Multiscale analysis of fMRI data

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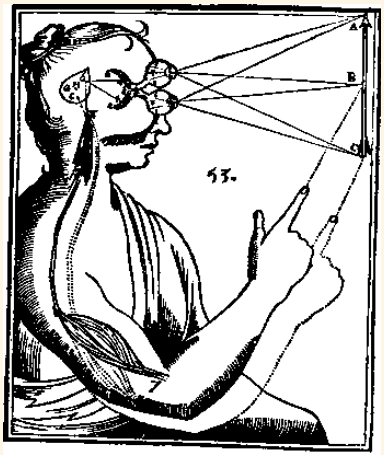
Outline

1. Introduction
2. FMRI projections on wavelet packets
3. Statistical properties of the projections
4. Detection of activation
5. Experiments

Introduction

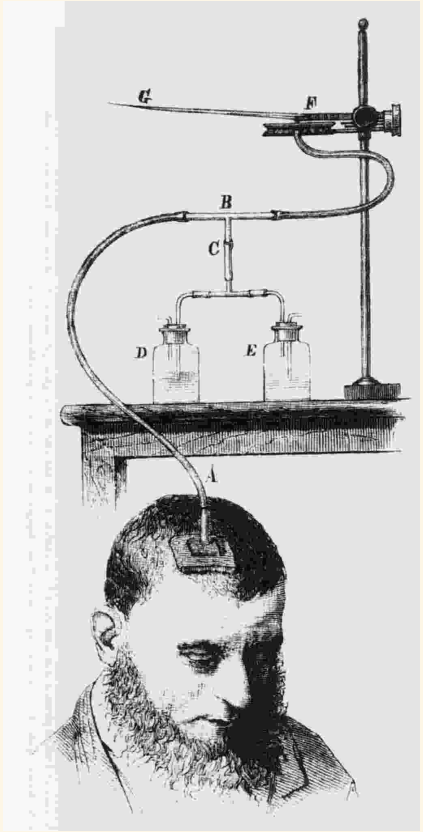
- functional imaging : delineation of functional anatomy in terms of spatial and temporal organization

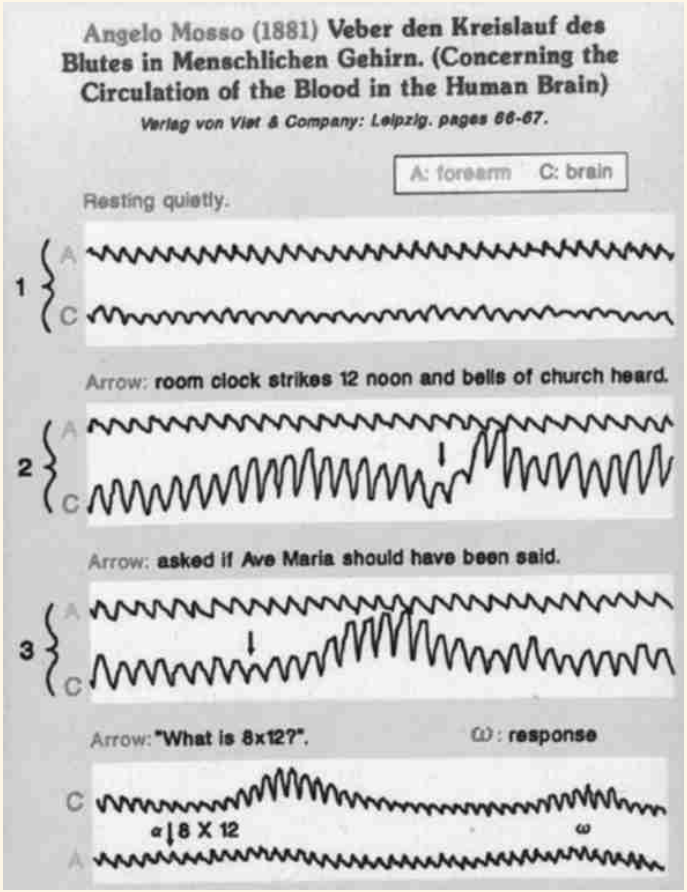


René Descartes *De homine* (1662)

Functional brain imaging : blood flow

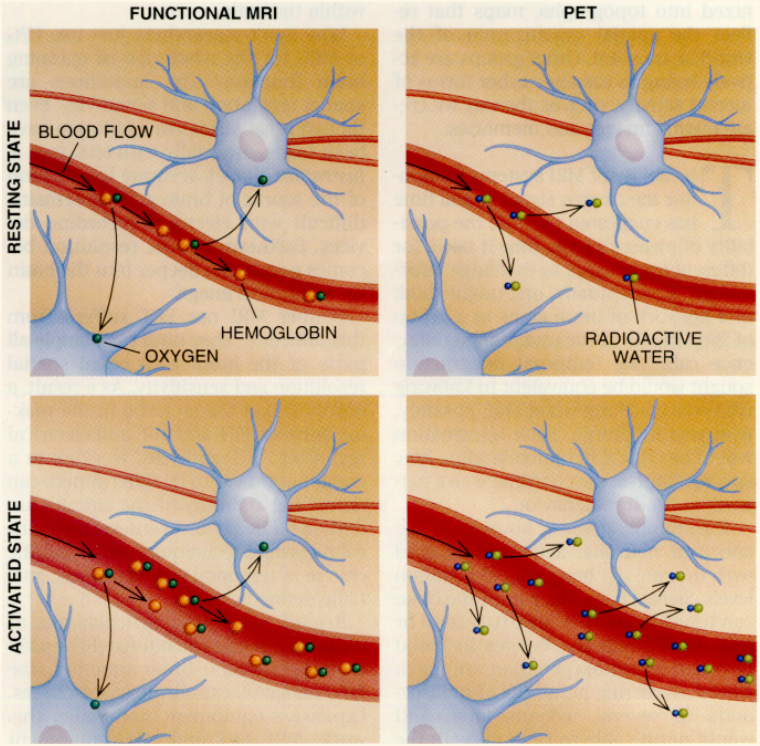
- hemodynamic changes induced by neuronal activity when a subject is submitted to sensory or cognitive stimulations.





Detection devices

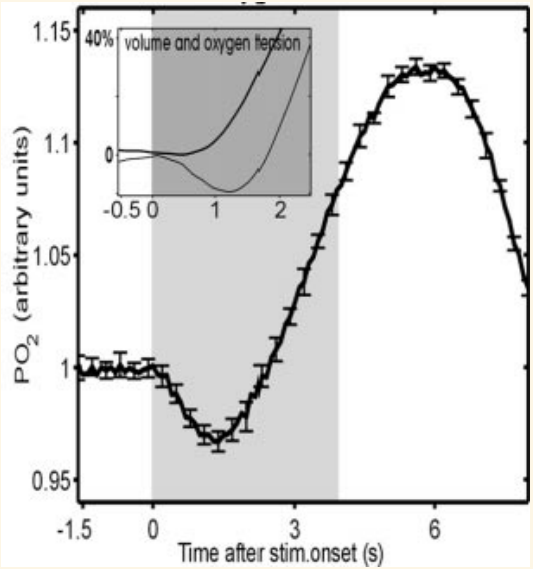
PET/fMRI



PET, fMRI : neuronal activity requires energy. Local increases in blood flow, and metabolism can be measured.

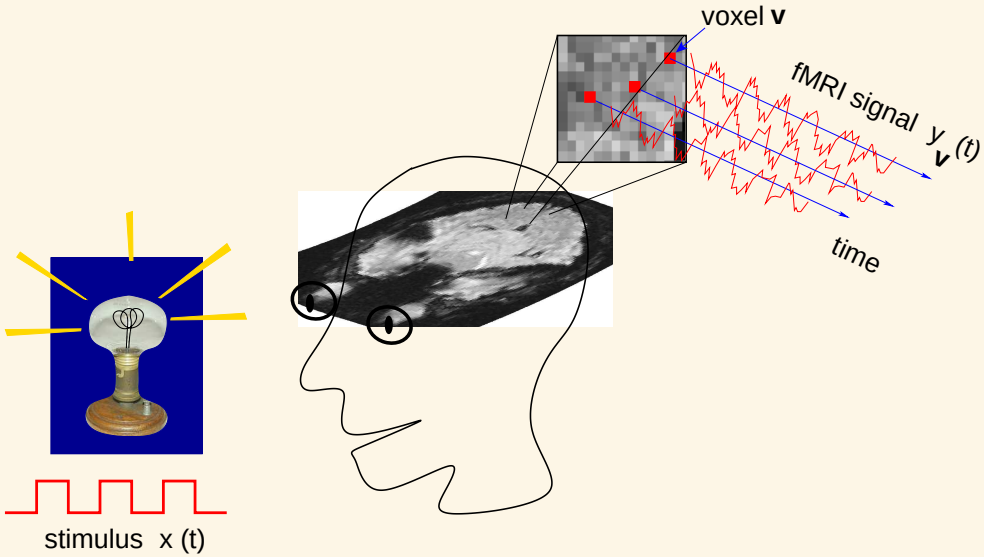
Oxygen concentration changes in the microcirculation

- Initial increase in oxygen consumption created by metabolic demand
- Increase in cerebral blood flow : oversupply of oxygenated blood
- oxygenated hemoglobin induces a difference in magnetic susceptibility relative to the surrounding
- imbalance between oxygen metabolism and oxygen supply is at the origin of the BOLD contrast



Microvascular oxygen concentration [Vanzetta and Grinvald, 1999].

Functional Magnetic Resonance Imaging (fMRI)



- Goal of the analysis : detect "activated" voxels $\mathbf{v}$ where changes in the fMRI signal $\mathbf{y}$ are triggered by the stimulus $\mathbf{x}$.

Analysis of fMRI data : Univariate statistical models

1. General Linear Model [Friston et al., 1995]

$$\mathbf{y_v} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}, \quad \boldsymbol{\varepsilon} \sim \mathcal{N}(0, \Sigma) \tag{1}$$

limitations :

- $\varepsilon(t)$ correlated
- var(ε) varies as a function of $\mathbf{v}$ [Chen et al., 2003]

2. Linear Time Invariant Model

$$\mathbf{y_v} = h_\mathbf{v} * \mathbf{x} \tag{2}$$

[Lange and Zeger, 1997, Genovese, 2000]
limitations :

- $h_\mathbf{v}$ haemodynamic response function depends on brain region, subject, etc.
- nonlinear relationship between $\mathbf{y_v}$ and $\mathbf{x}$ [Friston et al., 1998, Miller et al., 2001, Rees et al., 1997, Vazquez and Noll, 1998].

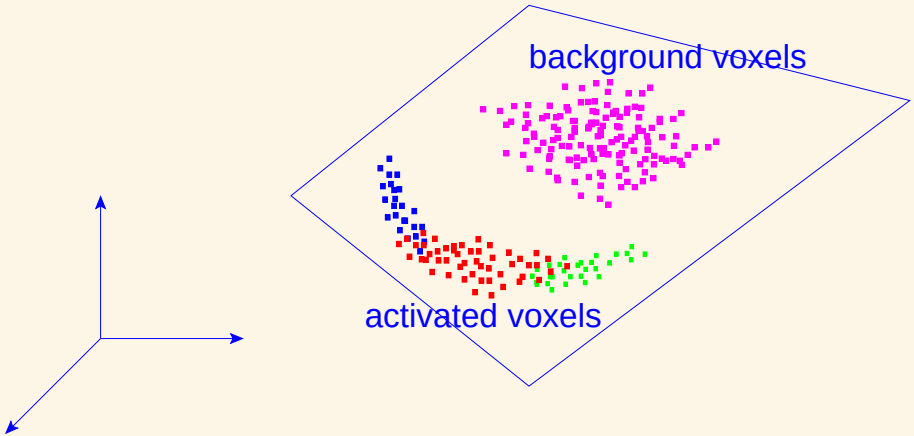
Analysis of fMRI data : Exploratory methods

1. principal component analysis
   [Lai and Fang, 1999, Gabbay et al., 2000]
   limitations :
   - components need to be orthogonal
   - interpretation of the components ?
2. independent component analysis
   [B.B.Biswal and Ulmer, 1999, McKeown, 2000]
   limitations :
   - component maps need to be independent
   - interpretation of the components ?
3. Clustering of the time series $\mathbf{y_v}$
   [Baumgartner et al., 1998, Golay et al., 1998, Meyer and Chinrungrueng, 200
   limitations :
   - performed in the time domain ($\mathbb{R}^{128}$!)

Goal of this work

- search for projections of the fMRI time series on a low dimensional subspace :

$\longrightarrow$ reveal the presence of activated time series.



- probability distribution of the projections (coefficients) : finite mixture of multivariate Gaussian densities
- estimate the parameters of the mixture, number of components, and interpret their physiological roles.

What type of projections ?

properties of the fMRI time series :

- non stationary $\rightarrow$ analyze transients, local features
- long range dependence ($1/f$ spectral behavior)
  [Zarahn et al., 1997, Fadili and Bullmore, 2002]
  $\rightarrow$ whiten the time series, stationary

good properties of the projections :

- rich library of waveforms well localized in time and in frequency
- fast search in the library

$\rightarrow$ library of wavelet packets

What can we learn from the wavelet packet coefficients of fMRI time series ?

- background signal: $y_{\mathbf{v}}(t) =$ constant $\rightarrow \alpha_{\mathbf{v}} \simeq 0$
  $\alpha_{\mathbf{v}} \sim \mathcal{N}(0, \sigma_b^2)$ [Chen et al., 2003]
- activated signal: $y_{\mathbf{v}}(t) =$ response triggered by stimulus
  if $\boldsymbol{\psi}$ is well chosen then $\alpha_{\mathbf{v}} \sim \mathcal{N}(\mu_k, \sigma_k^2)$ [Meyer and Shen, 2004]
- strength μ_k may vary as a function of $\mathbf{v}$
- $\alpha_{\mathbf{v}}$ stationary, uncorrelated

$$\text{corr}(\alpha(j,k), \alpha(j',k')) \sim O(|2^{-j}k - 2^{-j'}k'|^{\gamma-2p-1}),$$

  p vanishing moments

Joint distribution of the wavelet packet coefficients

- choose a small number K of wavelet packets $\boldsymbol{\psi}_{\gamma_k}$, (e.g. $K = 3$)
- for $\mathbf{v}$ all over the brain, compute $\alpha_{\mathbf{v}}(\gamma_k)$
- joint distribution of vector of coefficients $\boldsymbol{\alpha} = [\alpha(\gamma_0), \cdots, \alpha(\gamma_{K-1})]^T$
- $\boldsymbol{\alpha} \sim$ finite mixture of M multivariate Gaussian densities

$$p(\boldsymbol{\alpha}) = \sum_{m=1}^{M} \pi_m \boldsymbol{\phi}(\boldsymbol{\alpha}, \mu_m, \Sigma_m). \tag{3}$$

  $\boldsymbol{\phi}$: K-multivariate normal density,
  π_m : mixing parameters $\pi_m \geq 0$, $\sum \pi_m = 1$

- voxels with a similar activation strength are grouped together in the same component (irrespective of their relative spatial proximity).

Estimation of the parameters of the mixture

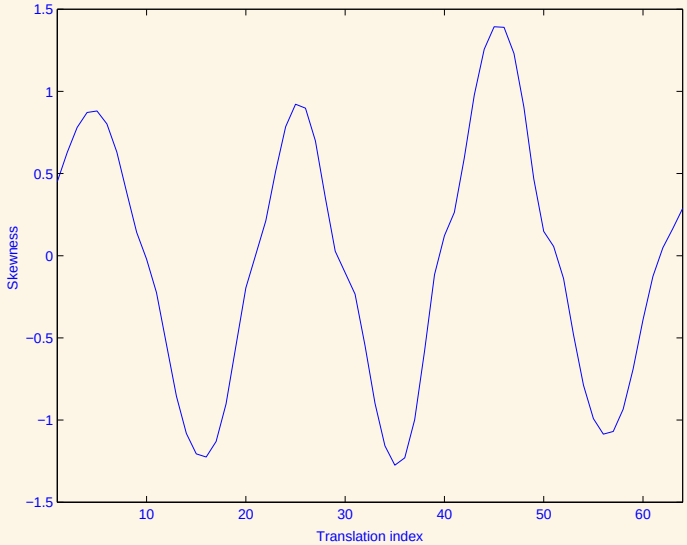
- maximum likelihood estimates $\hat{\mu}_m$, $\hat{\Sigma}_m$ and $\hat{\pi}_m$
- Expectation Minimization (EM) algorithm

How to find good a projection ?

- projection $= \boldsymbol{\psi}_\gamma$ nondecimated wavelet packet
- $\boldsymbol{\psi}_\gamma$ is a good projection if the distribution of the coefficients $\alpha_{\mathbf{v}}(\gamma)$ is asymmetric:
  - many small coefficients (=background),
  - few large coefficients (=activated region)
- maximize the skewness of the distribution of $\alpha_{\mathbf{v}}(\gamma)$ computed over all $\mathbf{v}$

$$E[(X - EX)^3] / E[(X - EX)^2]^{3/2} \tag{4}$$

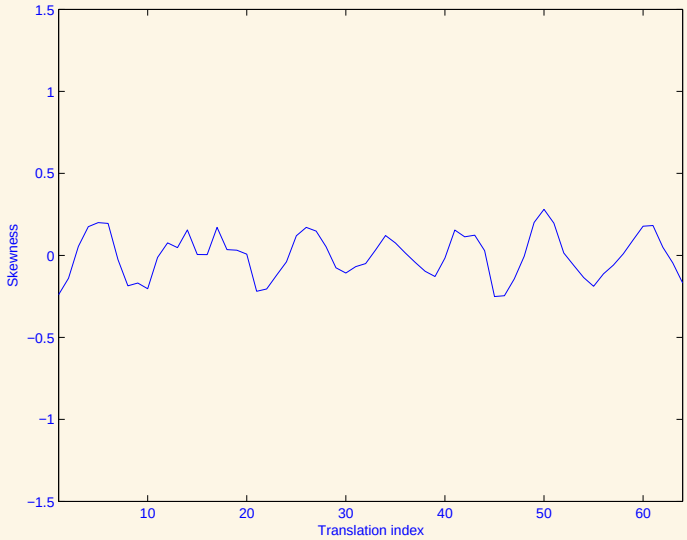
Skewness as a function of the translation index for a good projection



- periodic stimulus
- if $\boldsymbol{\psi}_\gamma$ is properly aligned:
  - response = large $\boldsymbol{\alpha}_{\mathbf{v}}(\gamma)$, background = small $\boldsymbol{\alpha}_{\mathbf{v}}(\gamma)$

  $\longrightarrow$ asymmetric distribution
- misalignment:
  - response = small $\boldsymbol{\alpha}_{\mathbf{v}}(\gamma)$, background = small $\boldsymbol{\alpha}_{\mathbf{v}}(\gamma)$

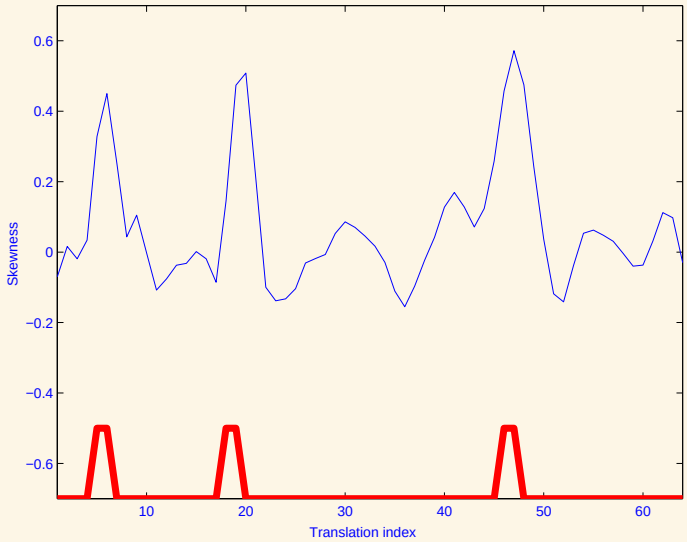
Skewness as a function of the translation index for a bad projection



- for all translation indexes:
  response = small $\boldsymbol{\alpha}_{\mathbf{v}}(\gamma)$, background = small $\boldsymbol{\alpha}_{\mathbf{v}}(\gamma)$

$\longrightarrow$ symmetric distribution

Skewness as a function of the translation index for a good projection



- 3 random stimuli
- for the right translation indexes:
  response = large $\boldsymbol{\alpha}_{\mathbf{v}}(\gamma)$, background = small $\boldsymbol{\alpha}_{\mathbf{v}}(\gamma)$

A spatial prior

- spatial distribution of the pattern of activation :
  not present in the mixture model
- activated patterns = small numbers of compact regions
- prior probability of the patterns of activation
- Markov random field
- detection of activation :

$$a_i = \begin{cases} 1 & \text{if } \mathbf{v}_i \text{ is activated,} \\ 0 & \text{if } \mathbf{v}_i \text{ is a background voxel.} \end{cases} \tag{5}$$

Parameter Estimation

- most likely activation pattern $\hat{\mathbf{a}}$:

$$\hat{\mathbf{a}} = \underset{(a_0,\cdots,a_4)}{\operatorname{argmax}} \; p(\mathbf{a}|\boldsymbol{\alpha}) \tag{6}$$

- Bayes' theorem

$$p(\mathbf{a}|\boldsymbol{\alpha}) \propto p(\boldsymbol{\alpha}|\mathbf{a})p(\mathbf{a}) \tag{7}$$

- coefficients conditionally independent given the activation map

$$p(\boldsymbol{\alpha}|\mathbf{a}) = \prod_j p(\boldsymbol{\alpha}_{\mathbf{v}_j}|\mathbf{a}) = \prod_j p(\boldsymbol{\alpha}_{\mathbf{v}_j}|a_j) \tag{8}$$

- $p(\boldsymbol{\alpha}_{\mathbf{v}_j}|a_j)$ computed at each voxel $\mathbf{v}_j$ from the mixture model
- $p(\mathbf{a})$: spatial prior
- optimization: simulated annealing

Experiments : synthetic data blended with in-vivo fMRI noise

- haemodynamic response [Glover, 1999] :

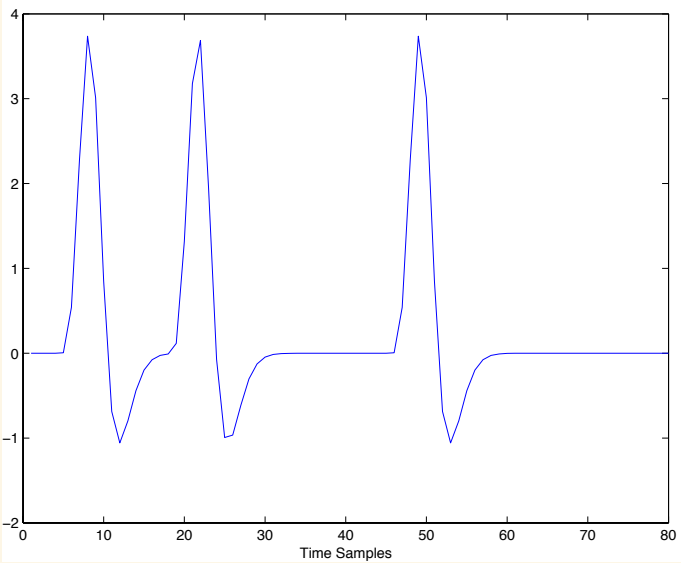
$$h(t) = A\left\{a_1(t-t_s)^5 e^{-(t-t_s)/t_1} - 0.4\, a_2(t-t_s)^2 e^{-(t-t_s)/t_2}\right\} \qquad (9)$$

- A = strength of the response
- fMRI signal = $h *$ stimulus + noise
- stimulus = 3 random events
- noise extracted from *in vivo* background time series

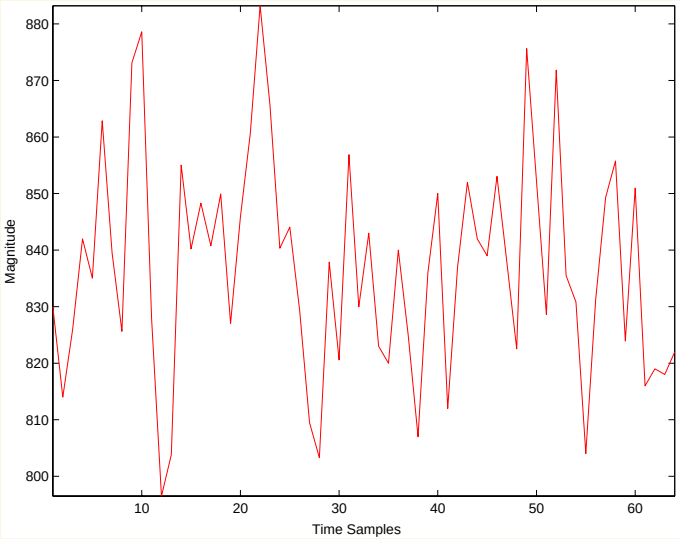
The synthetic datasets

- 4 datasets with uniform strength: $A = 1, 1.5, 2, 2.5,$
- 1 dataset with different strengths: A varies with $\mathbf{v}$
- 108 activated voxels (6.75%)
- gold standard: linear regression with perfect knowledge of $h(t)$ and the stimulus

Time series

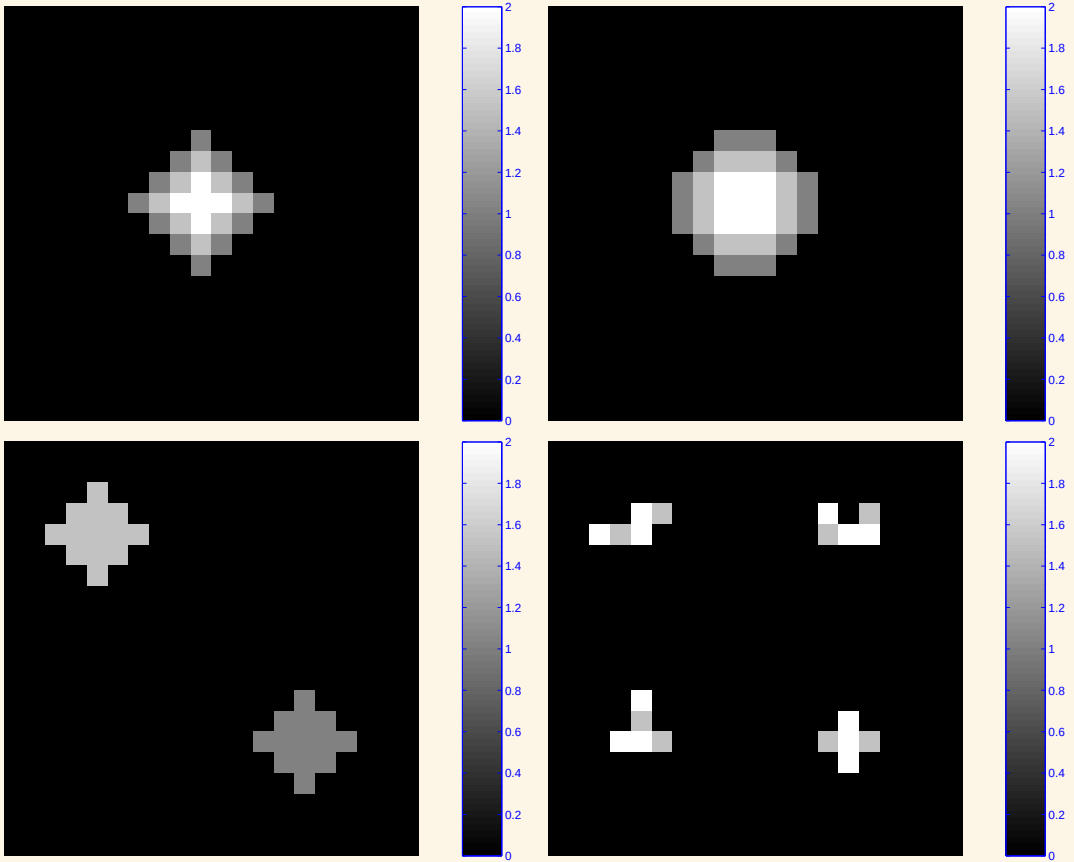


$h *$ stimulus

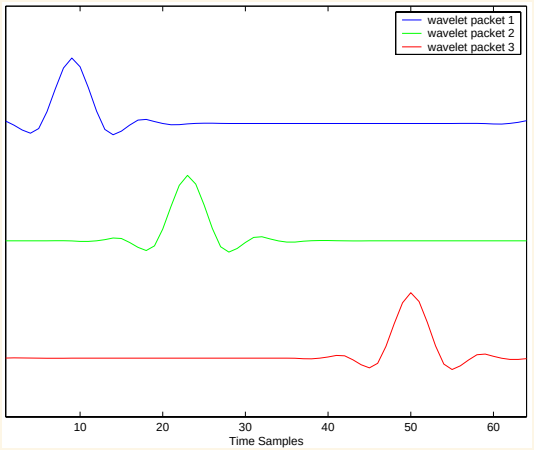


$h *$ stimulus $+$ noise, $A = 1$

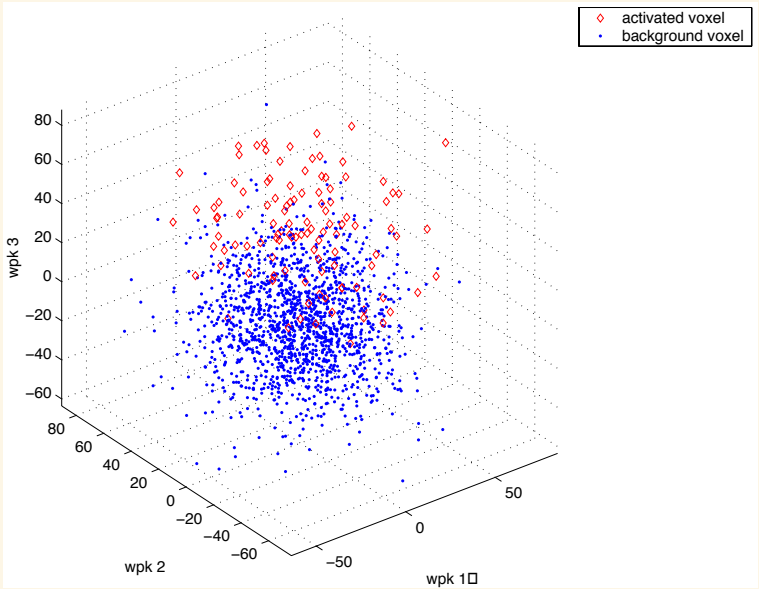
Dataset 5: activation patterns



Synthetic datasets: results

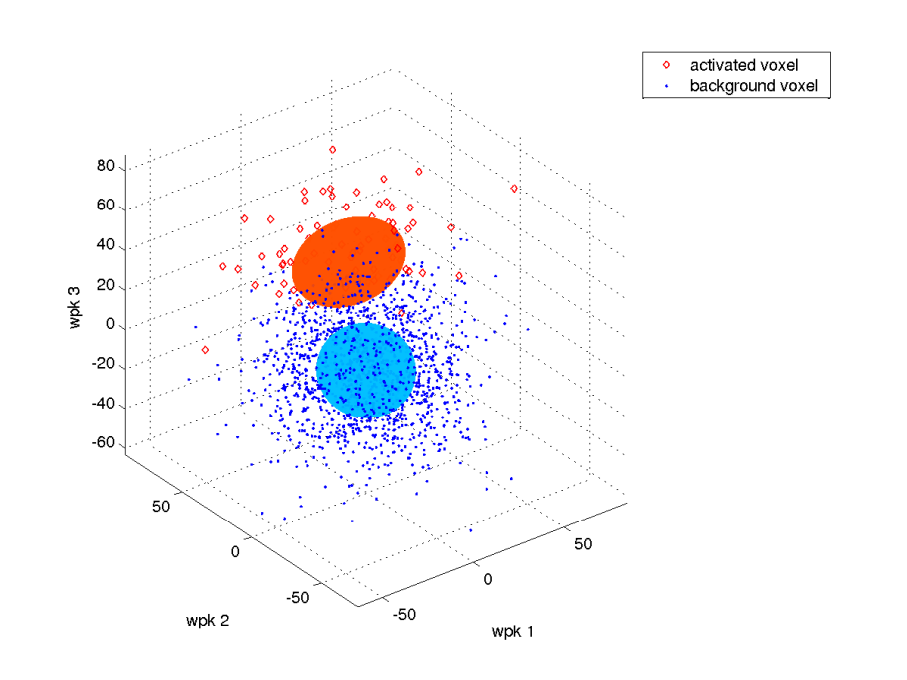


Projections (K=3)



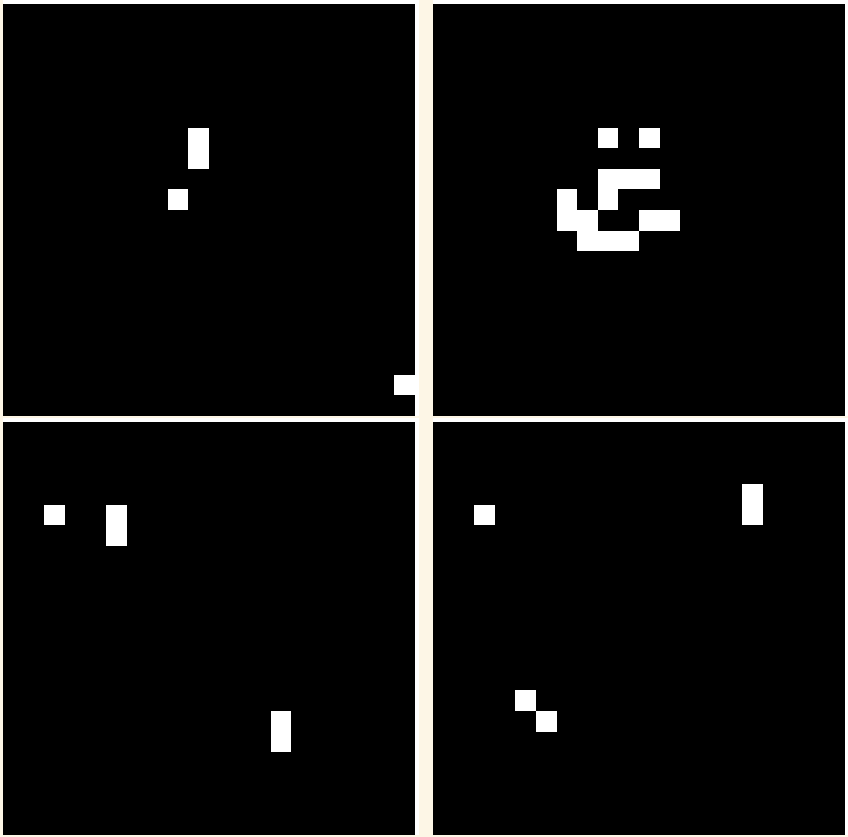
background (blue) and
activated (red) time series $(A = 1)$

Synthetic datasets: results



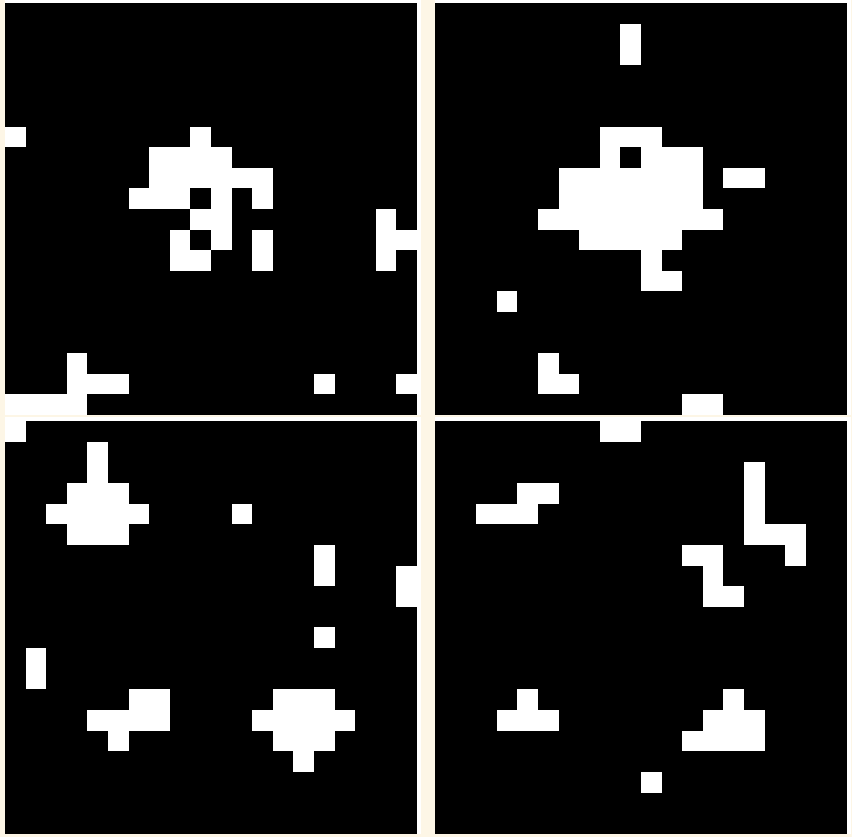
Classification between activated and background voxels $(A = 1)$

Synthetic datasets: activation maps



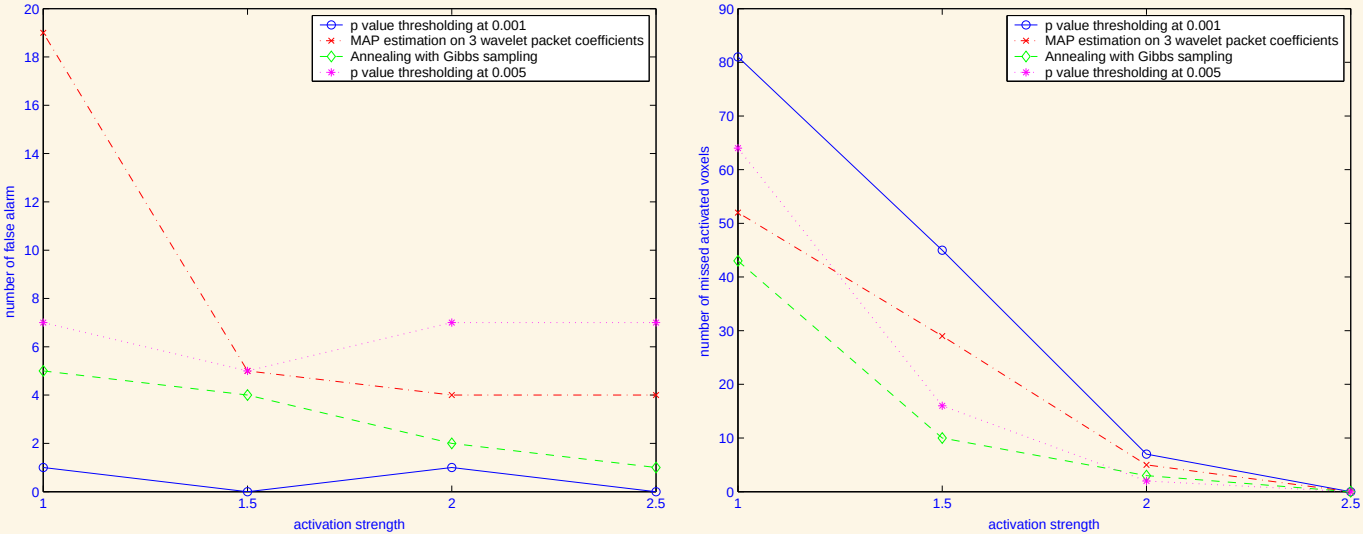
Activation maps obtained with the linear regression

Synthetic datasets: activation maps



Activation maps with our method $(A = 1)$

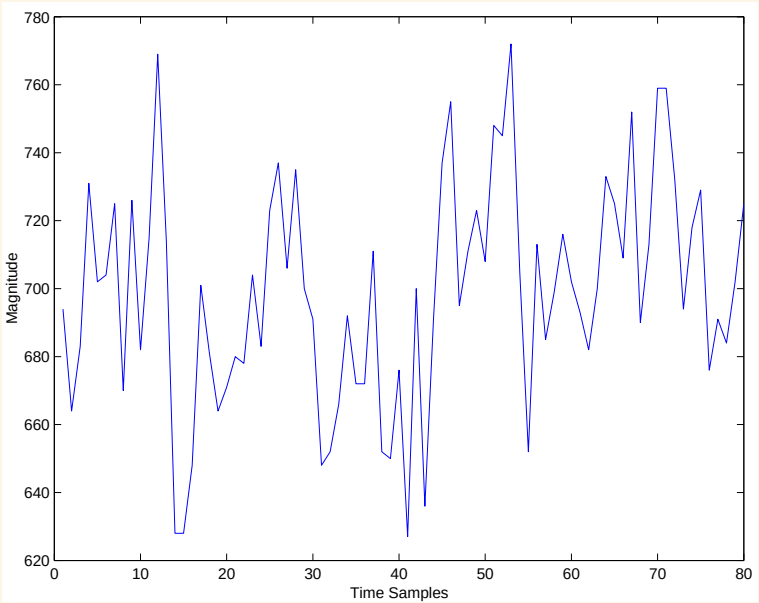
Performance



False alarm and missed activated voxels as a function of A.

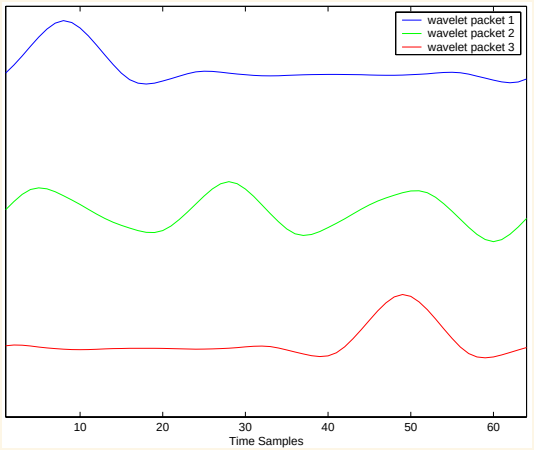
Experiments : in vivo data

- visual stimulus : periodic flashing checkerboard



Time series from an activated voxel

Experiments : in vivo data



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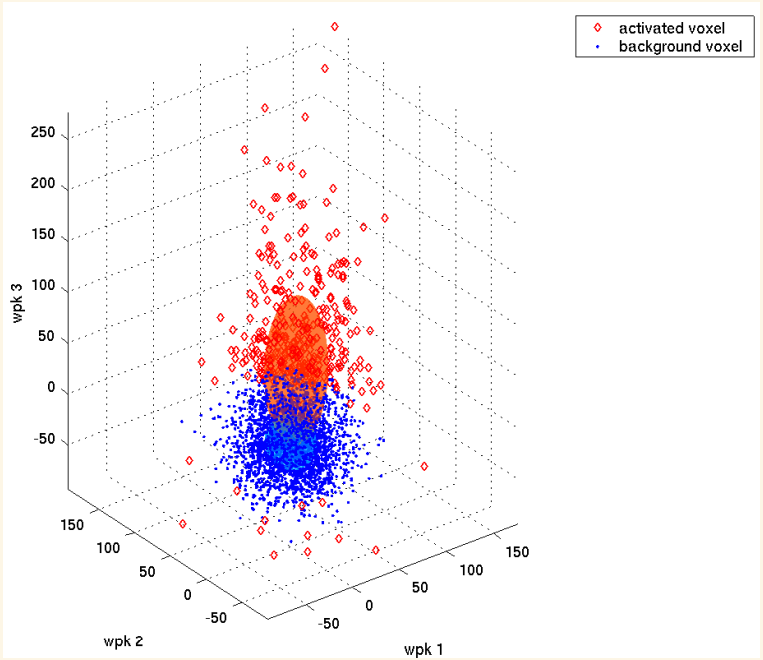
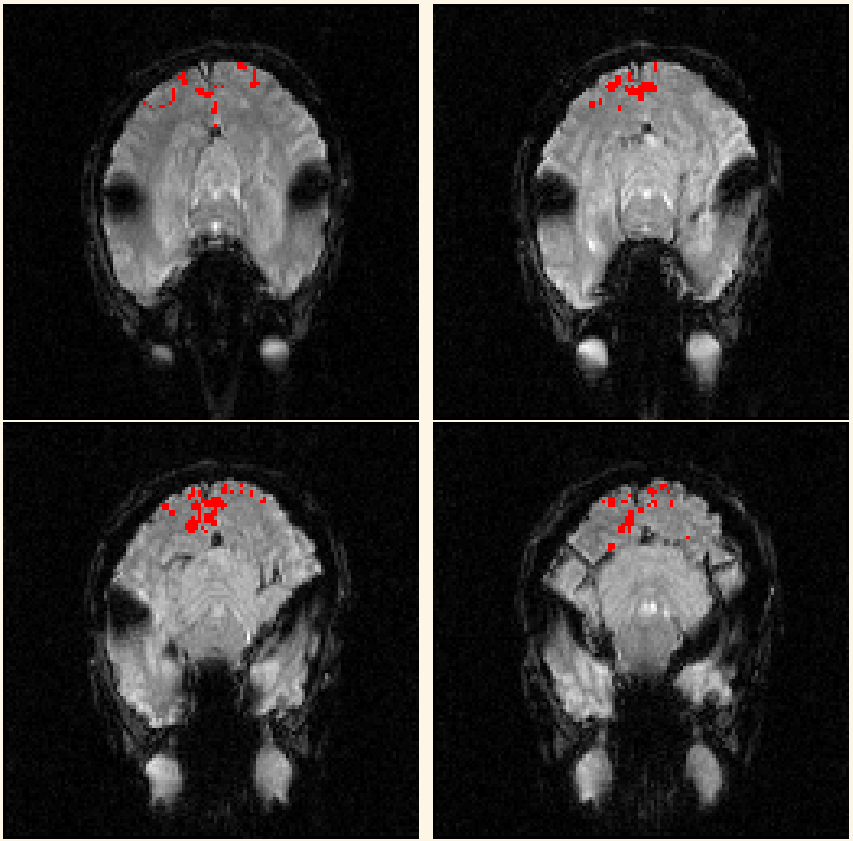


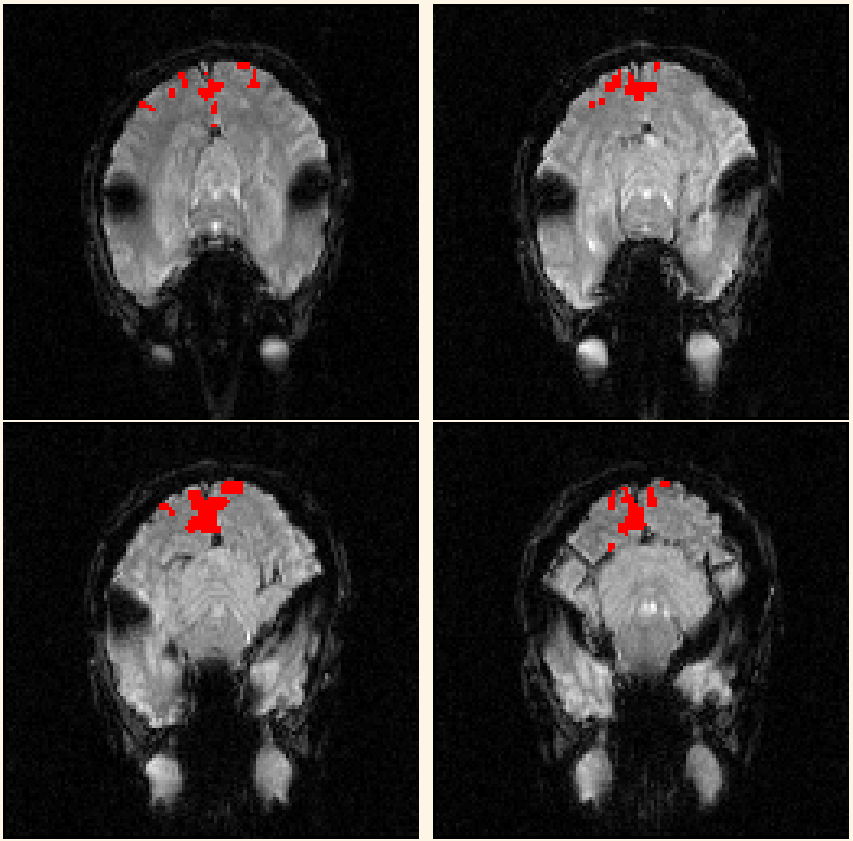
background (blue) and activated (red) time series

Visual stimulus: activation maps



Activation maps obtained with a linear model

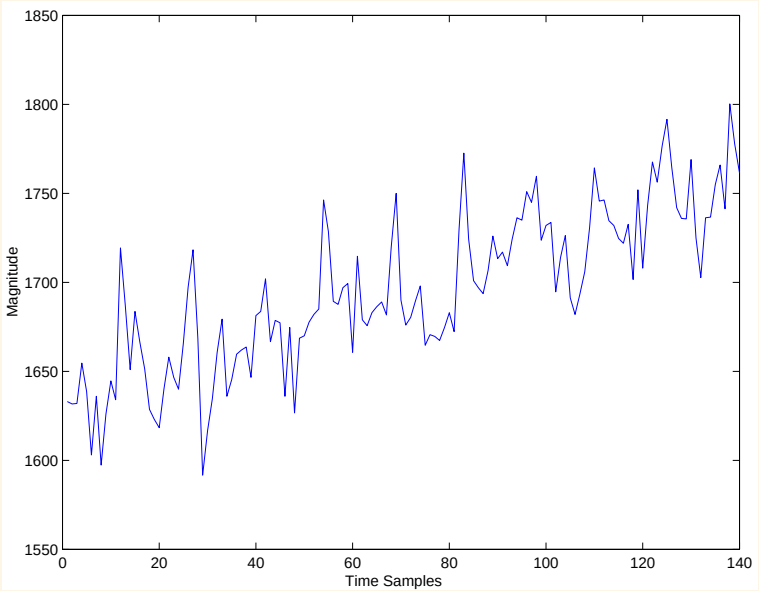
Visual stimulus: activation maps



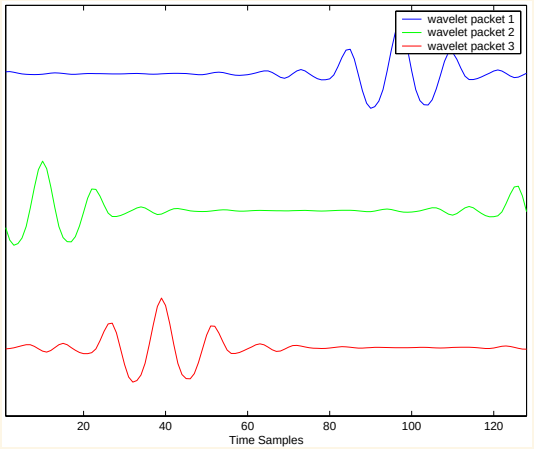
Activation maps obtained with our method

Experiments : in vivo data

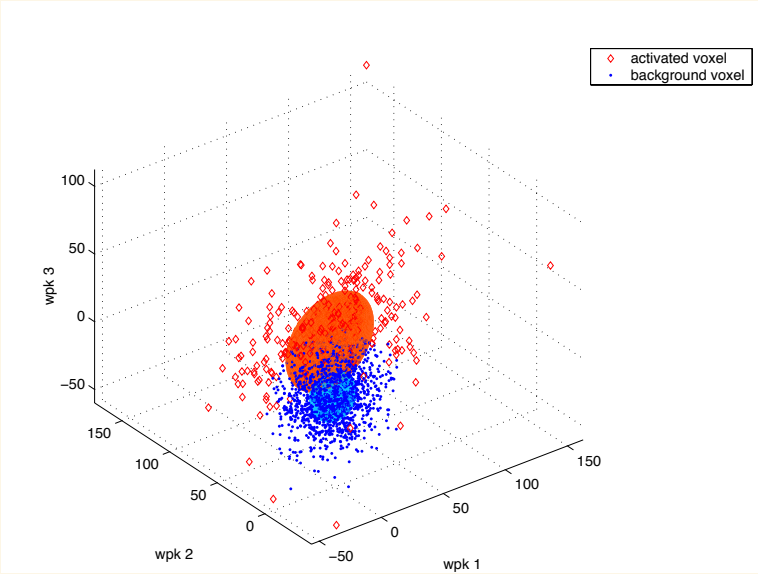
- visual-mental imagery : random presentation



Experiments : in vivo data

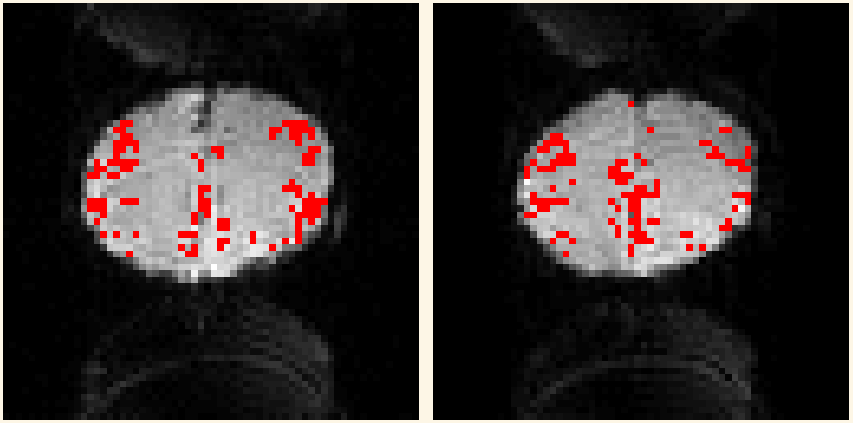


Projections (K=3)

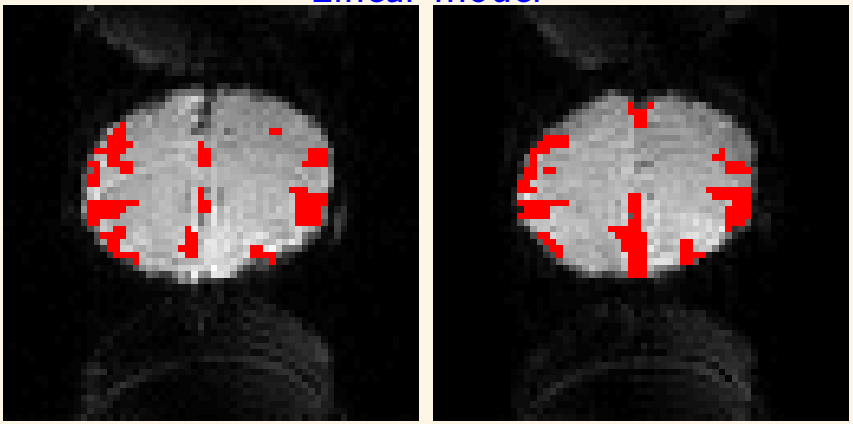


background (blue) and
activated (red) time series

Visual/Mental Imagery: activation maps



Linear model



Our method

Conclusion

- projection of the fMRI time series on a low dimensional subspace :
  - reveal the presence of activated time series.
  - probability distribution of the projections (coefficients) : finite mixture of multivariate Gaussian densities
  - estimate the parameters of the mixture, number of components, and interpret their physiological roles.
- spatial prior : activated voxels should be spatially clustered

Acknowledgment

- fMRI dataset collected by Dr. Jody Tanabe,

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