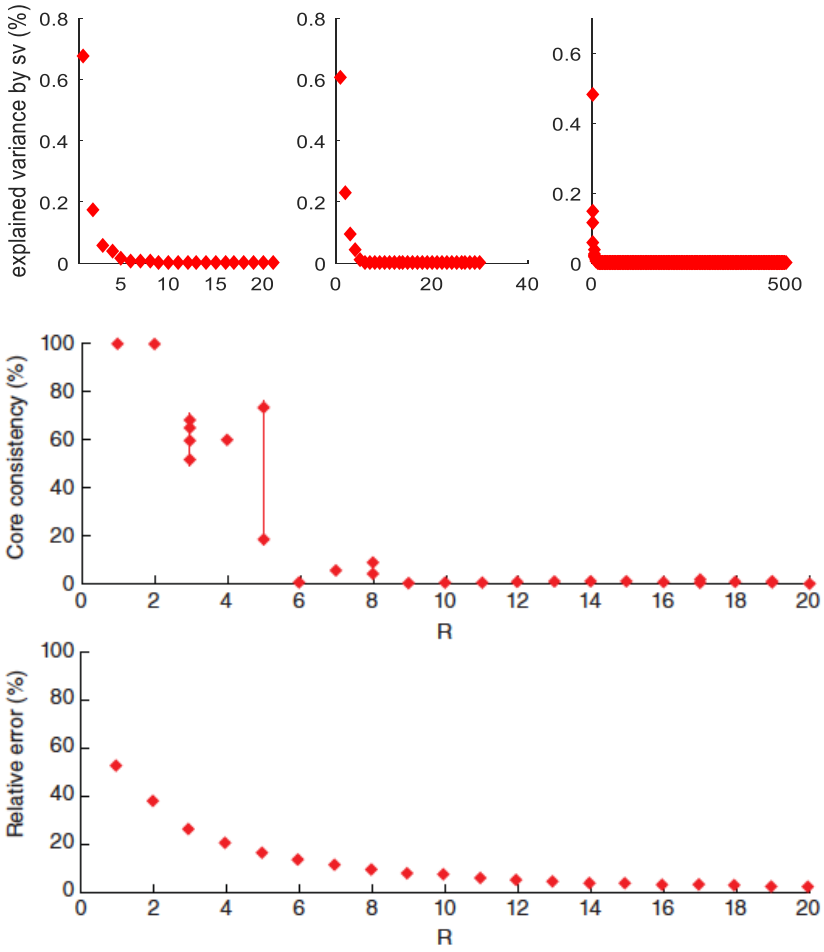


[Acar et al. 2007,
De Vos et al 2007]

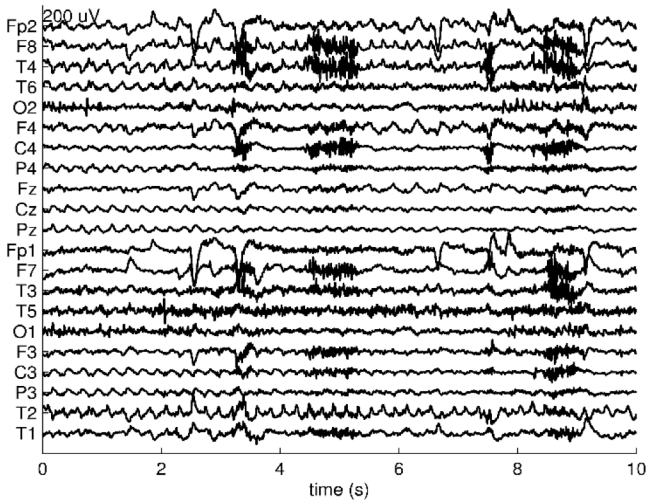
?

Tensor model selection

- Inspect multilinear singular values
- Vary R and inspect
  - Explained variance
  - Core consistency
- Run the model multiple times
  - Different initializations
  - Verify uniqueness



Tensor model selection



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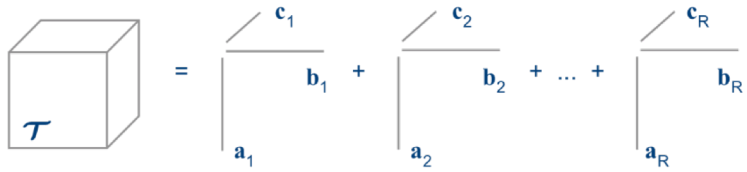

[Acar et al. 2007,
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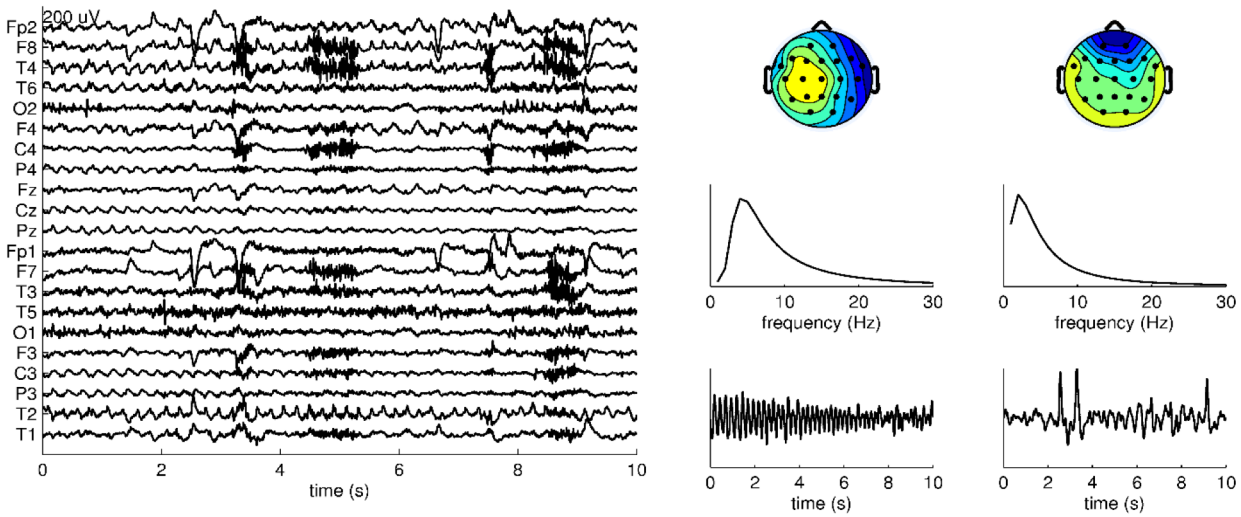
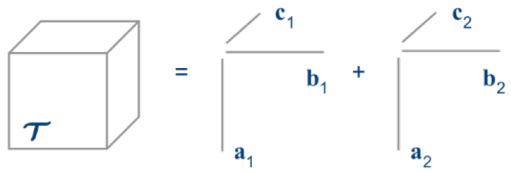
?

Tensor model selection



CPD:

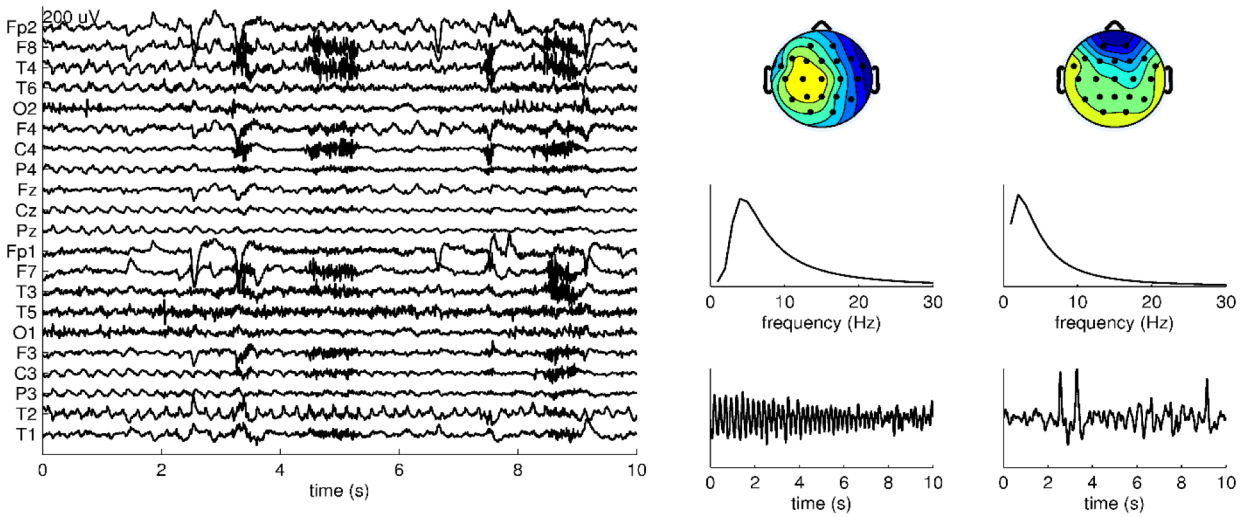


Diagnostic information:

- morphology
- topography
- frequency

[Acar et al. 2007,
De Vos et al 2007]

Tensor model selection



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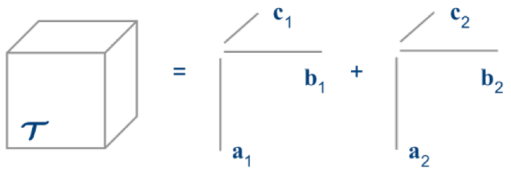
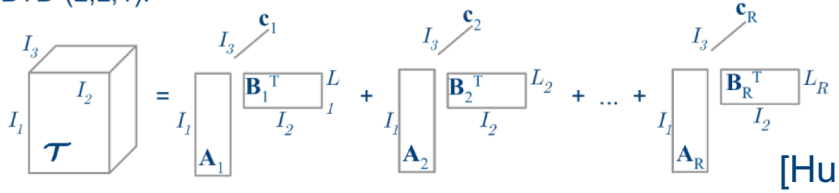


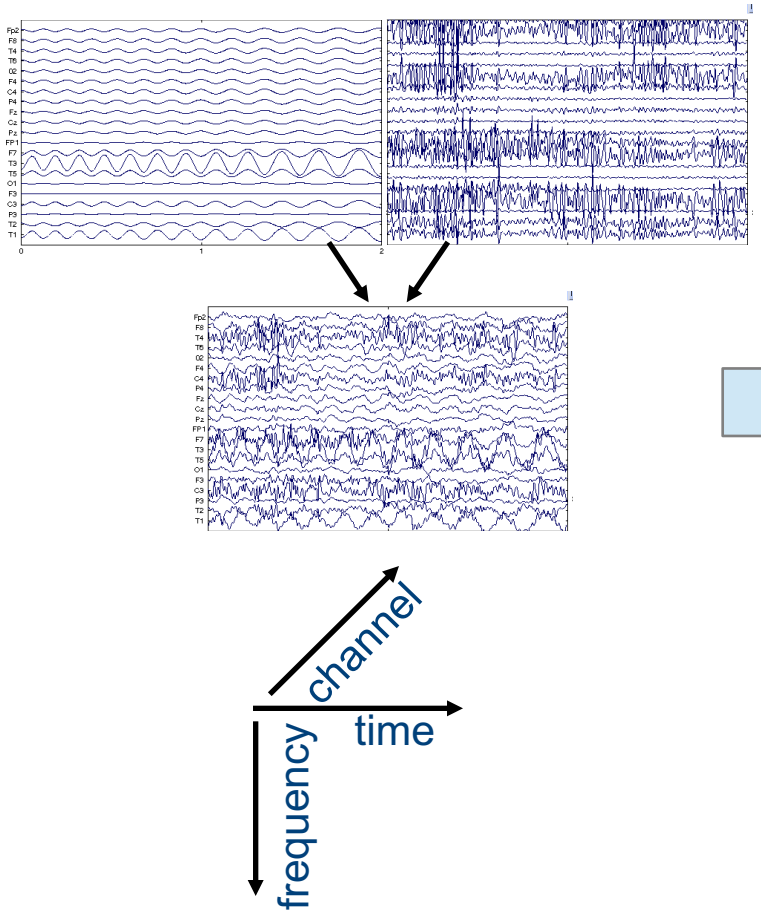
[Acar et al. 2007,
De Vos et al 2007]

BTD-(L,L,1):

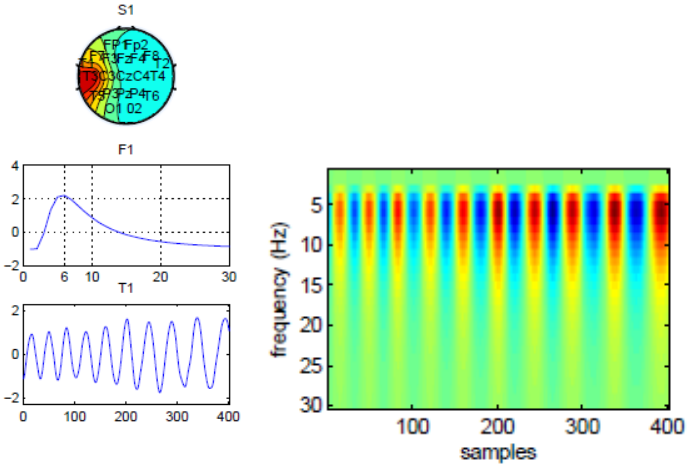


[Hunyadi et al 2014]

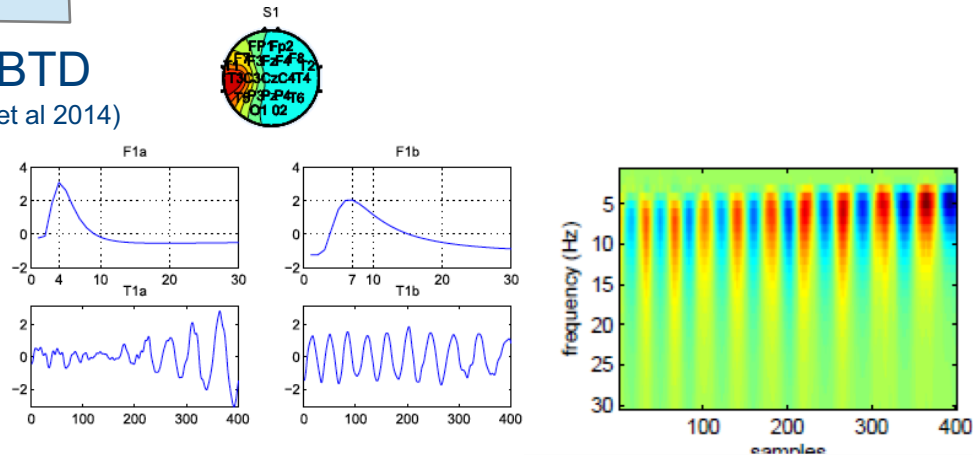
Signal model: oscillatory pattern



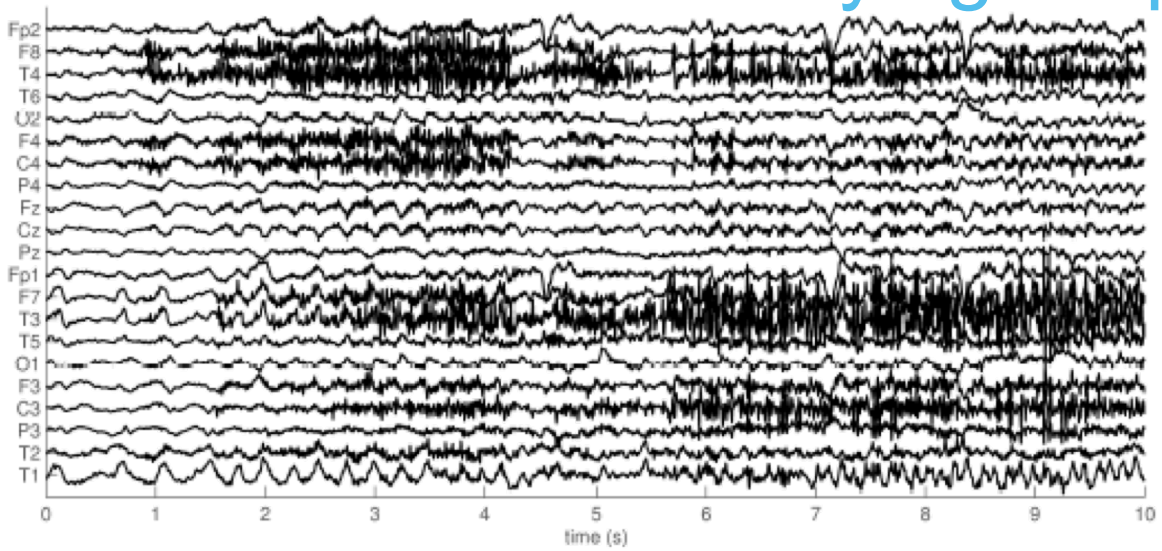
CWT-CPD
(Acar 2007,
De Vos 2007)



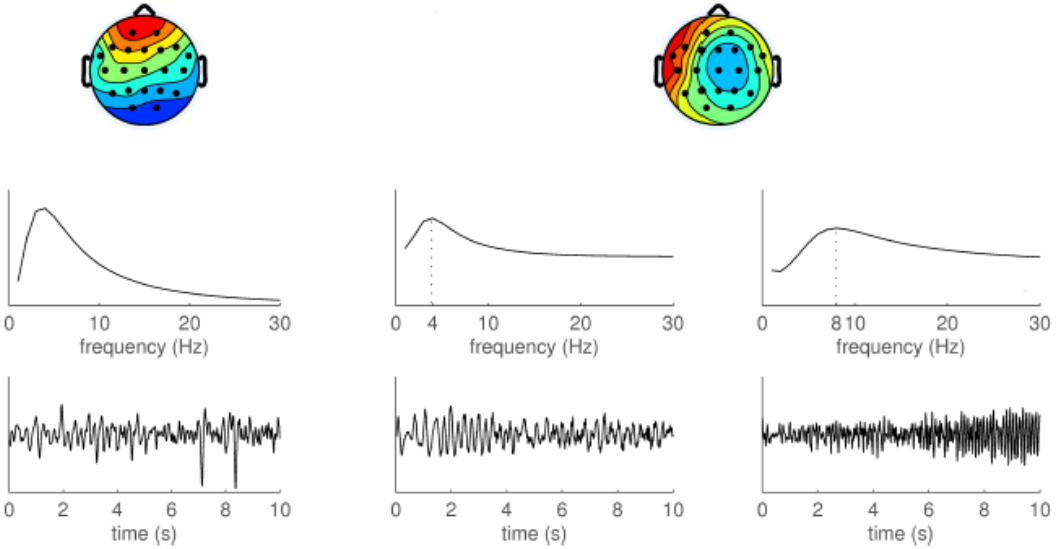
CWT-BTD
(Hunyadi et al 2014)



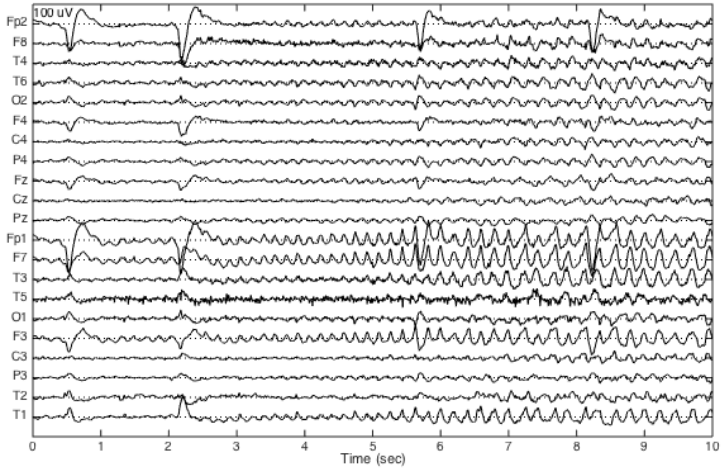
BTD of seizure 1: varying frequency

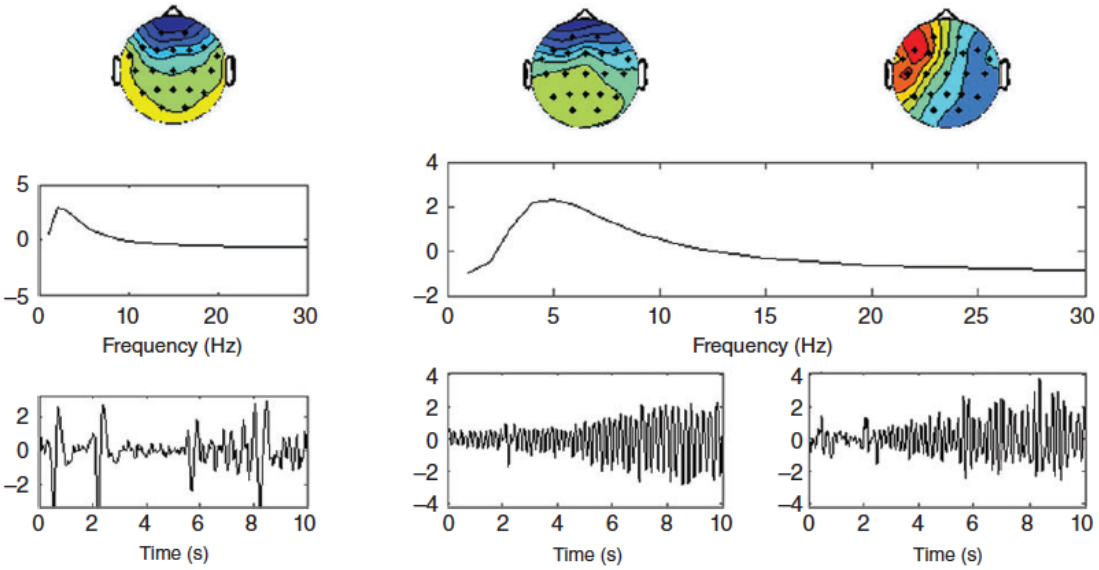


(a) Raw EEG



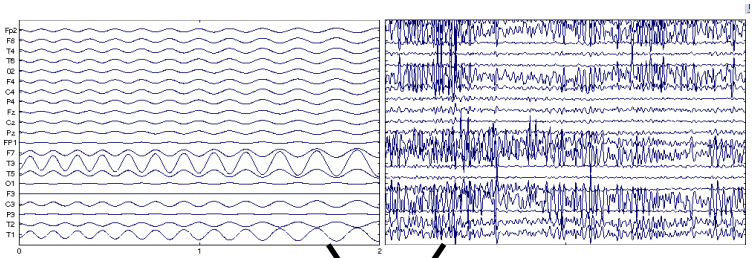
BTD of seizure 2: varying source

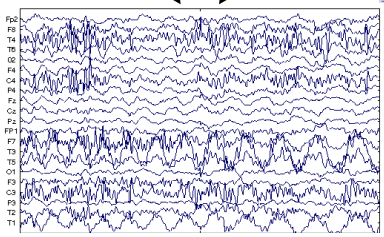


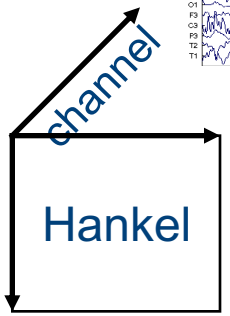


Signal model: sum of exp. damped sinusoids

BTD of Hankel expanded tensors



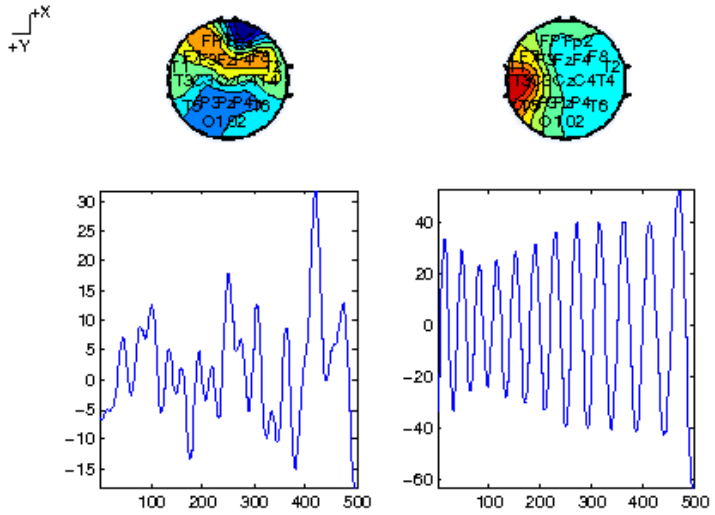




$$\begin{bmatrix} a_1 & a_2 & a_3 & \cdots & a_K \\ a_2 & a_3 & \cdots & a_K & a_{K+1} \\ a_3 & \cdots & a_K & a_{K+1} & a_{K+2} \\ \vdots & \iddots & \iddots & \iddots & \iddots \\ a_J & a_{J+1} & \cdots & a_{S-1} & a_S \end{bmatrix}$$

H-BTD

(De Lathauwer, 2011
Hunyadi et al. 2014)



Signal model: sum of exp. damped sinusoids

$$s_r(n) = \sum_{l_r=1}^{L_r} c_{l_r,r} z_{l_r,r}^n, \text{ with } 0 \le n \le N-1, 1 \le r \le R.$$

Sources: sum of exponentials

$$e^{-\alpha n}\cos(\omega n + \phi) = cz^n + c^*(z^*)^n, \text{ with } c = \frac{1}{2}e^{j\phi}$$

$$z = e^{-\alpha + j\omega}$$

Special case: sum of damped sinusoids

$$\mathbf{a}_{ch} = [a_{ch}(1)\ a_{ch}(2)\ \cdots\ a_{ch}(S)],$$

Hankelization

$$\mathbf{H}_{ch} = \begin{bmatrix} a_{ch}(1) & a_{ch}(2) & a_{ch}(3) & \cdots & a_{ch}(K) \\ a_{ch}(2) & a_{ch}(3) & \cdots & a_{ch}(K) & a_{ch}(K+1) \\ a_{ch}(3) & \cdots & a_{ch}(K) & a_{ch}(K+1) & a_{ch}(K+2) \\ \vdots & \iddots & \iddots & \iddots & \iddots \\ a_{ch}(J) & a_{ch}(J+1) & \cdots & a_{ch}(S-1) & a_{ch}(S) \end{bmatrix}$$

Rank(H) = L_r

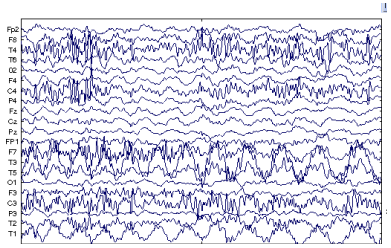
Linear combination of sources

$$H_r = V_r \cdot diag(c_{1,r}, c_{2,r}, \ldots, c_{L_r,r}) \cdot \hat{V}_r^T,$$

$$\mathbf{V}_r = \begin{bmatrix} 1 & 1 & \cdots & 1 \\ z_{1,r} & z_{2,r} & \cdots & z_{L_r,r} \\ \vdots & \vdots & \vdots & \vdots \\ z_{1,r}^{I-1} & z_{2,r}^{I-1} & \cdots & z_{L_r,r}^{I-1} \end{bmatrix}, \hat{\mathbf{V}}_r = \begin{bmatrix} 1 & 1 & \cdots & 1 \\ z_{1,r} & z_{2,r} & \cdots & z_{L_r,r} \\ \vdots & \vdots & \vdots & \vdots \\ z_{1,r}^{J-1} & z_{2,r}^{J-1} & \cdots & z_{L_r,r}^{J-1} \end{bmatrix}$$

Signal model: sum of exp. damped sinusoids

BTD of Hankel expanded tensors



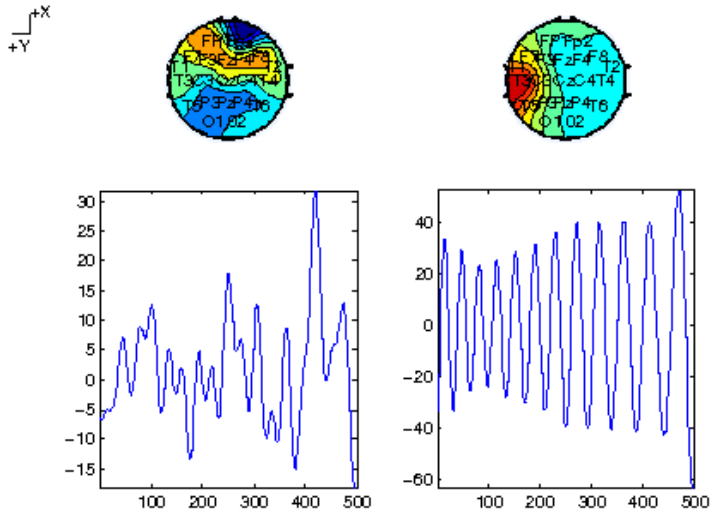
channel

Hankel

$$\begin{bmatrix} a_1 & a_2 & a_3 & \cdots & a_K \\ a_2 & a_3 & \cdots & a_K & a_{K+1} \\ a_3 & \cdots & a_K & a_{K+1} & a_{K+2} \\ \vdots & \iddots & \iddots & \iddots & \iddots \\ a_J & a_{J+1} & \cdots & a_{S-1} & a_S \end{bmatrix}$$

H-BTD

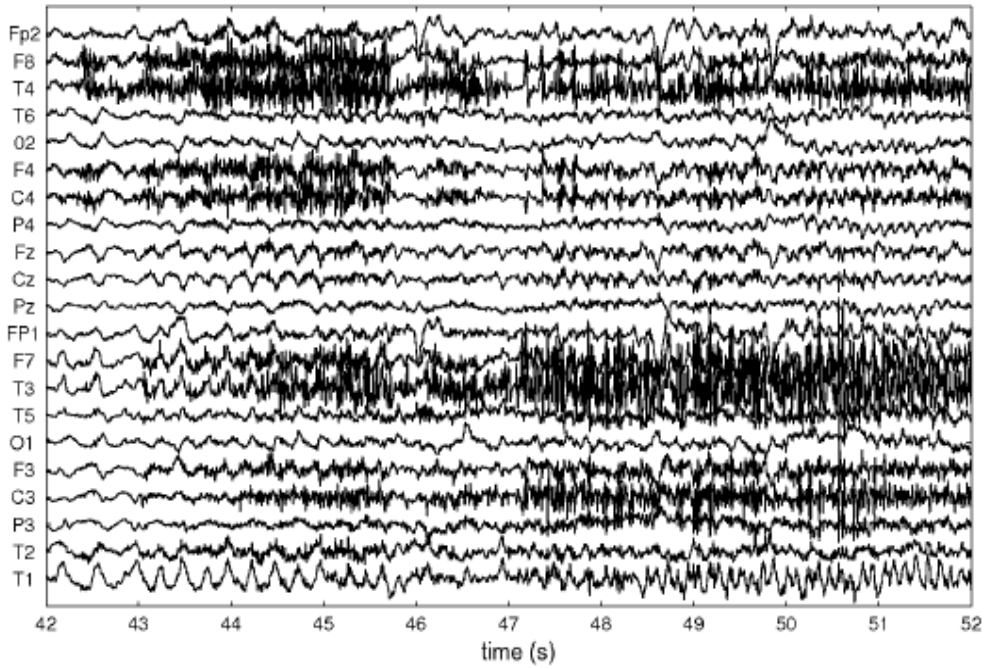
(De Lathauwer, 2011
Hunyadi et al. 2014)



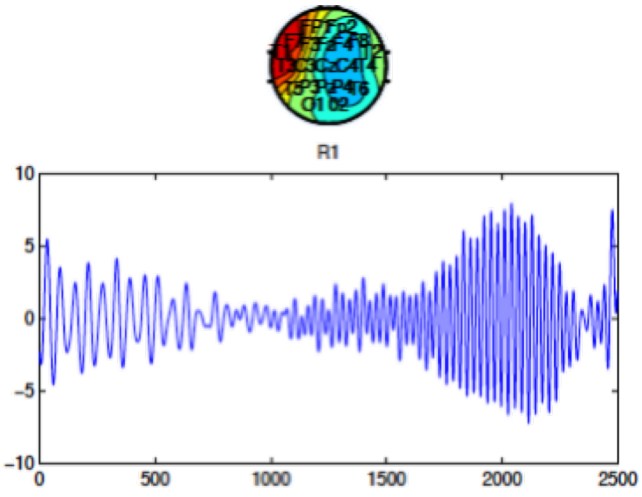
BTD-(L,L,1):

$$\mathcal{T} = \mathbf{A}_1 \mathbf{B}_1^{\mathrm{T}} \mathbf{c}_1 + \mathbf{A}_2 \mathbf{B}_2^{\mathrm{T}} \mathbf{c}_2 + \cdots + \mathbf{A}_R \mathbf{B}_R^{\mathrm{T}} \mathbf{c}_R$$

H-BTD of seizure 1



(a) Raw EEG

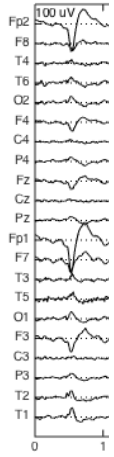


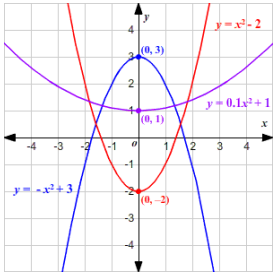
(d) H-BTD

L_r=6

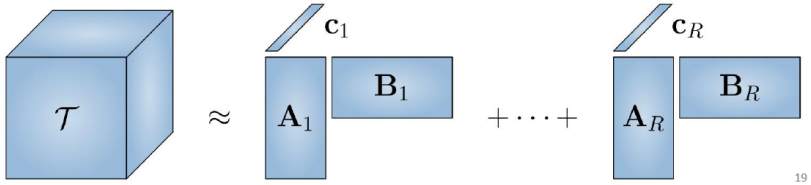
Eye blink artifact

- If too L too high, the seizure and eye blink component will be intermixed
- See demo!
- Solution:
  - Model and remove eye blink before performing H-BTD
  - Eye blink ~ quadratic function
  - Löwnerization: f(x) sampled at two distinct points sets X={x_1, $x_{2,..}$ x_I } and Y={y_1, $y_{2,..}$ y_J }



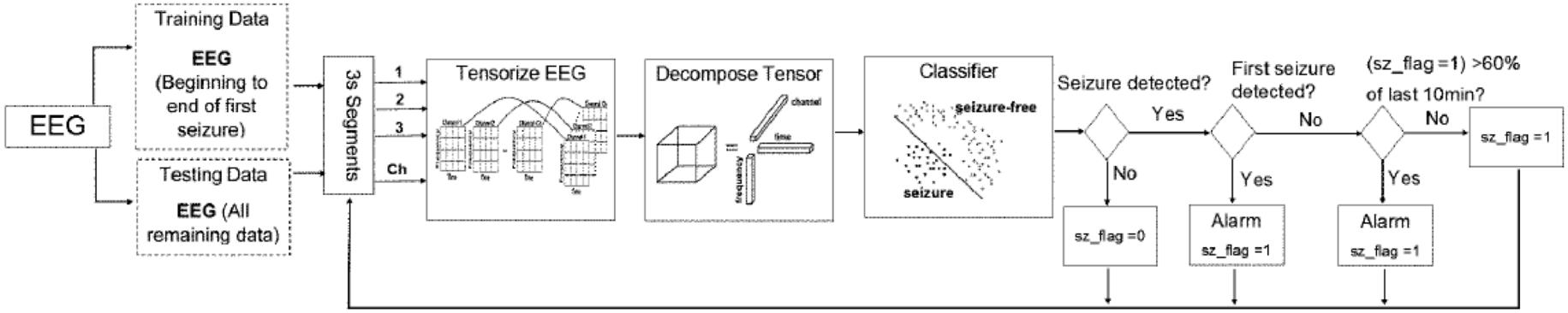


$$\mathbf{L} = \begin{bmatrix} \frac{f(x_1)-f(y_1)}{x_1-y_1} & \frac{f(x_1)-f(y_2)}{x_1-y_2} & \cdots & \frac{f(x_1)-f(y_J)}{x_1-y_J} \\ \frac{f(x_2)-f(y_1)}{x_2-y_1} & \frac{f(x_2)-f(y_2)}{x_2-y_2} & \cdots & \frac{f(x_2)-f(y_J)}{x_2-y_J} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{f(x_I)-f(y_1)}{x_I-y_1} & \frac{f(x_I)-f(y_2)}{x_I-y_2} & \cdots & \frac{f(x_I)-f(y_J)}{x_I-y_J} \end{bmatrix}$$

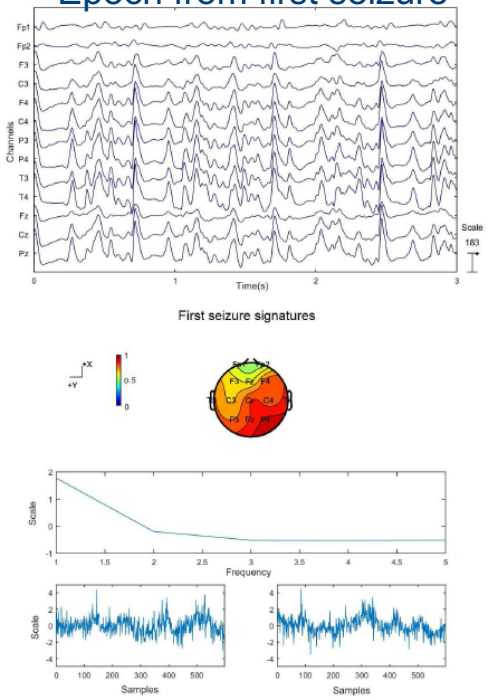


$$\operatorname{rank}(\mathbf{L}) = \delta = \deg(f).$$

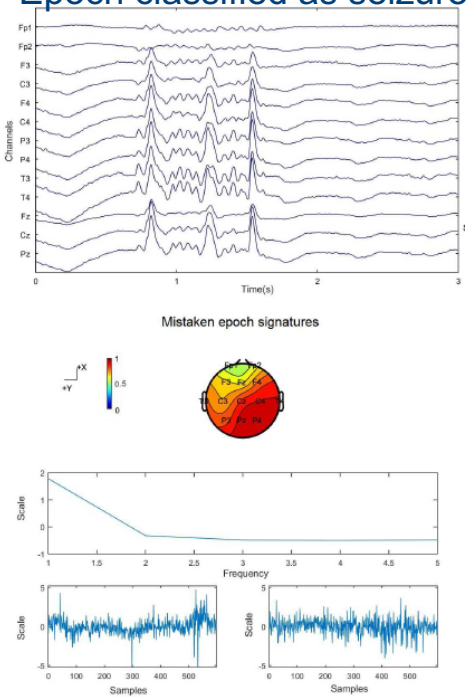
Application: automated seizure detection



Epoch from first seizure



Epoch classified as seizure



[Rodriguez Aldana 2017]

Application: Localization of seizure onset zone

1. Few seizures -> long hospital stay
2. EEG resolution not great
3. Epileptic activity in deep structures not picked up

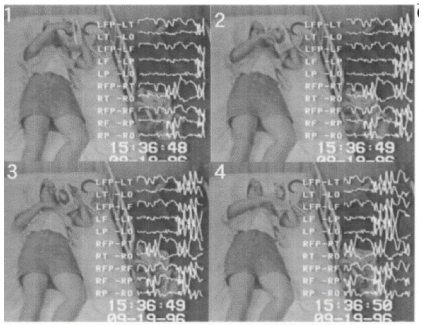
Therefore…

Presurgical evaluation

Epileptogenic zone

- Hypothetical region
- Use of complementary techniques

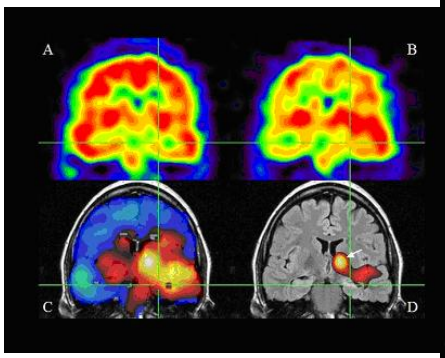
Ictal Video-EEG monitoring



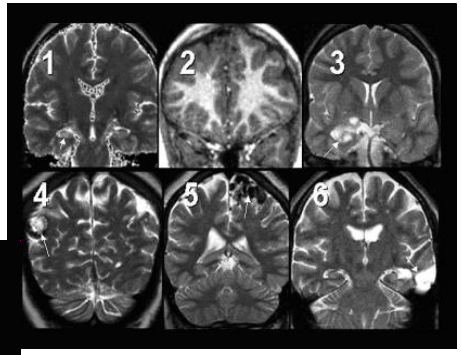
[Y. Shirasaka, I. Mitsuyoshi Brain and Development 1999]

Interictal EEG-fMRI

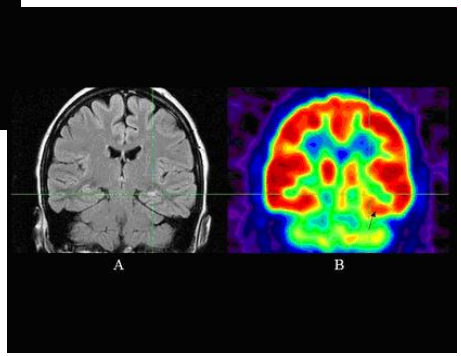
http://fmri.uib.no/



SISCOM



Structural MRI



PET

+ Psychological and psychiatric evaluation

EEG-correlated fMRI

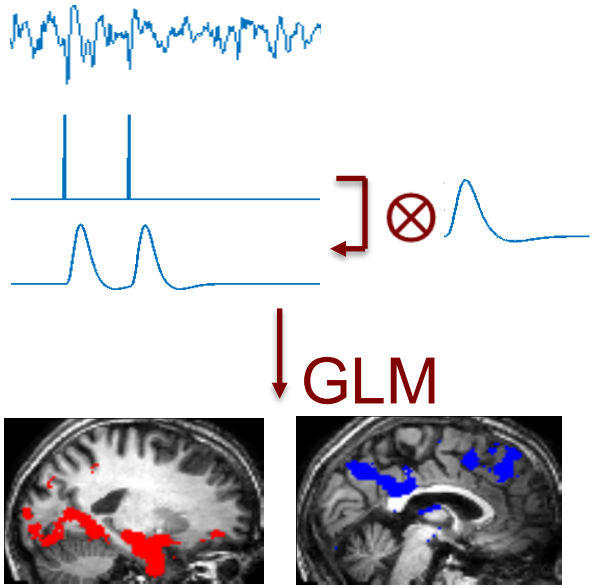
1. Find interictal spikes on EEG
2. Create a vector of spike timing
3. Create a regressor by convolving the timing vector with the HRF
4. Create regressors based on various confounders (e.g. head movement)
5. Analyze fMRI time series within the general linear model (GLM):

$$Y = X\beta + e$$

6. Solution in the LS sense:

$$\beta = (X^T X)^{-1} X^T y + e$$

7. Activation maps are obtained by statistical hypothesis testing of β values



EEG-correlated fMRI

Success stories:

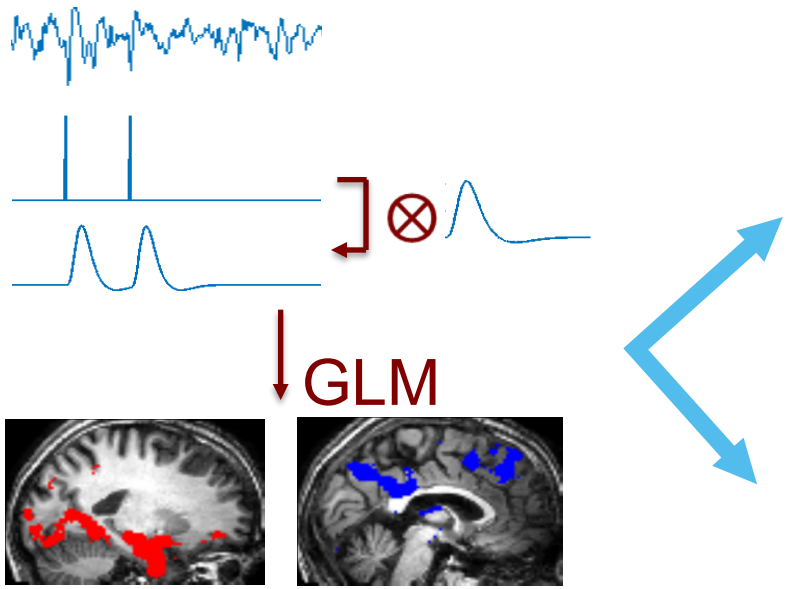
- IED-related BOLD changes in focal and generalized epilepsy *[Gotman 2006]*
- Instrumental in presurgical evaluation *[Zijlmans 2007, Pittau 2012]*

Hypothetically, the network is:

- active during interictal spikes
- focal and coincides with the true epileptogenic zone

But…

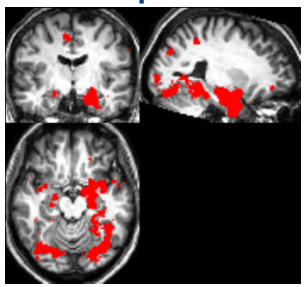
EEG-correlated fMRI



40-70% EEG-fMRI studies fail due to lack of interictal spikes

[Grouiller et al. 2011]

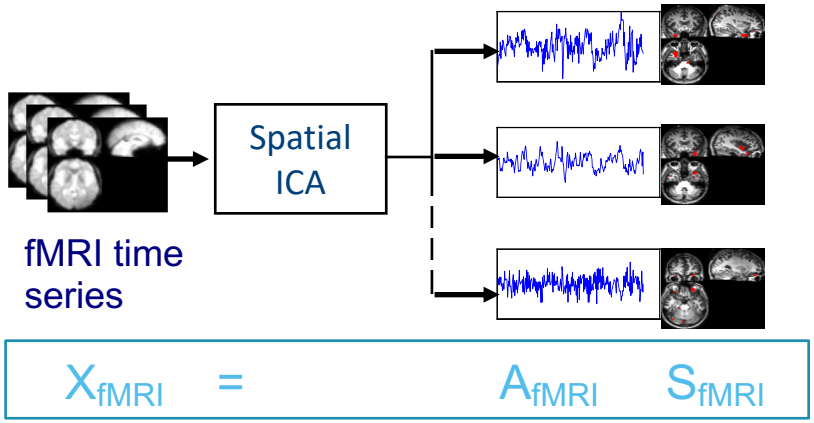
Widespread activation



ICA of interictal fMRI

[Rodionov et al 2007]

- EEG-positive cases
- Selection based on temporal regressor and GLM-based activation map



Spatial ICA vs Temporal ICA

- Temporal ICA: used in EEG
- fMRI: too few time points for robust statistics in the temporal mode
- fMRI Spatial mode:
  - vectorization of the 3D volume of voxels
  - Voxel x time matrices
  - Independence in the voxel mode: super-Gaussian distributions (Infomax); high kurtosis (fastICA)

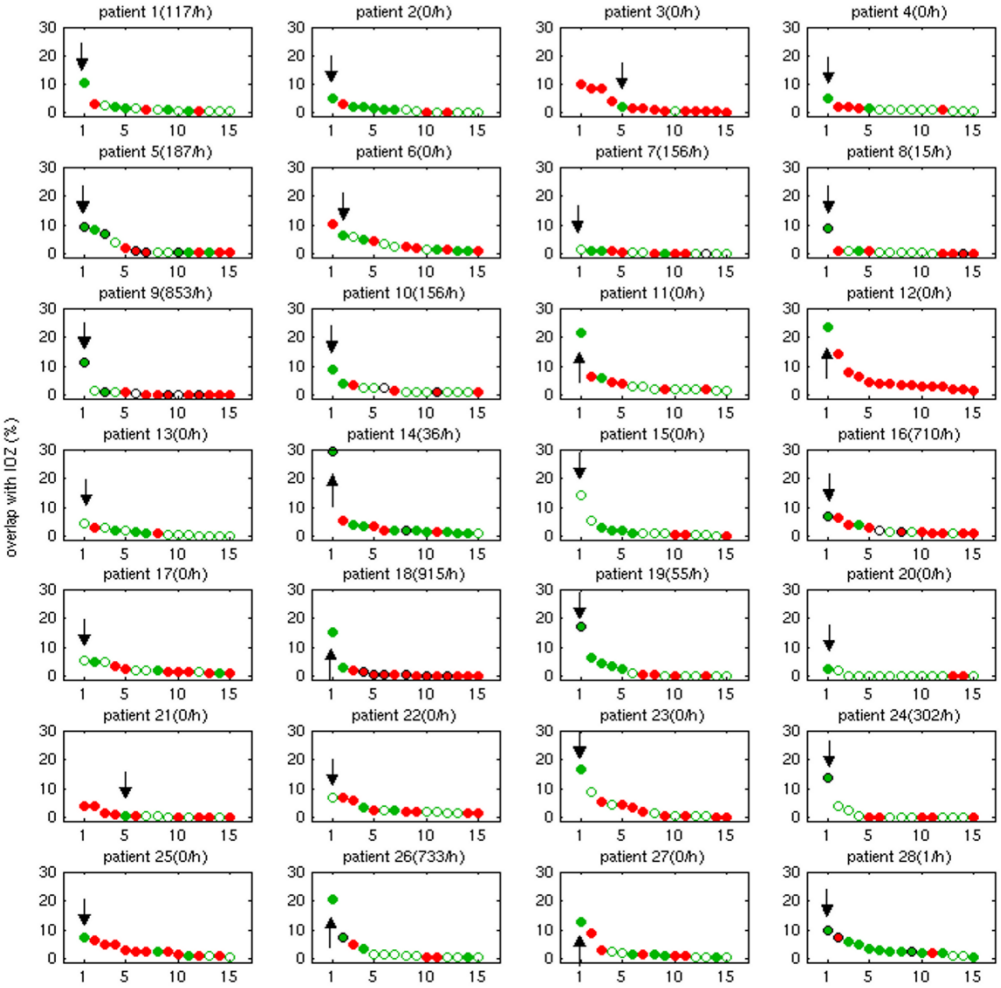
ICA of EEG-negative fMRI

- Data acquisition:
  - Simultaneous EEG-fMRI recordings
    - 10-22 minute long sessions
    - 2-4 sessions per individual
  - 28 patients refractory epilepsy patients
    - Presurgical evaluation ➔ concordant results ➔ known EZ
    - EEG-positive group: 11 had clinically concordant spikes
    - EEG-negative group: 17 patient had no clinically concordant spikes
  - 12 healthy controls
- Analysis:
  - Group ICA on all sessions for each individual separately
  - Overlap between each IC and known EZ
  - Artifact-related ICs rejected manually

ICA of EEG-negative fMRI

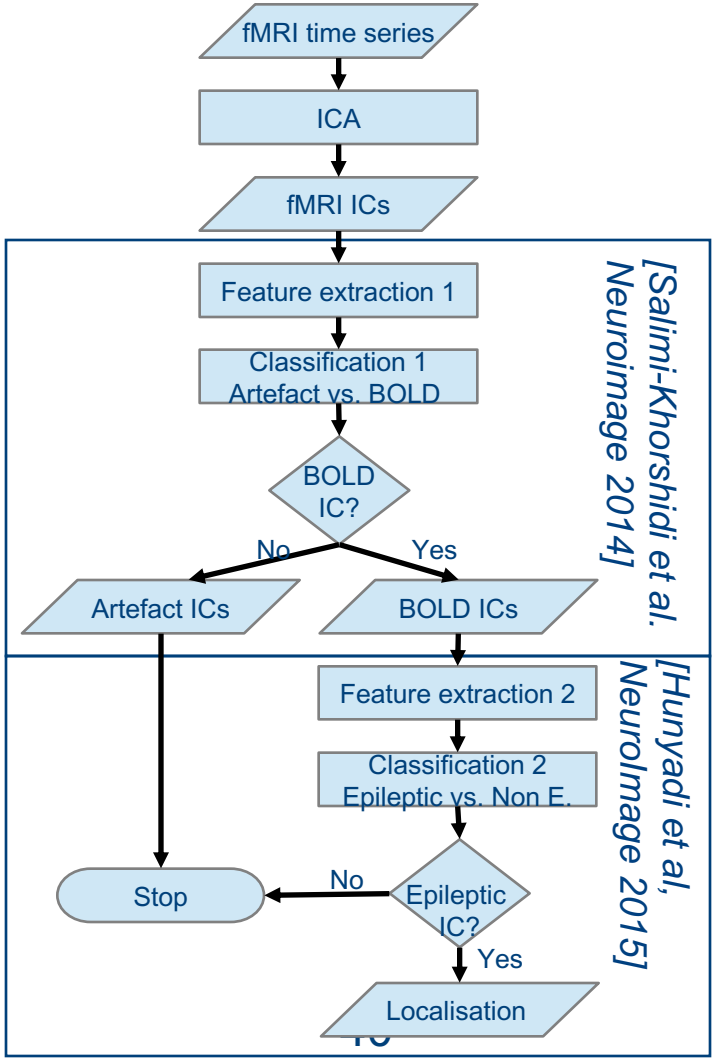
Results:

- Epileptic IC (↓, eIC) was identified as the IC with the largest overlap with the EZ, after excluding artefacts (•).
- ICA revealed epileptic sources overlapping with the EZ also in patients without spikes.
- Overlaps are significantly larger than in control group

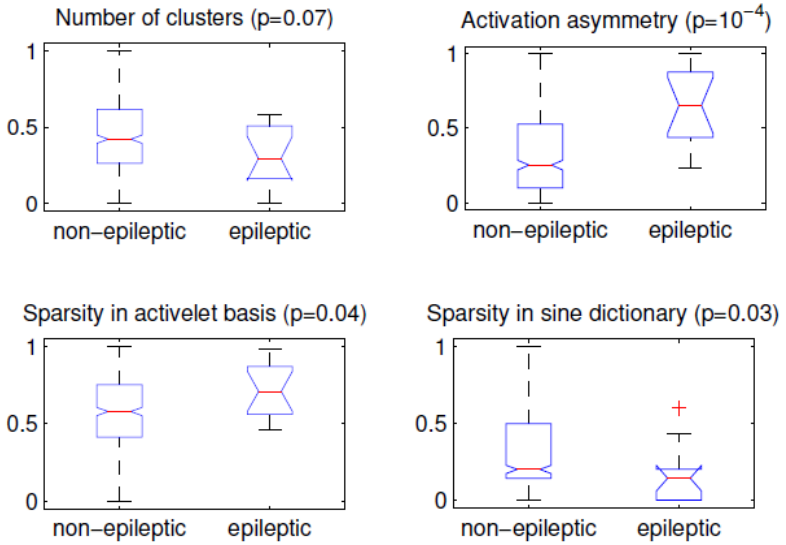


[Hunyadi et al 2013]

Selecting the epileptic IC



Feature extraction 2:



Classification 2:

- LS-SVM with linear kernel and modified decision function:

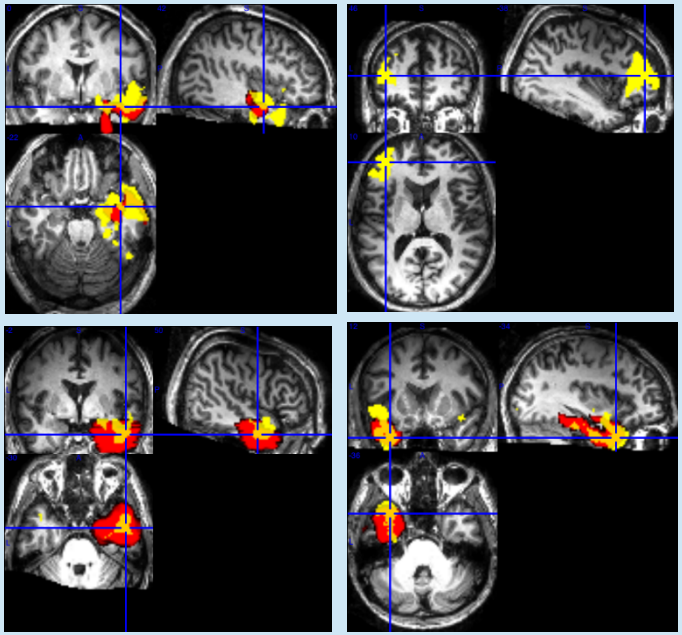
$$y(x_i) = \begin{cases} 1 & \text{if } \arg\max_{\mathbf{x}}(\mathbf{w}^T \boldsymbol{\varphi}(\mathbf{x})) = i \text{ and } \mathbf{w}^T \boldsymbol{\varphi}(\mathbf{x}) + b > 0 \\ 0 & \text{otherwise.} \end{cases}$$

Outcome in EEG-negative cases

- Training set: 12 EEG-positive cases
- A selection was made in 1 out of 13 controls: 92% specificity
- A selection was made in 11 out of 18 patients

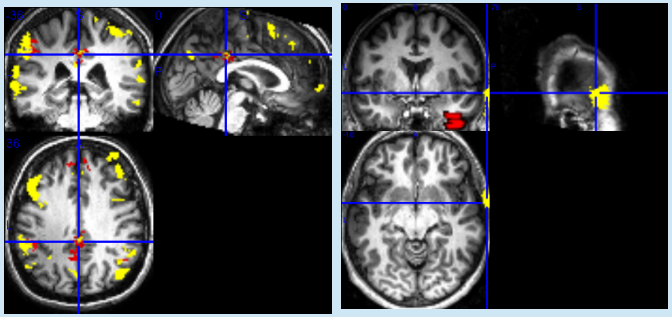
Informative (4)

Concordant with the EZ (4)



Misleading (0)

Non-informative (7)



ECN (average of 6 selected maps)

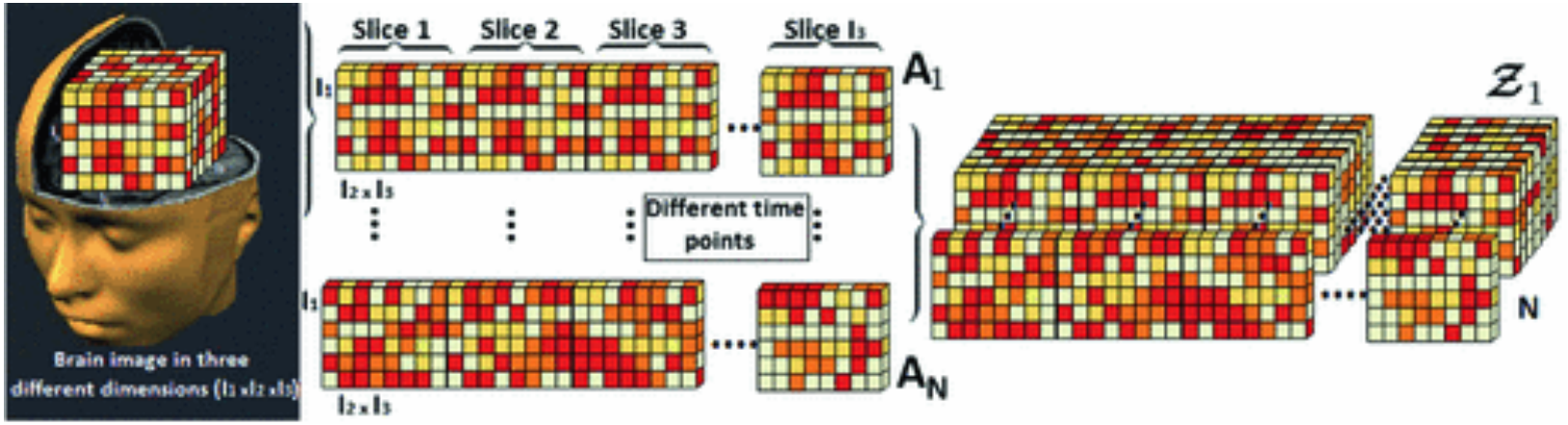
Artefact

Related to epilepsy:
[Zhang et al. 2009]

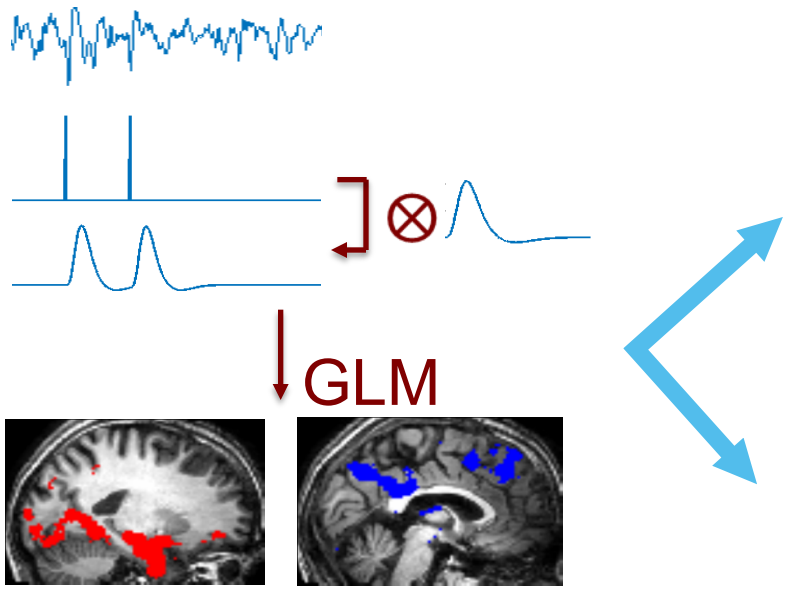
Tensor-based fMRI analysis

- Tensor-PICA [Beckmann&Smith2005]:
  - Extension of previous model for multisession fMRI
  - Sessions have equal time courses (task-based fMRI)
  - Voxel x time x sessions OR voxel x time x subjects
  - CPD with independence constraint

- BTD-(L,L,1) for spatially folded fMRI [Chatzichristos2017]



EEG-correlated fMRI



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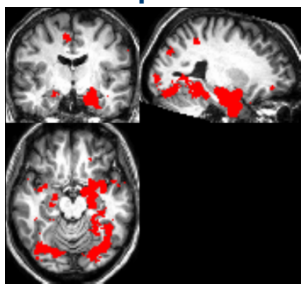


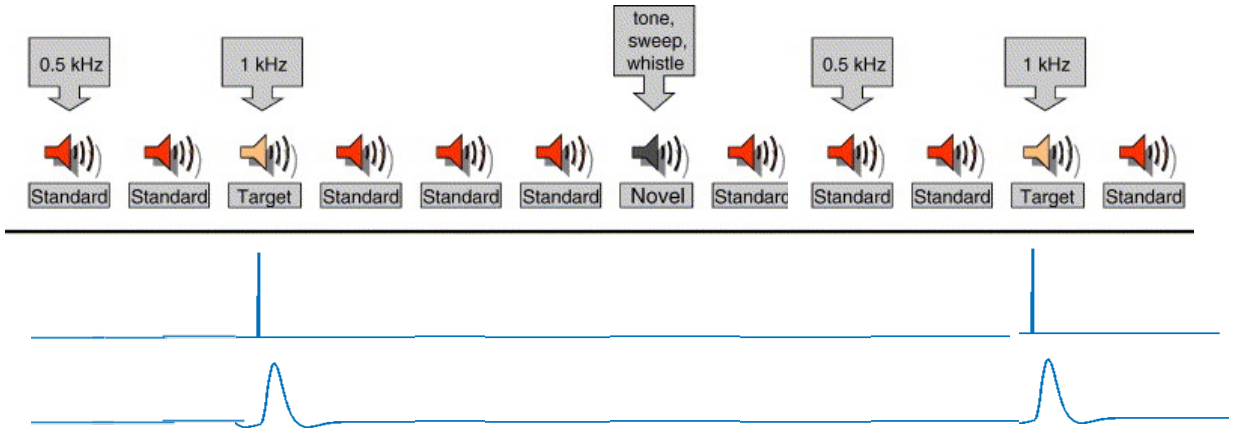
We need better spatiotemporal resolution

- Symmetric EEG-fMRI integration
- Find a common mode of variation
- Joint decomposition (BSS) where signatures in this mode are shared
  - Subject / patient
    - JointICA
    - Multichannel jointICA
    - CPD
  - Time

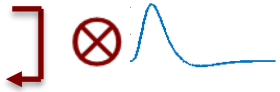
We need better spatiotemporal resolution

- Symmetric EEG-fMRI integration
- Find a common mode of variation
- Joint decomposition (BSS) where signatures in this mode are shared
  - **Subject / patient**
    - JointICA
    - Multichannel jointICA
    - CPD
  - Time

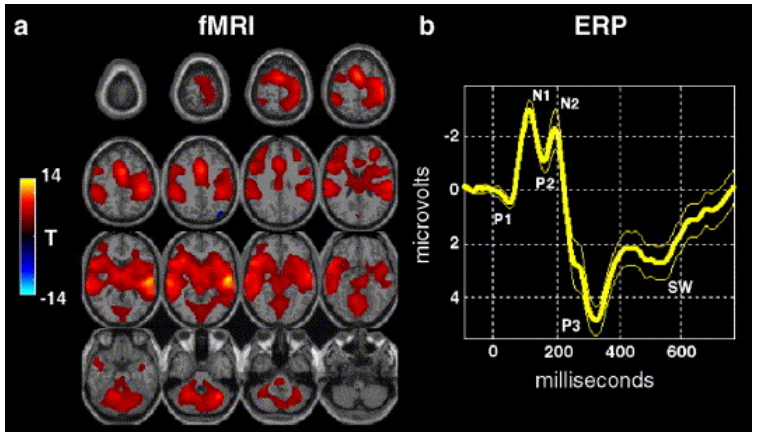
Study cognitive function with EEG-fMRI



Peak at 5s!



GLM

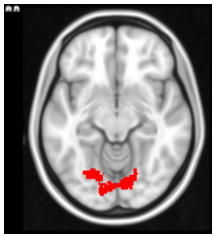


[Calhoun2006]

EEG-fMRI fusion via BSS

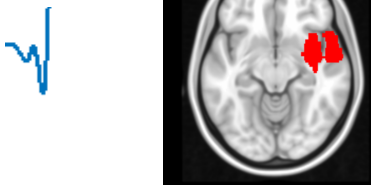
s_1(EEG) s_1(fMRI)

s_2(EEG) s_2(fMRI)

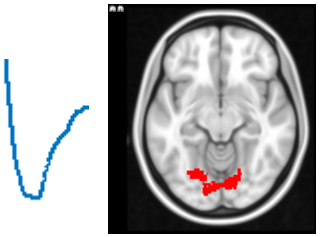


EEG-fMRI fusion via BSS

s_1(EEG) s_1(fMRI)



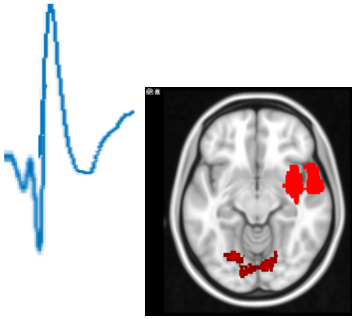
s_2(EEG) s_2(fMRI)



a_{11}

a_{12}

x_1(EEG) x_1(fMRI)

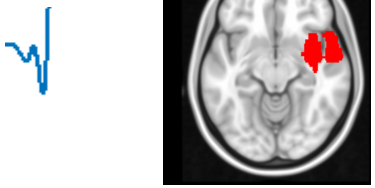


$x_1(EEG) = a_{11}s_1\ (EEG) + a_{12}s_2\ (EEG)$

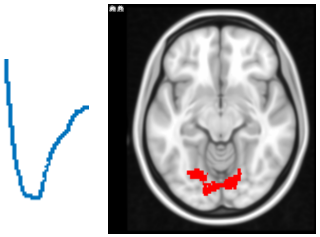
$x_1(fMRI) = a_{11}s_1\ (fMRI) + a_{12}s_2\ (fMRI)$

EEG-fMRI fusion via BSS

s_1(EEG) s_1(fMRI)



s_2(EEG) s_2(fMRI)



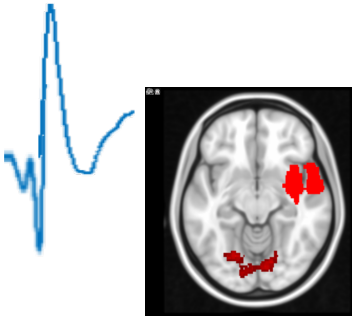
a_{11}

a_{21}

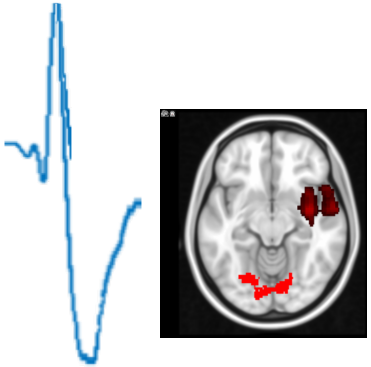
a_{12}

a_{22}

x_1(EEG) x_1(fMRI)



x_2(EEG) x_2(fMRI)



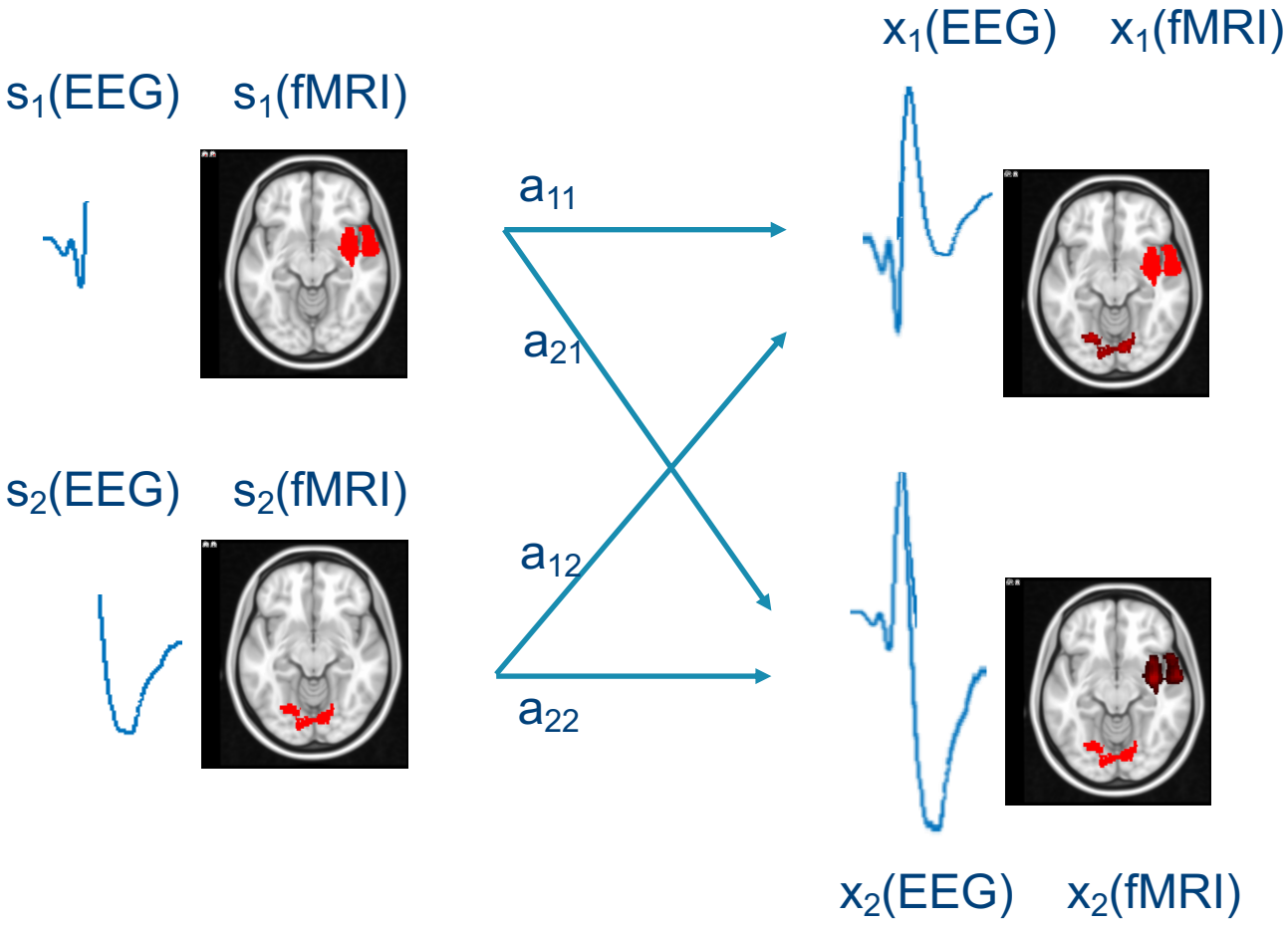
$x_1(EEG) = a_{11}s_1(EEG) + a_{12}s_2(EEG)$

$x_1(fMRI) = a_{11}s_1(fMRI) + a_{12}s_2(fMRI)$

$x_2(EEG) = a_{21}s_1(EEG) + a_{22}s_2(EEG)$

$x_2(fMRI) = a_{21}s_1(fMRI) + a_{22}s_2(fMRI)$

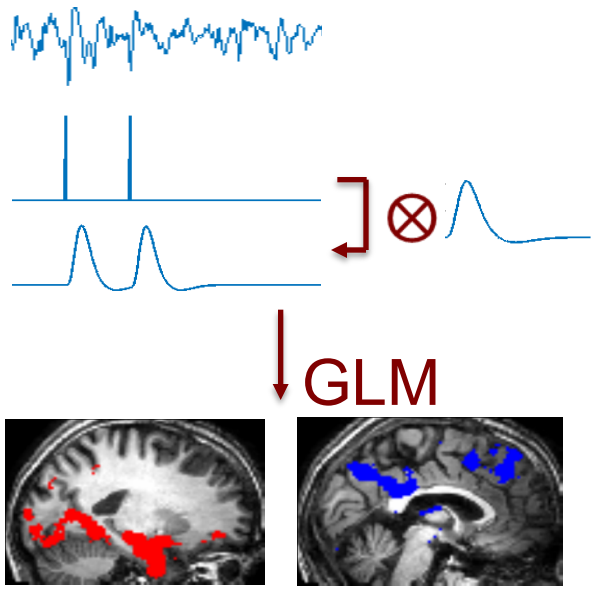
EEG-fMRI fusion via BSS



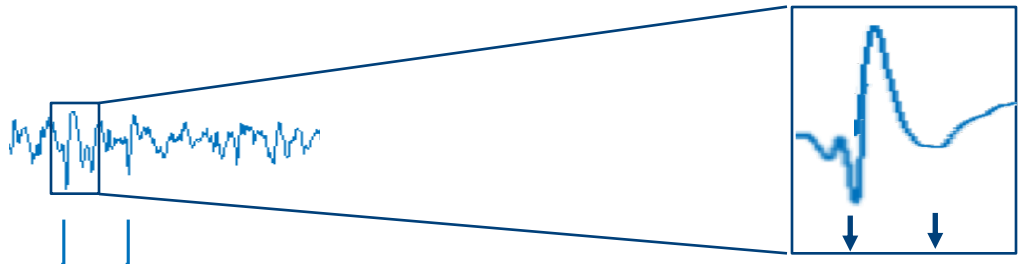
$X(EEG)=AS(EEG)$

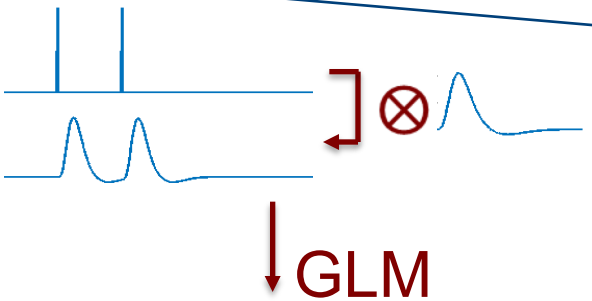
$X(fMRI)=AS(fMRI)$

EEG-correlated fMRI



Traditional GLM-based analysis

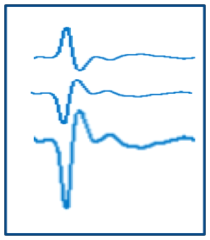




Spikes and slow waves reflect **different neural processes**. In GLM, they are **modelled as one** entity, causing **widespread activation.**

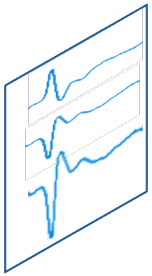
Goal: Disentangle the different neural processes from multisubject **EEG-fMRI** in order to obtain a better spatiotemporal characterization

Data representation

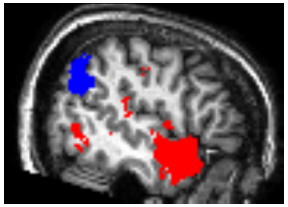


$\overline{\text{IED}}_1$

Data representation



$\overline{IED}_1$

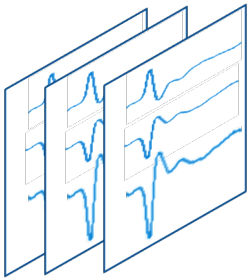


Masked fMRI activation maps (GLM)

vectorization

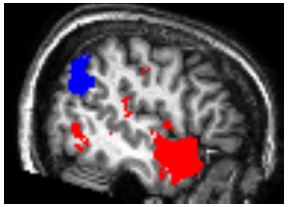
Data representation

$\overline{IED}_2$



x_{EEG}

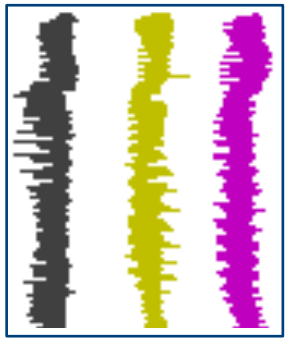
$\overline{IED}_1$ $\overline{IED}_3$



Masked fMRI activation maps (GLM)

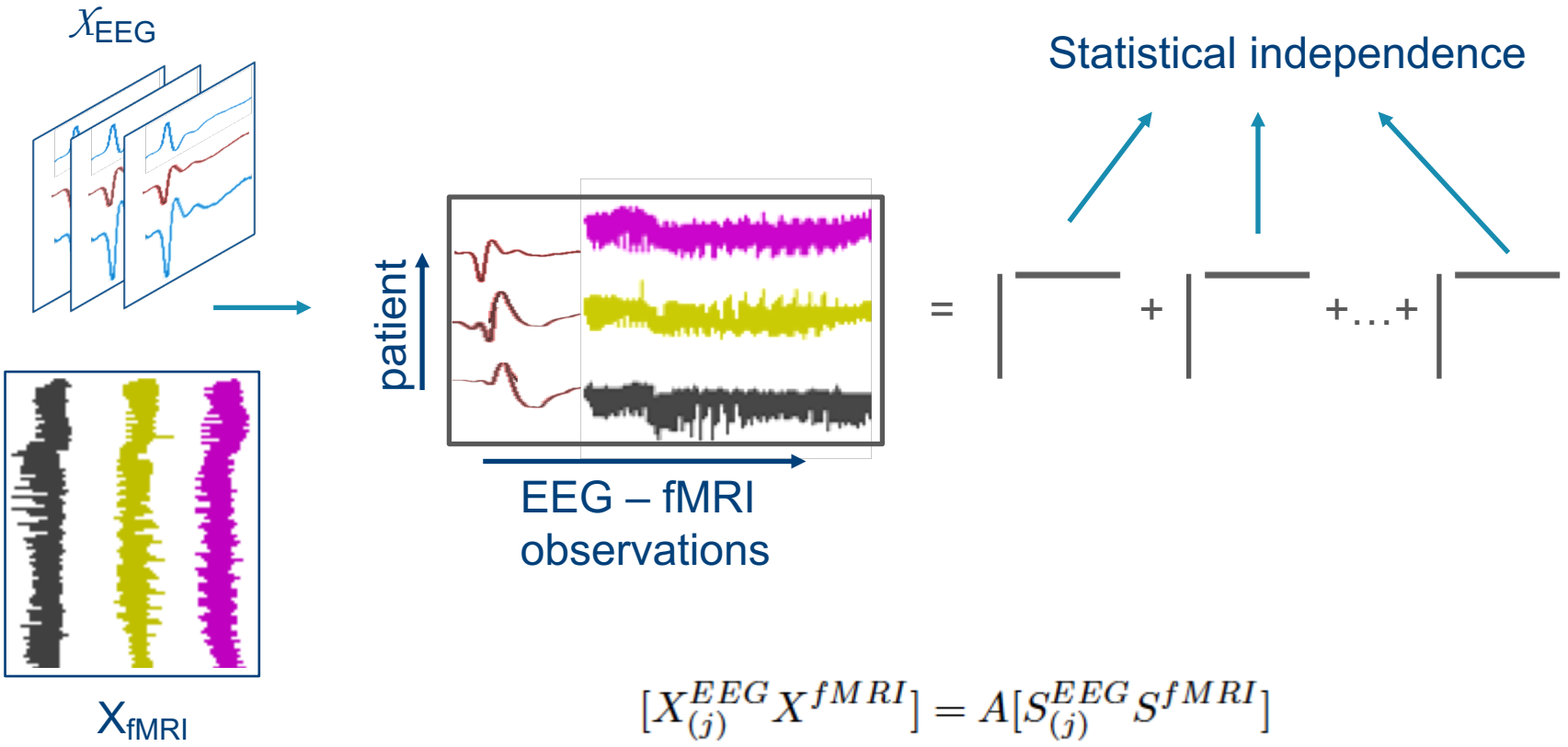
vectorization

X_{fMRI}



im_1 im_2 im_3

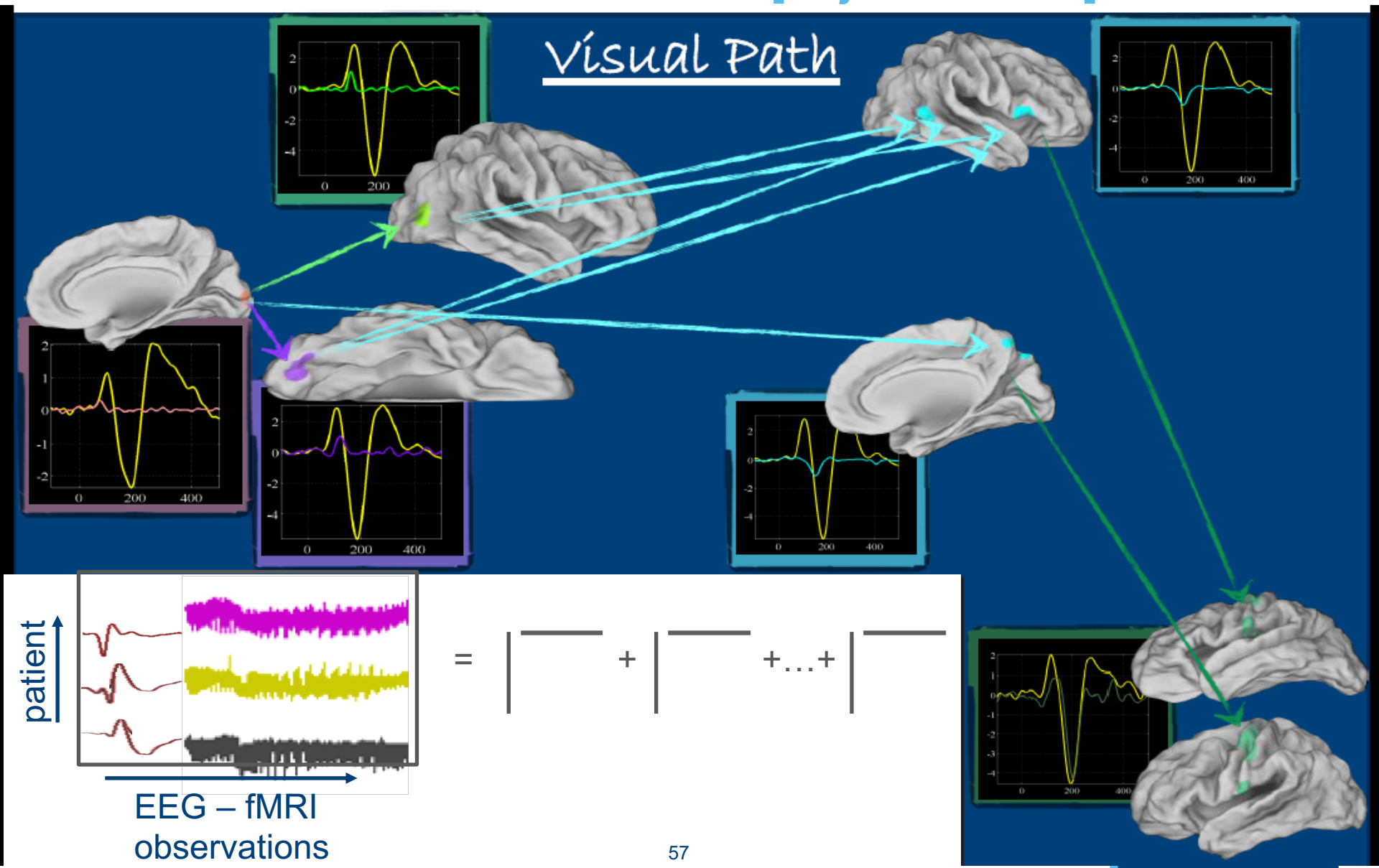
Joint blind source separation (1): jointICA



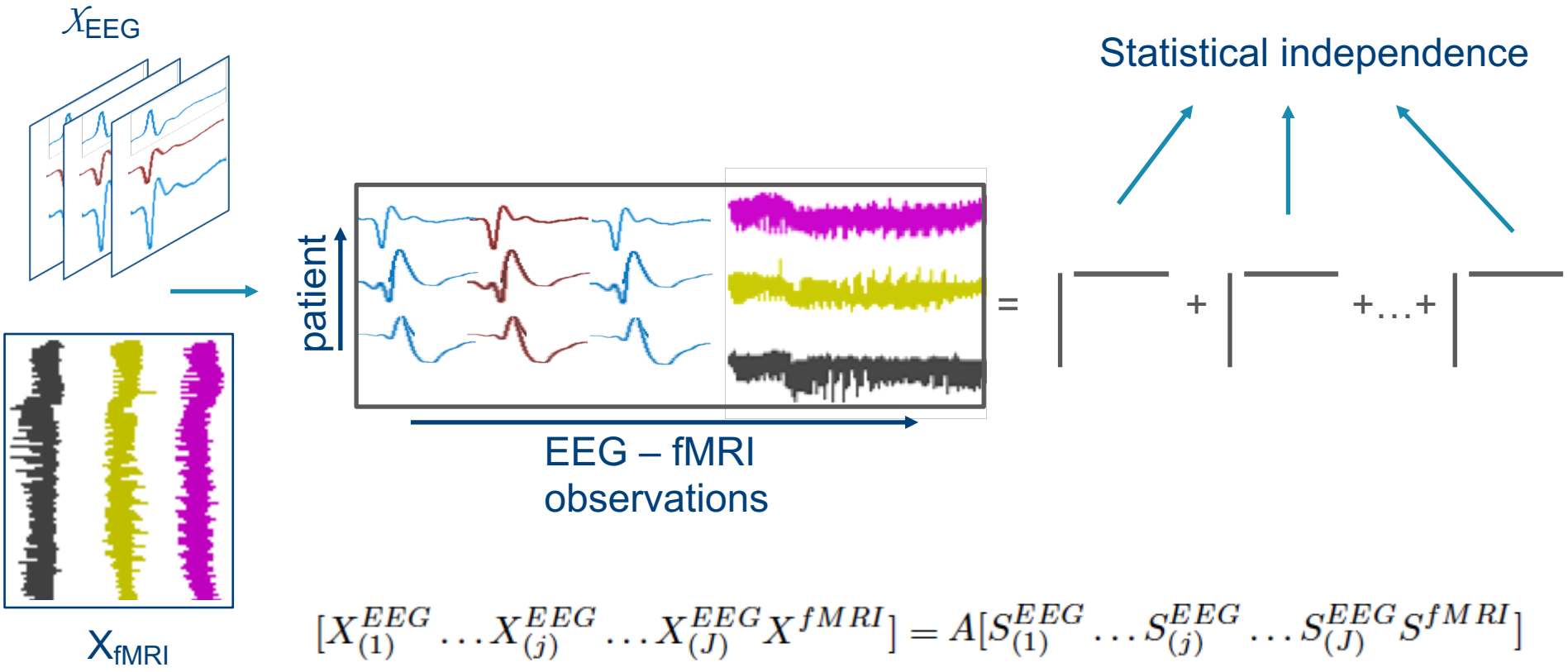
$$[X_{(j)}^{EEG} X^{fMRI}] = A[S_{(j)}^{EEG} S^{fMRI}]$$

[Calhoun 2006]

JointICA: Visual detection task [Mijovic 2012]



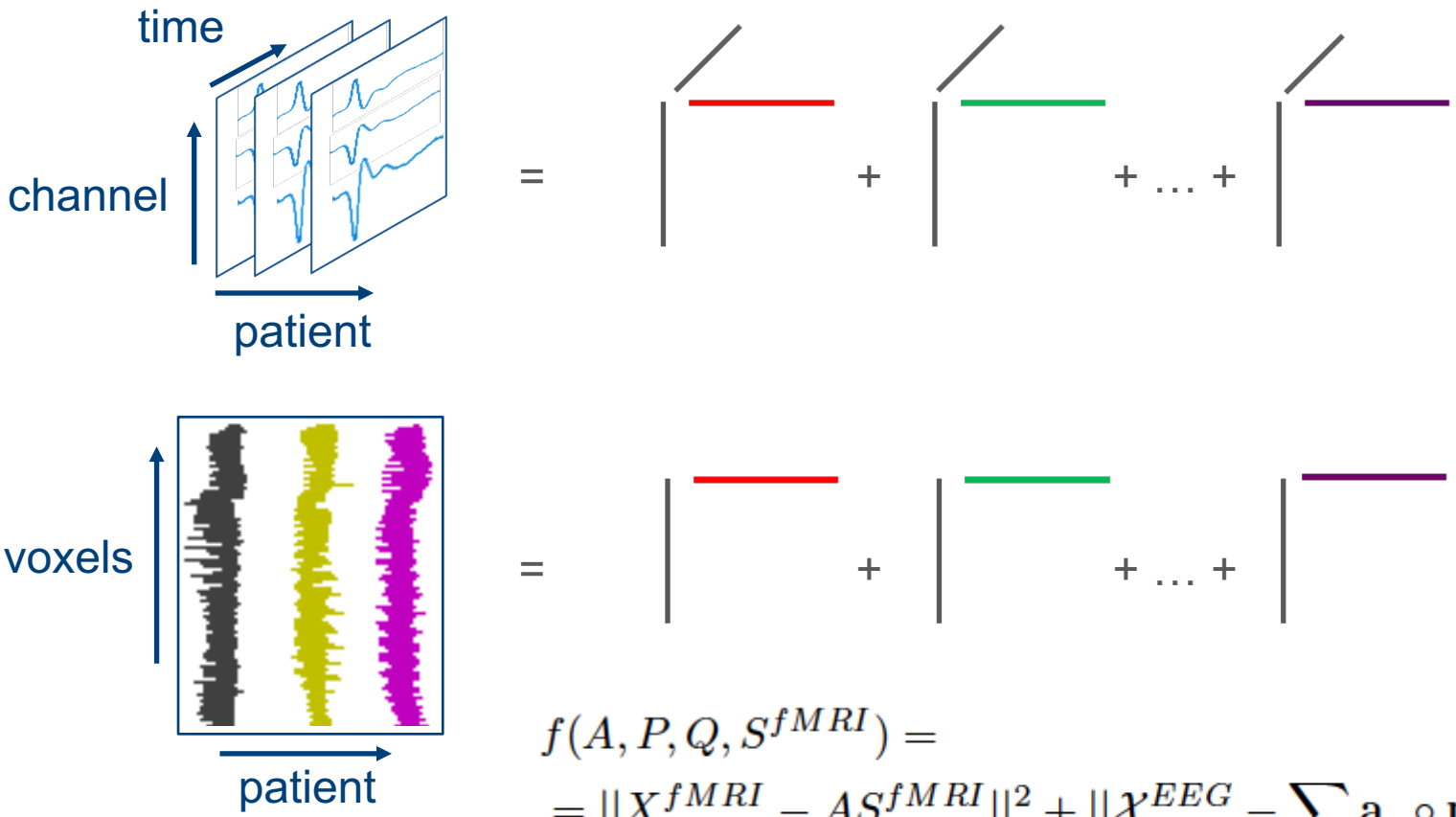
Joint blind source separation (2): t-jointICA



$$[X_{(1)}^{EEG} \dots X_{(j)}^{EEG} \dots X_{(J)}^{EEG} X^{fMRI}] = A[S_{(1)}^{EEG} \dots S_{(j)}^{EEG} \dots S_{(J)}^{EEG} S^{fMRI}]$$

[Swinnen 2014]

Joint blind source separation (3): Coupled tensor-matrix factorization



$$f(A,P,Q,S^{fMRI}) =$$
$$= ||X^{fMRI} - AS^{fMRI}||^2 + ||\mathcal{X}^{EEG} - \sum_R \mathbf{a}_r \circ \mathbf{p}_r \circ \mathbf{q}_r||^2$$

[Acar 2014, Hunyadi 2016]

Experiments

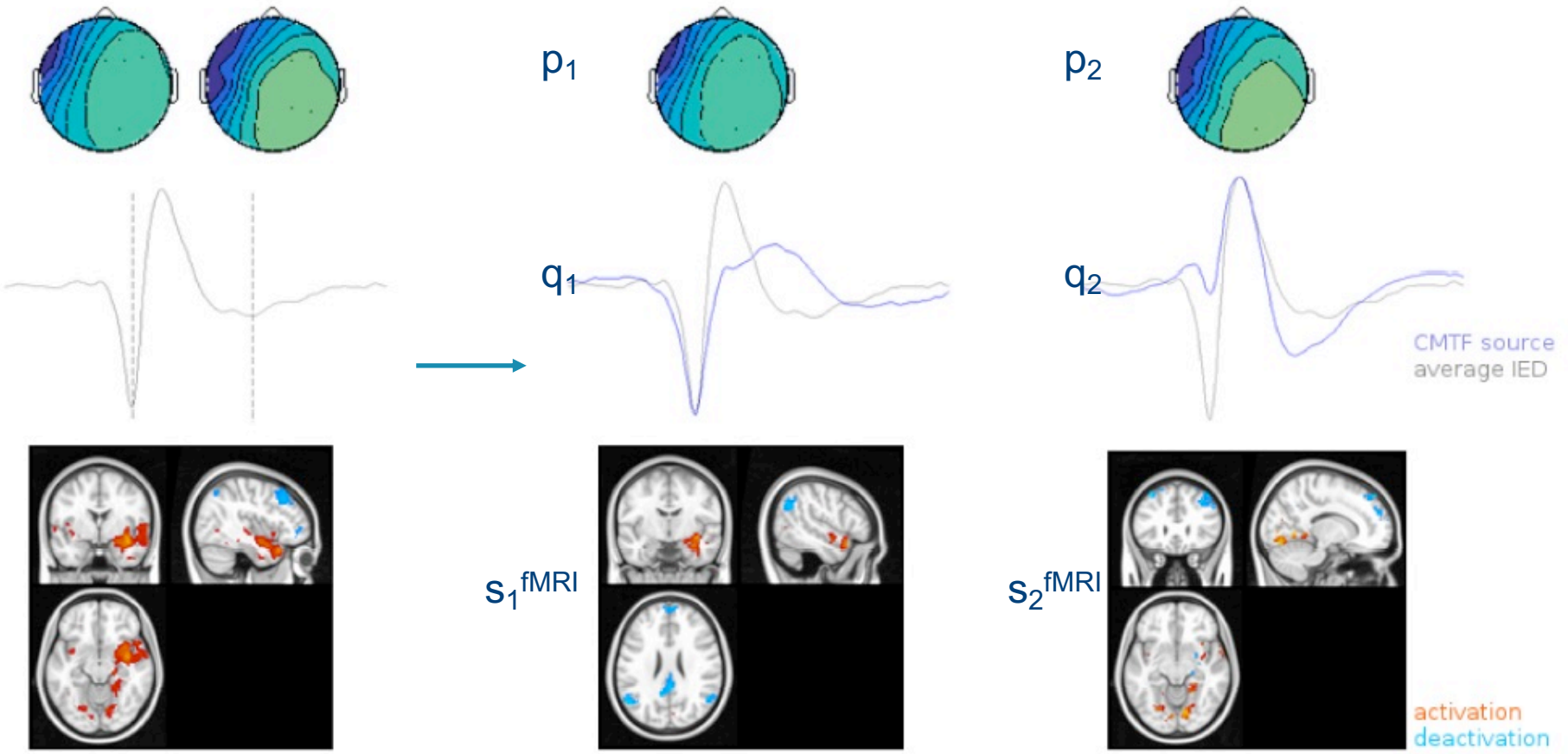
Dataset

- 10 temporal lobe epilepsy (TLE) patients, 5 right, 5 left
- To get a consistent set, the EEG and the fMRI of the LTLE patients are mirrored

Model selection

- R=2 was chosen

Results: epileptic network



average IED and GLM-based activation map

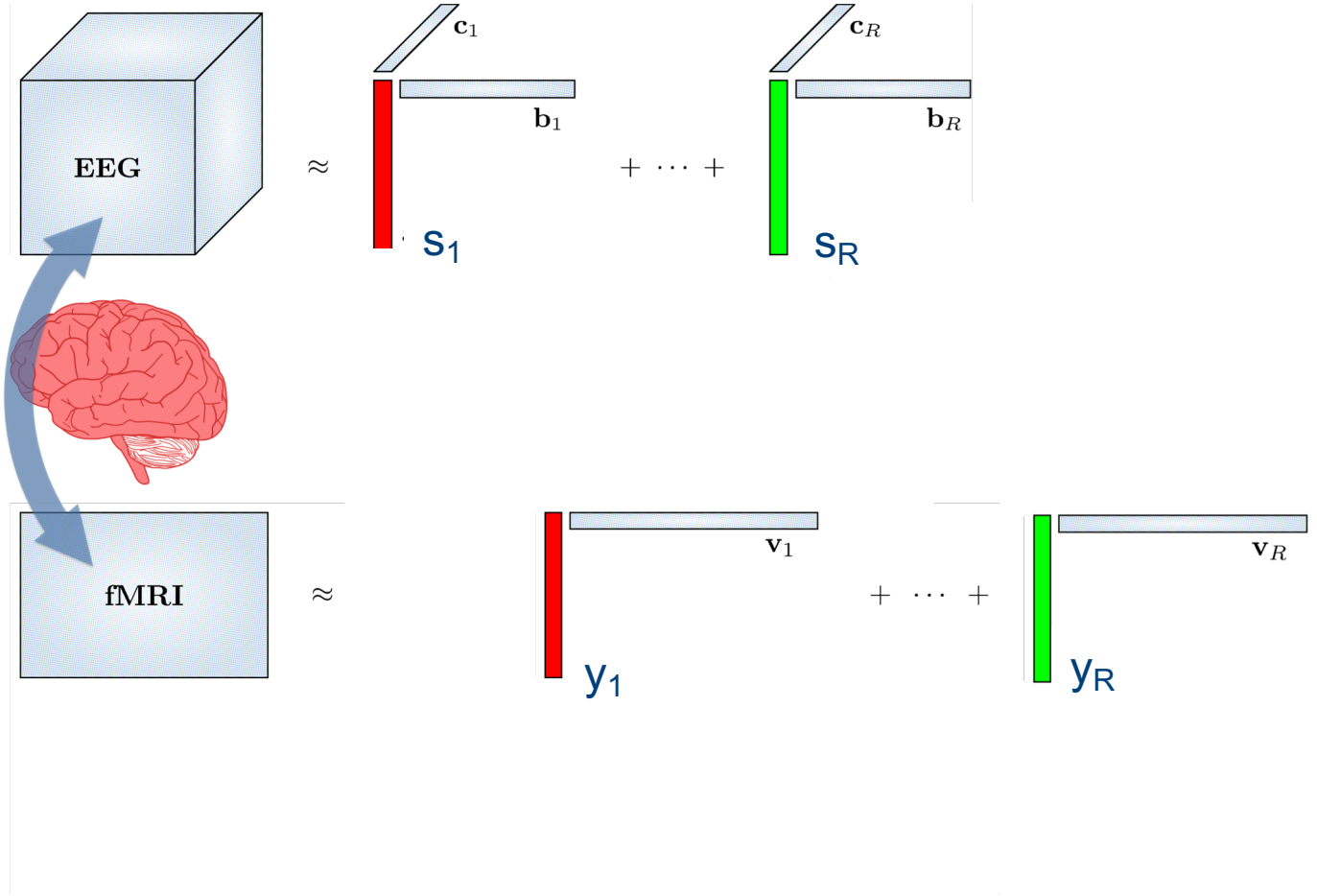
"onset"

"propagation / inhibition"

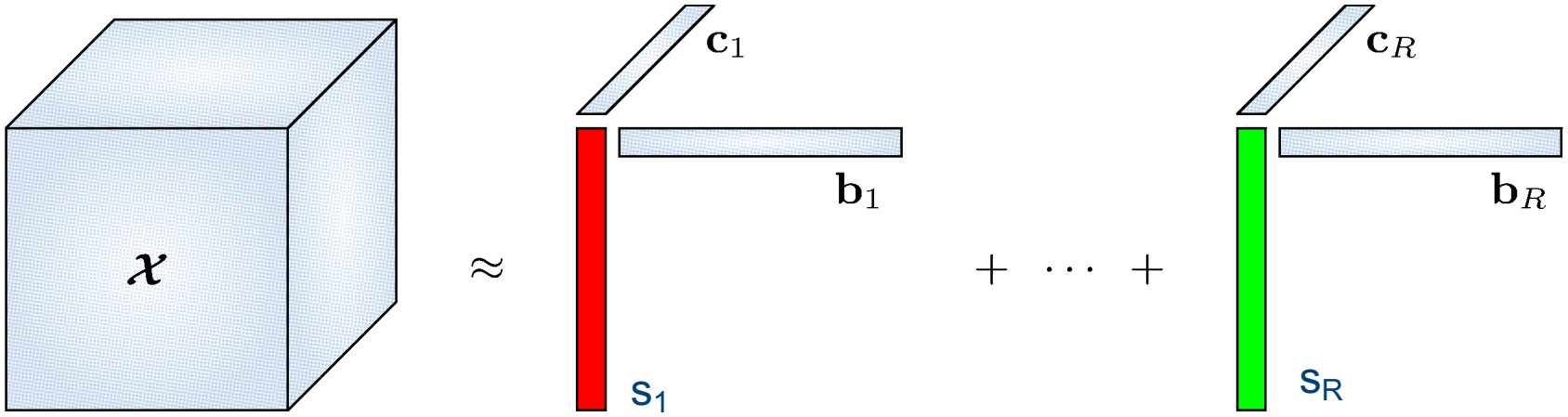
We need better spatiotemporal resolution

- Symmetric EEG-fMRI integration
- Find a common mode of variation
- Joint decomposition (BSS) where signatures in this mode are shared
  - Subject / patient
    - JointICA
    - Multichannel jointICA
    - CPD
  - **Time**

EEG-fMRI fusion in the temporal mode



The proposed approach



EEG decomposed into components

1 component / source = temporal pattern (s)
+ activity over channels (b)
+ activity over frequencies (c)

Hemodynamic coupling

$$y(t) = h(t) * s(t)$$

modelled time course in 1 voxel

$$y(t) = \sum_{u=1}^{L} h(t-u)s(u)$$

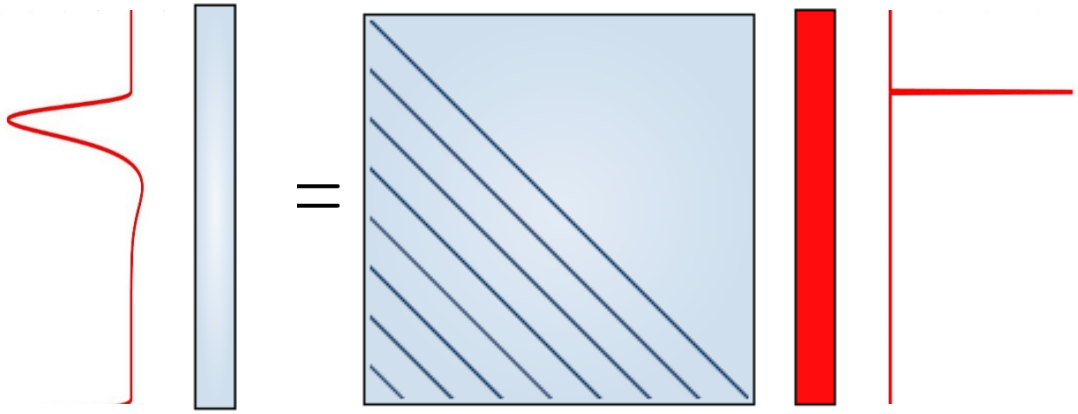
$$\begin{bmatrix} y(0) \\ y(1) \\ y(2) \\ \vdots \\ y(N) \end{bmatrix} = \begin{bmatrix} h(0) & 0 & 0 & \cdots & 0 & 0 \\ h(1) & h(0) & 0 & \cdots & 0 & 0 \\ h(2) & h(1) & h(0) & \cdots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ h(N) & h(N-1) & h(N-2) & \cdots & h(1) & h(0) \end{bmatrix} \begin{bmatrix} s(0) \\ s(1) \\ s(2) \\ \vdots \\ s(N) \end{bmatrix}$$

Hemodynamic coupling

$$y(t) = h(t) * s(t)$$

$$y(t) = \sum_{u=1}^{L} h(t-u)s(u)$$

modelled time course in 1 voxel

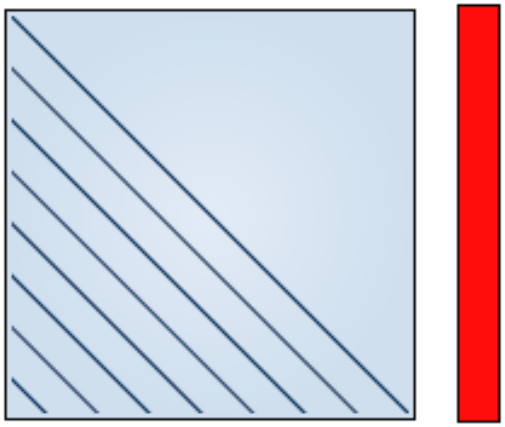


Hemodynamic coupling

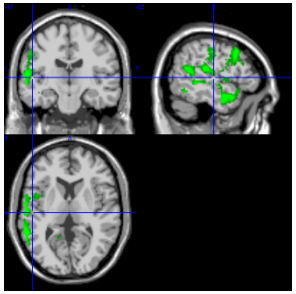
$$y(t) = h(t) * s(t)$$

$$y(t) = \sum_{u=1}^{L} h(t-u)s(u)$$

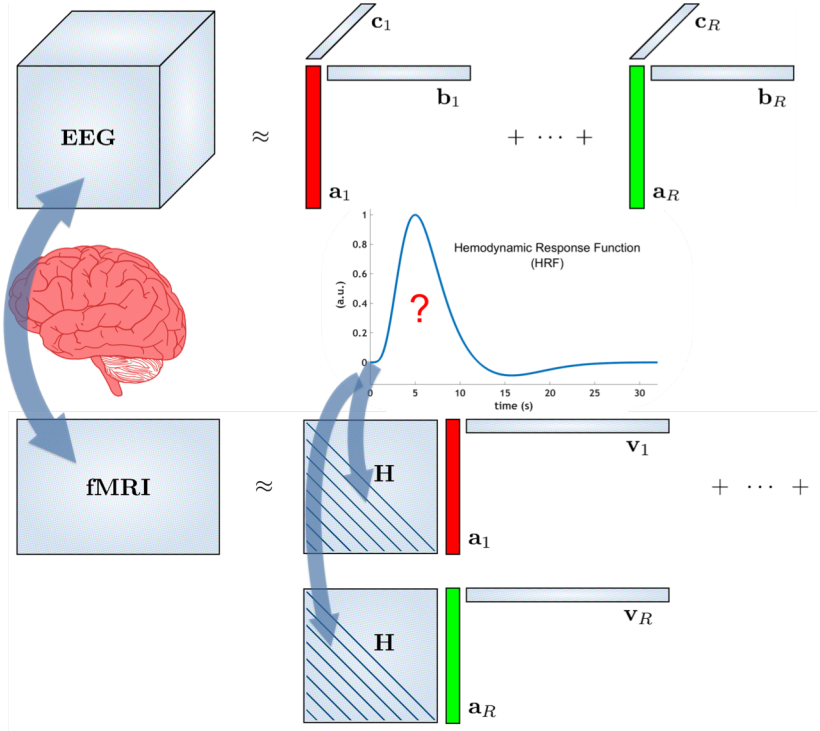
modelled time course in 1 voxel



activation pattern over voxels



EEG-fMRI fusion in the temporal mode



$$J(\mathbf{A},\mathbf{B},\mathbf{C},\mathbf{V},\theta) = \|\boldsymbol{\mathcal{X}} - \sum_{r=1}^{R} \mathbf{a}_r \otimes \mathbf{b}_r \otimes \mathbf{c}_r\|^2 + \qquad (3)$$

$$\|\mathbf{Y} - \sum_{r=1}^{R} (\mathbf{H}(\theta)\mathbf{a}_r) \otimes \mathbf{v}_r\|^2 \ , \ \text{s.t. } \mathbf{A}, \mathbf{C} \geq 0$$

[Van Eyndhoven 2016]

Advantages of the approach

In a simualtion study, it was shown that

- Proposed appraoch can estimate subject-specific HRF
- Accounting for HRF variability results in more accurate characterization of neural sources of activity
  - In spatial / temporal / spectral domain
- Proposed approach can deal with
  - different changes in HRF waveform
  - spatially / temporally correlated noise

Summary

- EEG and fMRI measure a mixture of brain and non-brain sources, resulting in low SNR
- Tensor-based blind source separation is a powerful way to deal with this problem
- Successful applications in EEG and in fMRI
- Fusion of EEG-fMRI for better spatiotemporal resolution
- Tensor-based fusion along a common mode of variation

Thank you!

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| Universidad de Oriente, Cuba

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