Multi-subject Bayesian joint detection & estimation in fMRI

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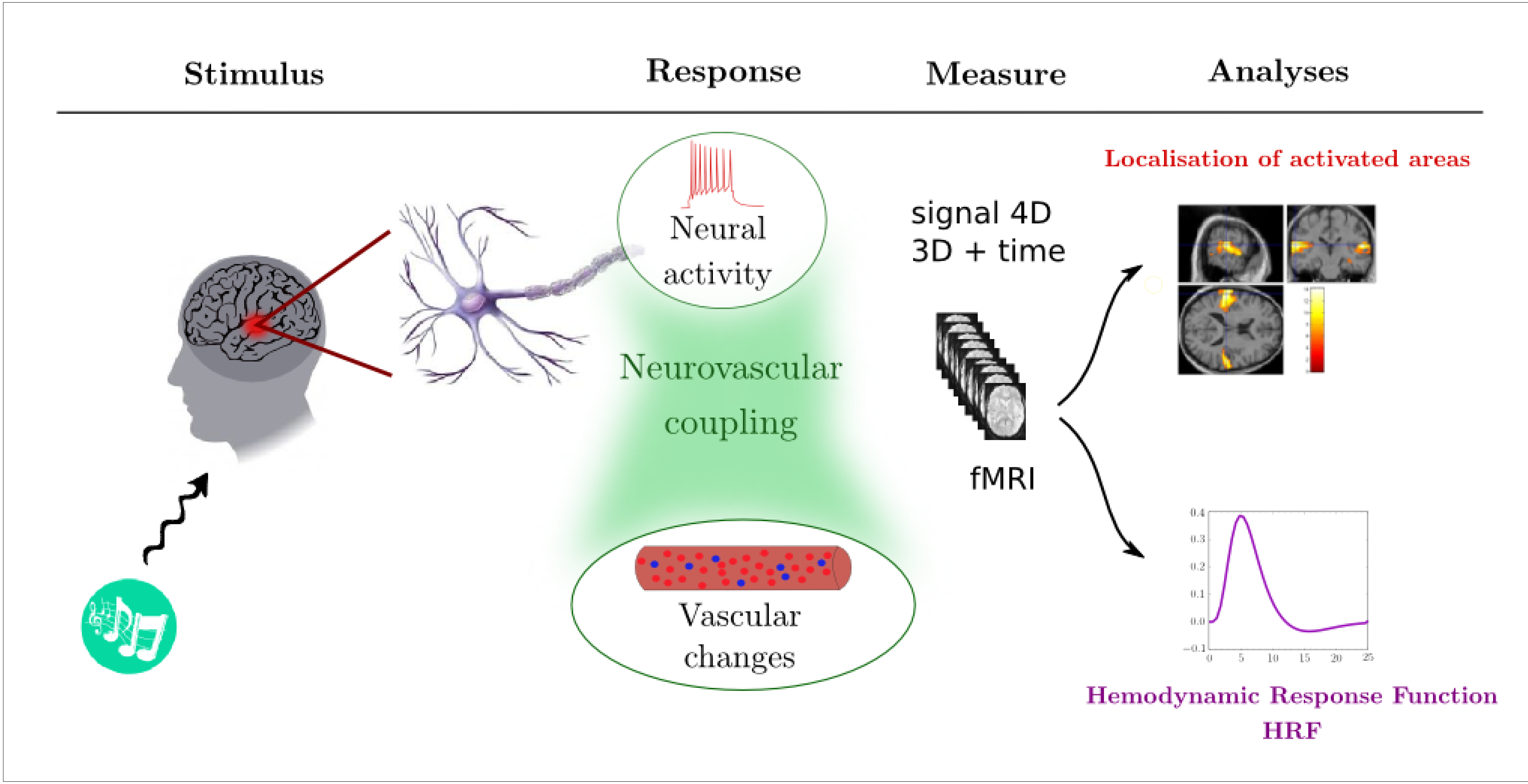
University of Warwick

Brain Activity Measurement in fMRI



fMRI: BOLD effect

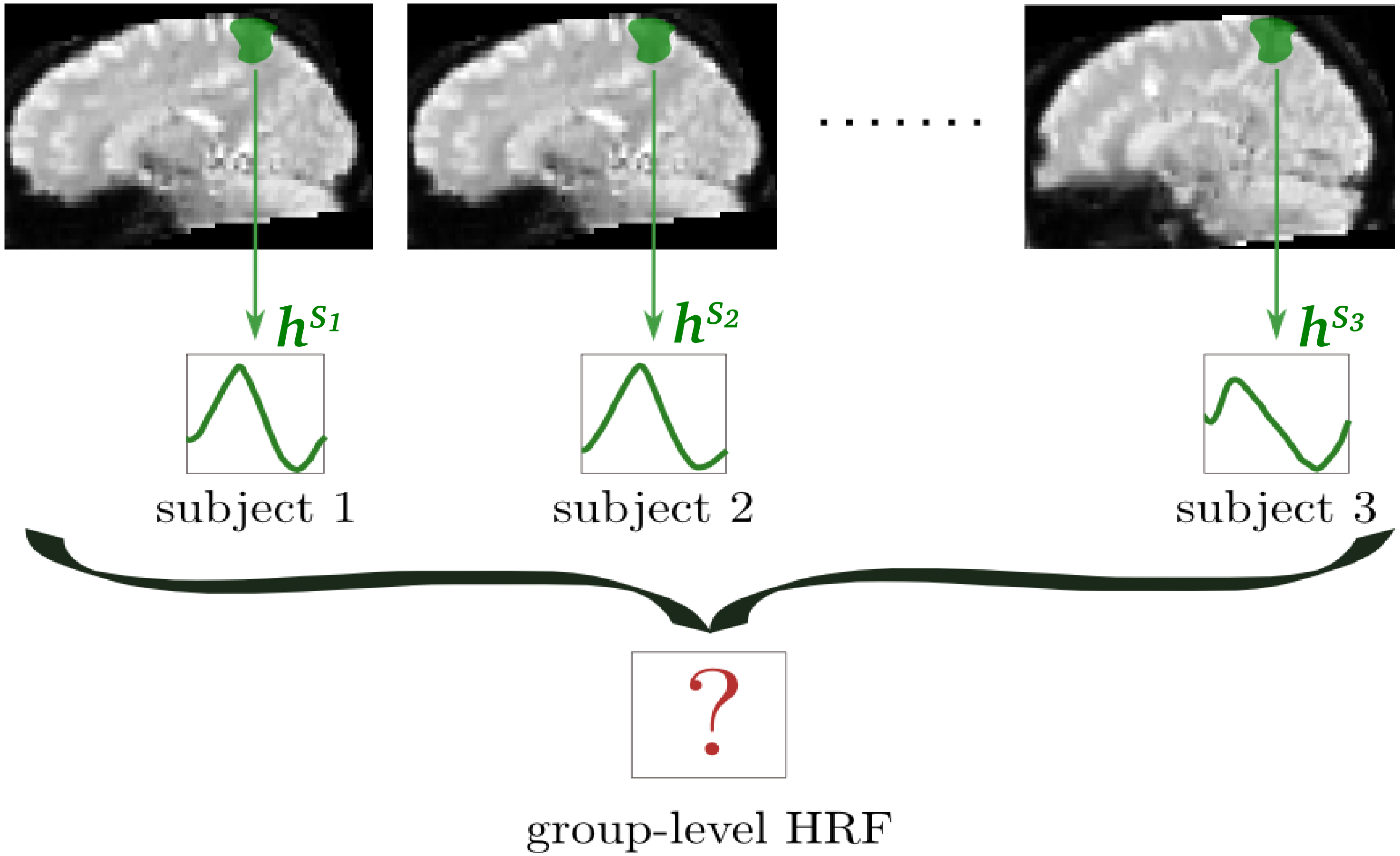
Blood oxygenation level dependent signal

[Ogawa et al., *PNAS* 1990]

Motivations

→ **HRF shape estimation at the group-level:**

- Group comparisons (patients vs controls, young vs elderly subjects)
- Effect of treatment (Placebo vs Drug) in clinical trials
- Compare hemodynamic variability sources (region, condition, ...)



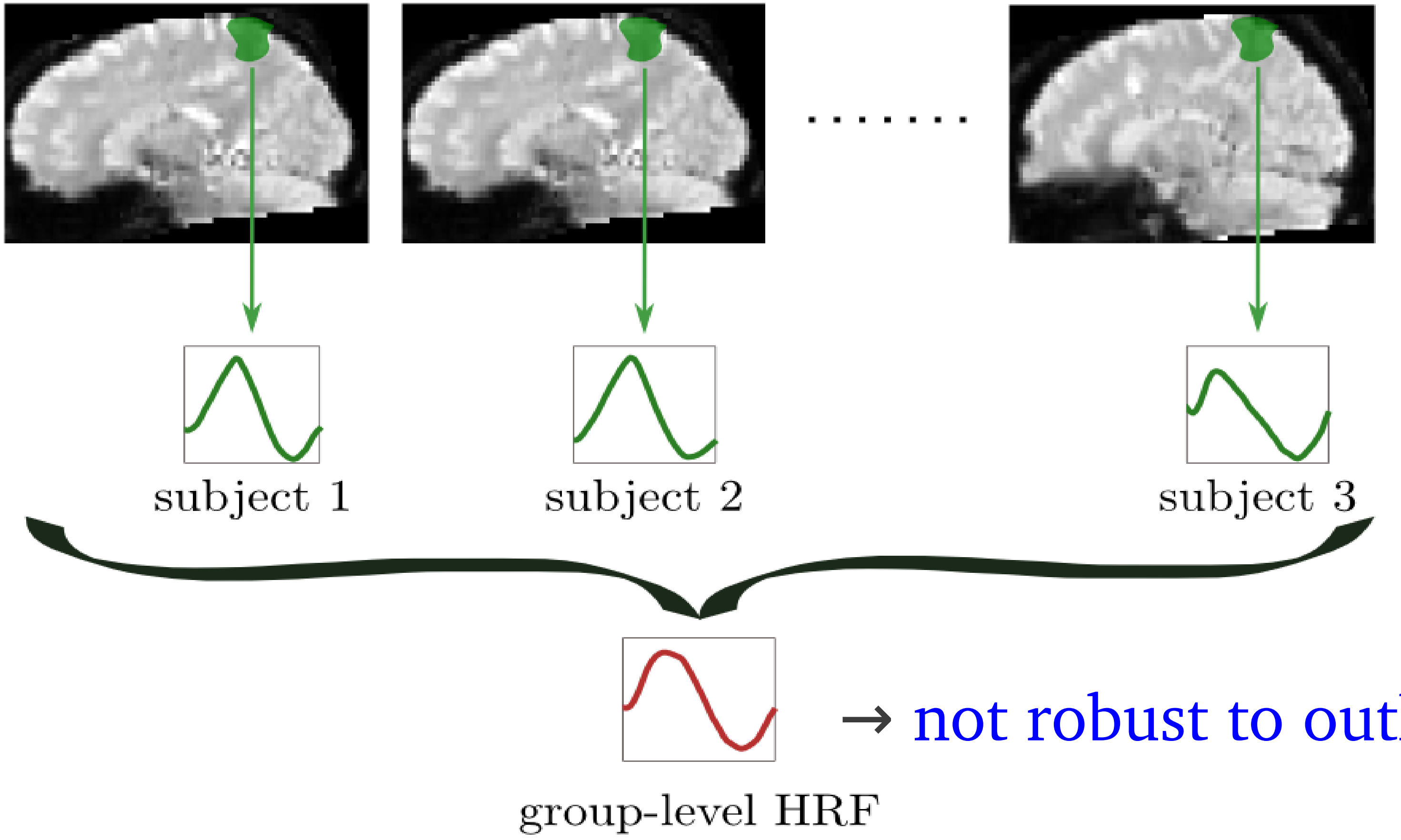
Outline

- Current approaches
- Bayesian joint detection & estimation (JDE) formalism
- Multi-subject extension
- Results
- Conclusions

Group-level HRF estimation

Classical approach:

1/ Perform subject-by-subject estimation
2/ Average over subjects

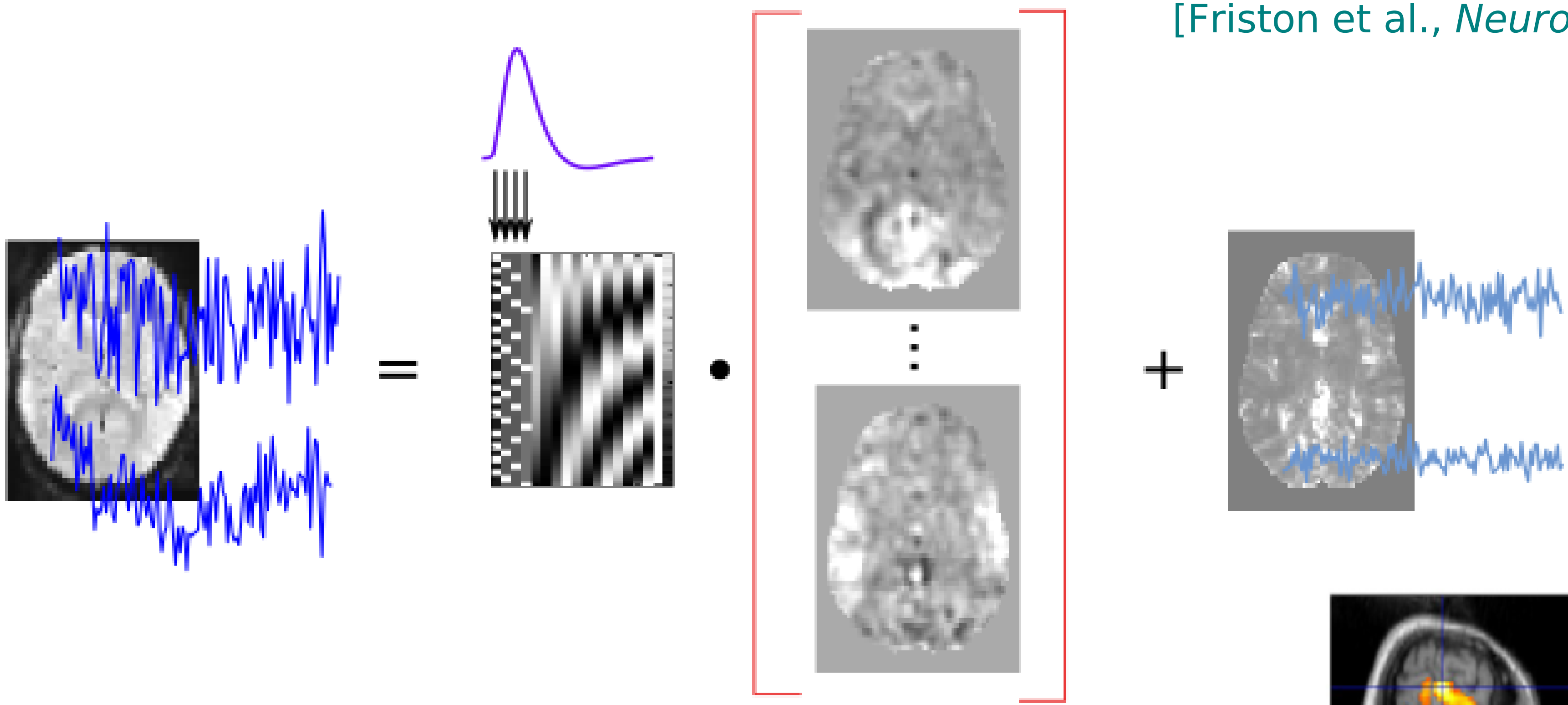


→ not robust to outliers

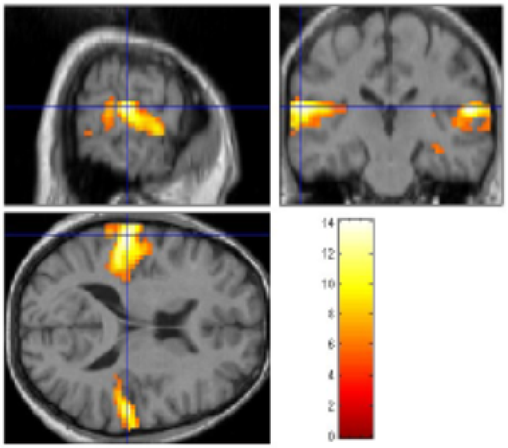
Standard brain mapping analysis

General Linear Model: $\boldsymbol{y}_j = \boldsymbol{X}\boldsymbol{\beta}_j + \boldsymbol{b}_j$

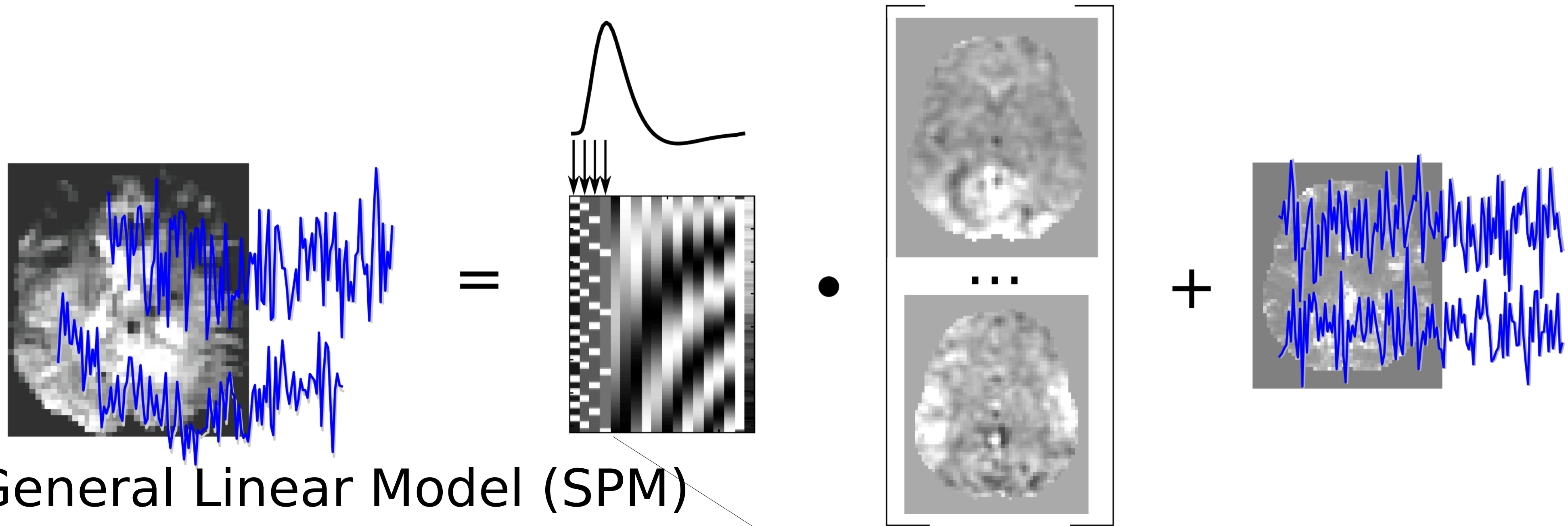
[Friston et al., *NeuroImage* 1995]



Effects of interest



HRF recovery within the GLM

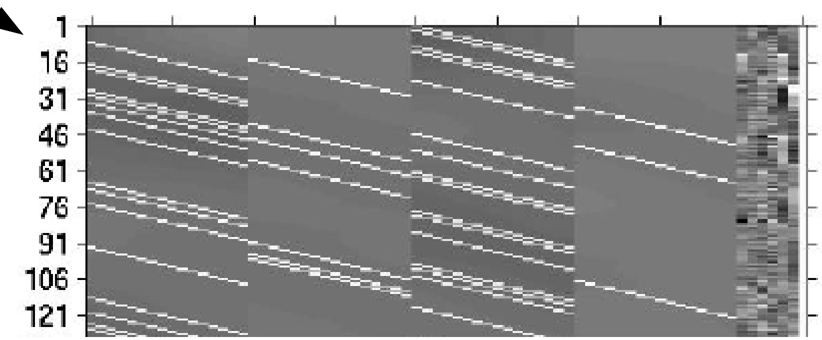


General Linear Model (SPM)

[Frackowiak et al., *Hum. Brain Func. 1997*]

- HRF variability :
  - Within-subject, between-subjects, between-groups (children, patients, ...)
    [Miezin et al., *NeuroImage* 2000;
    D'Esposito et al, *NeuroImage* 2003;
    Handwerker et al, *NeuroImage* 2004]

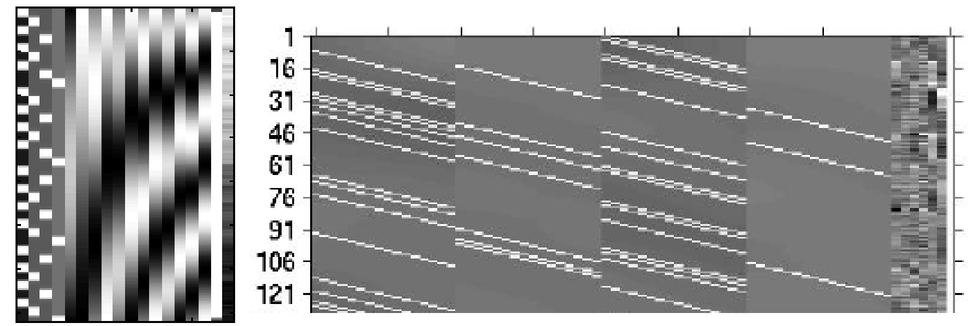
Finite Impulse Response (FIR)

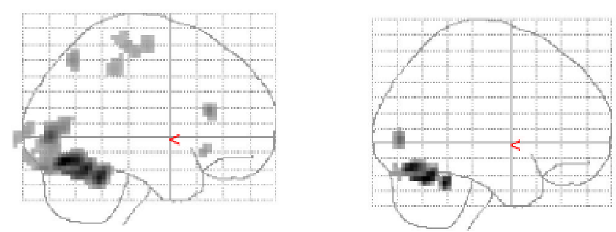


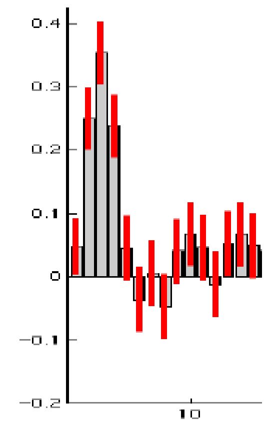
[Henson et al., *Hum. Brain Func.* - Chap. 10]

HRF recovery within the GLM

- Limits of the FIR model:
  - Synchronous paradigms
  - Putative loss of sensitivity
  - Lack of robustness





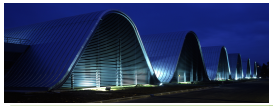


[Henson et al., *Hum. Brain Func.* - Chap. 10]

- Interplay between detection and estimation

➡ **Joint** detection and estimation (JDE)

[Makni et al., *IEEE TSP* 2005, *NeuroImage* 2008]



Group-level HRF estimation

Multi-subject inference:

- Semi-parametric *univariate* estimation framework

$$h^s_{j,m}(t) = A^s_{j,m}.h^G_{j,m}\left(\frac{t + D^s_{j,m}}{W^s_{j,m}}\right)$$

[Zhang et al., *NeuroImage* 2013]

- Semi-parametric joint Detection-Estimation *univariate* framework [Degras & Lindquist, *NeuroImage* 2014]

- Non-parametric Bayesian JDE *multivariate* framework

[Badillo et al, *IEEE PRNI* 2014]

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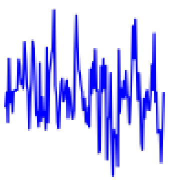
Forward Modeling of fMRI Time Series

[Makni et al., *NeuroImage* 2008]
[Vincent et al., *IEEE TMI* 2010]

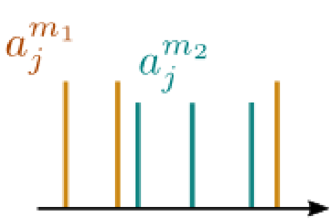
Binary onsets matrix

$$\boldsymbol{y}_j = \sum_{m=1}^{M} a_j^m \boldsymbol{X}^m \boldsymbol{h}_\gamma + \underbrace{\boldsymbol{P}\,\boldsymbol{\ell}_j}_{drift} + \underbrace{\boldsymbol{b}_j}_{noise}$$

[Voxel j
condition $m \in [\![1; M]\!]$



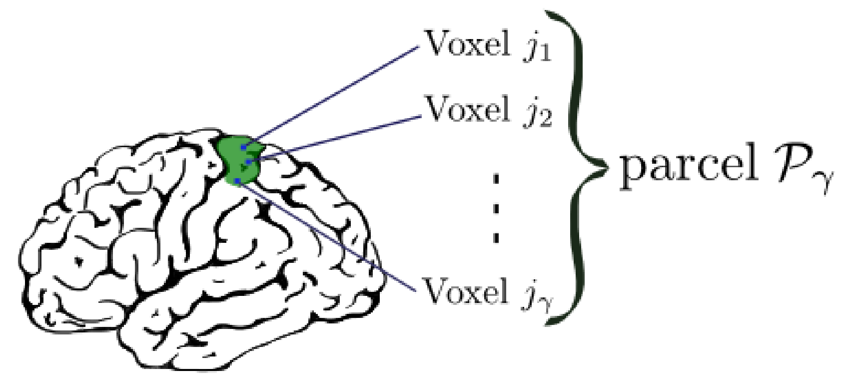
Activation detection
Response amplitudes



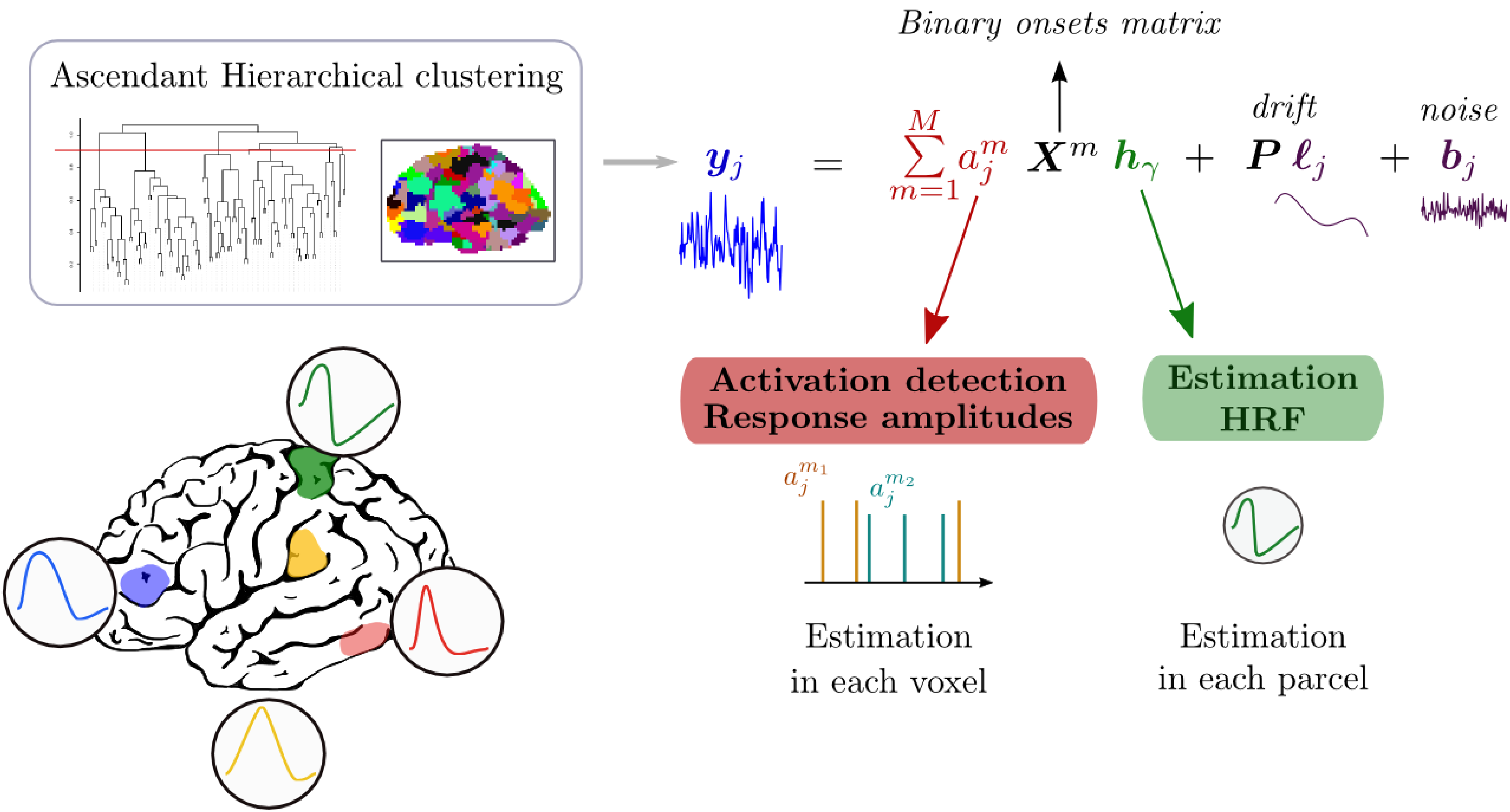
Estimation
in each voxel

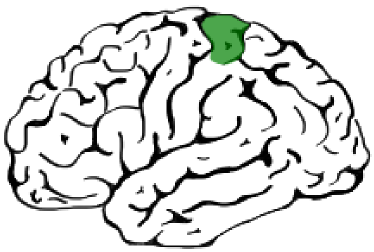
Estimation
HRF

Estimation
in each parcel

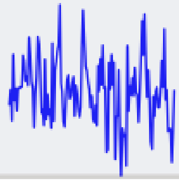


Whole Brain Analysis





$$\boldsymbol{y}_j = \sum_{m=1}^{M} \boxed{a_j^m} \bullet \boldsymbol{X}^m \boxed{\boldsymbol{h}_\gamma} + \boldsymbol{P}\,\boldsymbol{\ell}_j + \boldsymbol{b}_j$$



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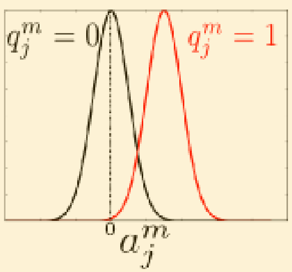
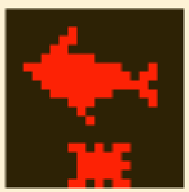
LIKELIHOOD

Spatial Mixture Models

Gaussian Mixture Model





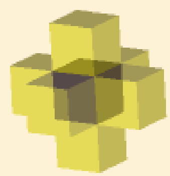
$$(a_j^m | q_j^m = i) \sim \mathcal{N}(\mu_i^m, \sigma_i^{m^2})$$

$$\boldsymbol{\theta}^m = \{\beta^m, v_0^m, \mu_1^m, v_1^m\}$$

Ising field

3D

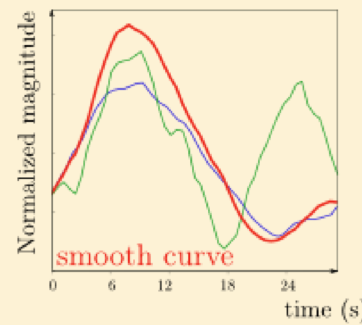
neighbourhood: 6-connexity



$$Pr(\boldsymbol{q}^m | \beta^m) = \frac{\beta^m \sum_{j \sim k} w_{j,k} I(q_j^m = q_k^m)}{Z(\beta_m)}$$

Smoothing constraint

$$\boldsymbol{h} \sim \mathcal{N}(0, \sigma_h^2 \boldsymbol{R})$$



$$\theta_{\boldsymbol{h}} = \sigma_{\boldsymbol{h}}^2$$

White noise

$$\boldsymbol{b}_j \sim \mathcal{N}(0, \sigma_j^2)$$

$$\theta_{0,j} = \sigma_j^2$$

or

AR(1)

$$\boldsymbol{b}_j \sim \mathcal{N}(0, \sigma_j^2 \Lambda^{-1})$$

$$\theta_{0,j} = [\sigma_j^2, \rho_j]$$

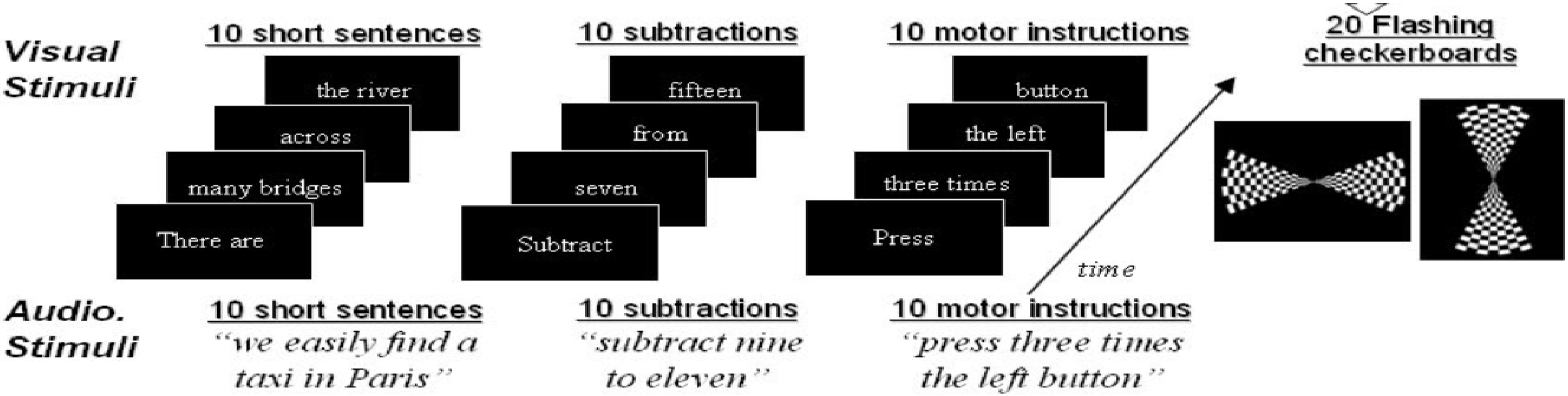
JOINT *A POSTERIORI* LAW

$$p(\boldsymbol{h}_\gamma, \boldsymbol{A}, \boldsymbol{L}, \boldsymbol{\Theta} | \boldsymbol{Y}) \propto p(\boldsymbol{Y}, \boldsymbol{h}_\gamma, \boldsymbol{A}, \boldsymbol{L}, \boldsymbol{\theta}_0)\, p(\boldsymbol{A} | \boldsymbol{\theta}_{\boldsymbol{A}})\, p(\boldsymbol{h}_\gamma v_{\boldsymbol{h}_\gamma}) p(\boldsymbol{L} | v_\ell)\, p(\boldsymbol{\theta}_0)\, p(\boldsymbol{\theta}_{\boldsymbol{A}})\, p(v_{\boldsymbol{h}_\gamma}, v_\ell)$$

- Hybrid MH-Gibbs sampling
- Posterior mean estimates
- Faster VEM alternative

[Vincent et al., *IEEE TMI* 2010]
Risser et al., *JSPS* 2011]
[Chaari et al., *IEEE TMI* 2013]

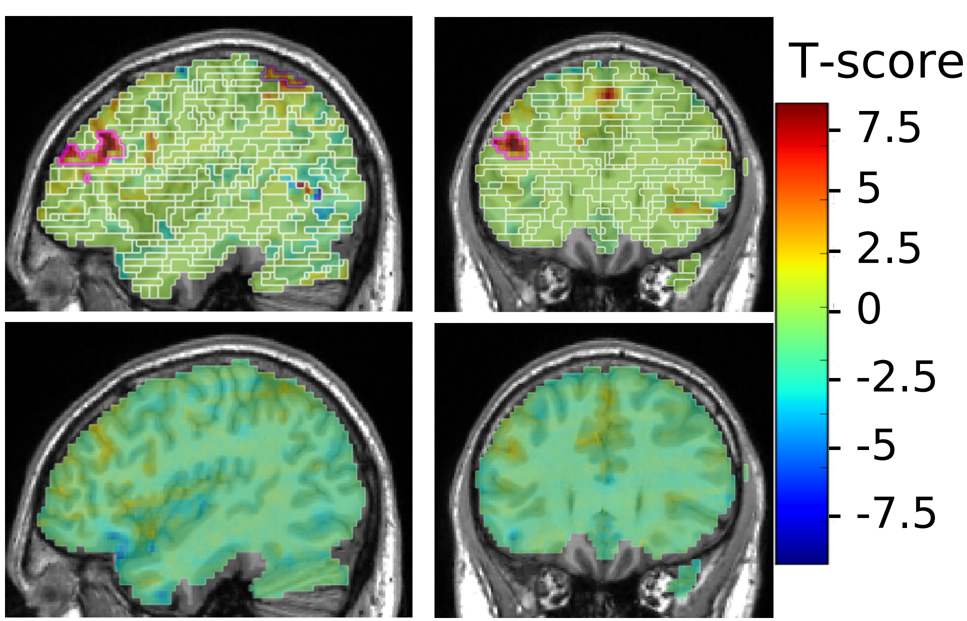
Within-subject Results



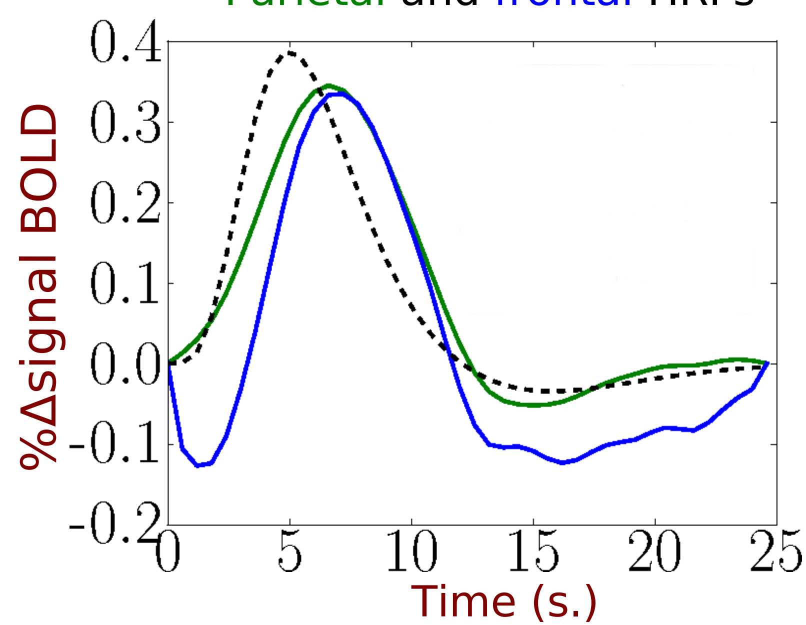
Computation – *Sentence* contrast

JDE
MCMC & VEM

GLM



Parietal and frontal HRFs



[Chaari et al, *IEEE TMI* 2013; Badillo et al, *NeuroImage* 2013]

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Multi-Subject JDE Forward Model

data *drift* *noise*

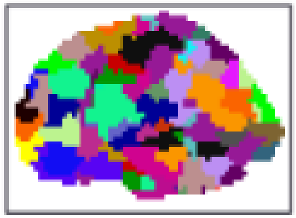
$$\boldsymbol{y}_j^s = \sum_{m=1}^{M} a_j^{m,s} \boldsymbol{X}^m \boldsymbol{h}_\gamma^s + \boldsymbol{P}\boldsymbol{\ell}_j^s + \boldsymbol{b}_j^s$$

voxel j
conditions m=1:M
subject s=1:S

$a_j^{m,s}$

$\boldsymbol{h}_\gamma^s$

subject-specific



Group parcellation

MS-JDE Supplementary Prior

data · *drift* · *noise*

$$\boldsymbol{y}_j^s = \sum_{m=1}^{M} a_j^{m,s} \boldsymbol{X}^m \boldsymbol{h}_\gamma^s + \boldsymbol{P}\boldsymbol{\ell}_j^s + \boldsymbol{b}_j^s$$

$$\left.\begin{array}{l} a_j^{m,s} \\ \boldsymbol{h}_\gamma^s \end{array}\right\}$$ **subject-specific**

HRF Priors:

- $\boldsymbol{h}_\gamma^s \sim \mathcal{N}(\boldsymbol{h}_\gamma^G, v_{\boldsymbol{h}_\gamma^s} \boldsymbol{R})$ $\quad \boldsymbol{R} = (\boldsymbol{D}_2^T \boldsymbol{D}_2)^{-1}$
- $\boldsymbol{h}_\gamma^G \sim \mathcal{N}(0, v_{\boldsymbol{h}_\gamma^G} \boldsymbol{\Sigma}_G)$

$$\boldsymbol{\Sigma}_G = (\boldsymbol{D}_2^T \boldsymbol{D}_2)^{-1}$$

MS-JDE Supplementary Prior

data *drift* *noise*

$$\boldsymbol{y}_j^s = \sum_{m=1}^{M} a_j^{m,s} \boldsymbol{X}^m \boldsymbol{h}_\gamma^s + \boldsymbol{P}\boldsymbol{\ell}_j^s + \boldsymbol{b}_j^s$$

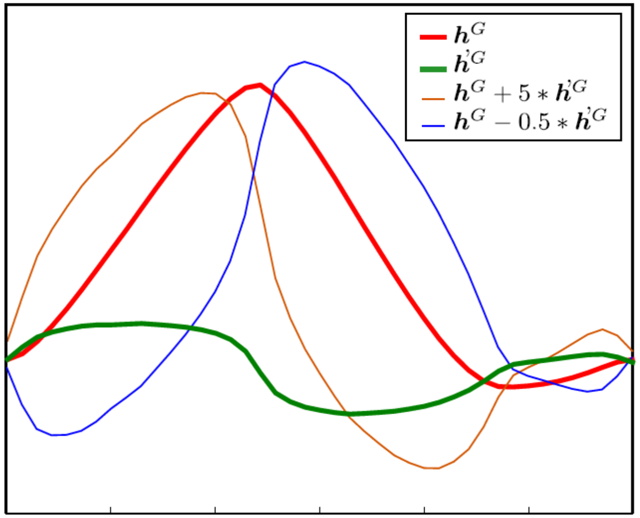
$$\left.\begin{array}{l} a_j^{m,s} \\ \boldsymbol{h}_\gamma^s \end{array}\right\}$$ **subject-specific**

HRF Priors:

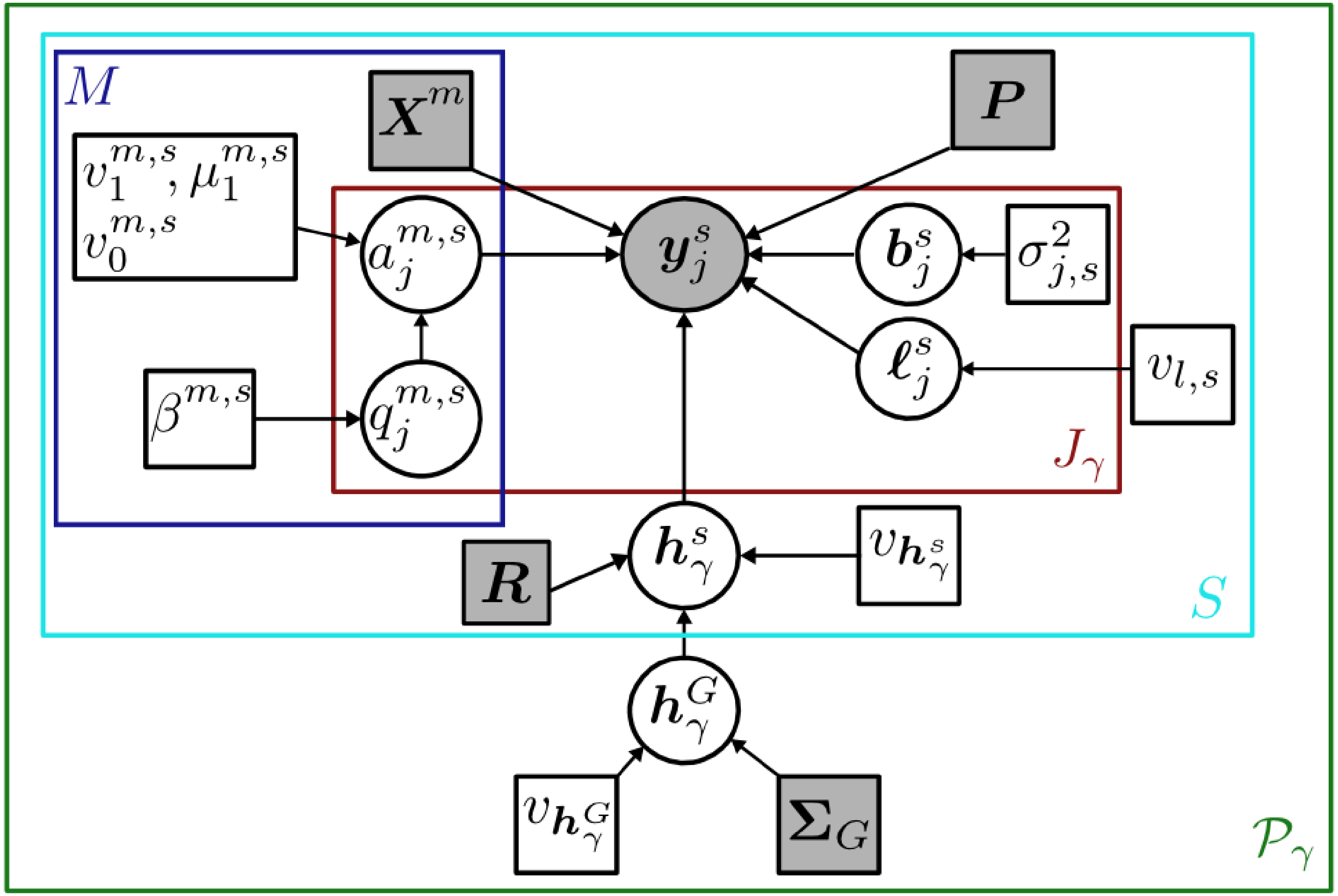
- **Potential subject-specific shift of the peak**

$$\boldsymbol{h}_\gamma^s \sim \mathcal{N}(\boldsymbol{h}_\gamma^G + \alpha_s \boldsymbol{h}'^G_\gamma, v_{\boldsymbol{h}_\gamma^s} \boldsymbol{R})$$

can be generalized to other population distribution (eg, mixtures, Student)



MS-JDE Directed Acyclic Graph



MCMC implementation: see [Badillo et al, IEEE PRNI 2014] for details

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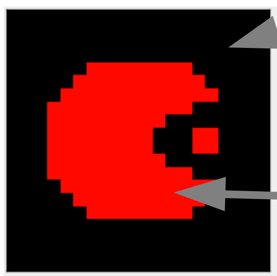
Simulated Data

→ **Fast event-related paradigm**

TR=1s; N=300 scans, SOA~3.6s, 1run

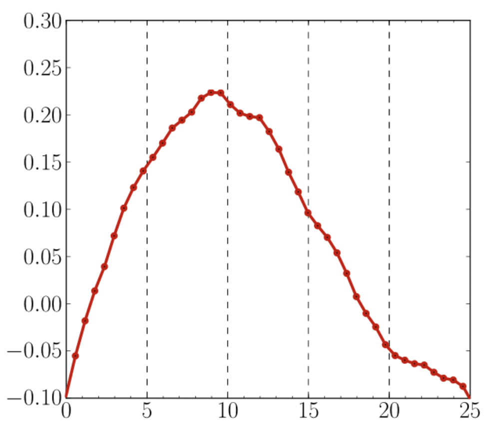
→ **Simulation of activated areas**



q=0

q=1

→ **Group-level HRF**



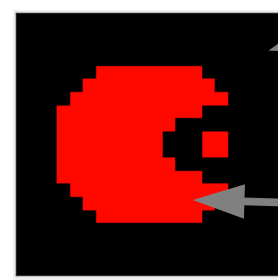
→ **Subject-level HRF**

$$\boldsymbol{h}_\gamma^s \sim \mathcal{N}(\boldsymbol{h}_\gamma^G, v_{\boldsymbol{h}_\gamma^s} \boldsymbol{R})$$

Simulation of 4D data:

$$\boldsymbol{y}_j^s = \sum_{m=1}^{M} a_j^{m,s} \boldsymbol{X}^m \boldsymbol{h}_\gamma^s + \boldsymbol{P} \boldsymbol{\ell}_j^s + \boldsymbol{b}_j^s$$

- 400 time points
- Response levels:

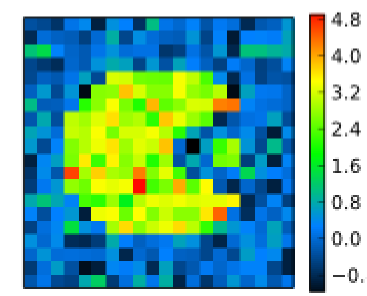


q=0

$a_j^{m,s} \sim \mathcal{N}(0, 0.25)$

q=1

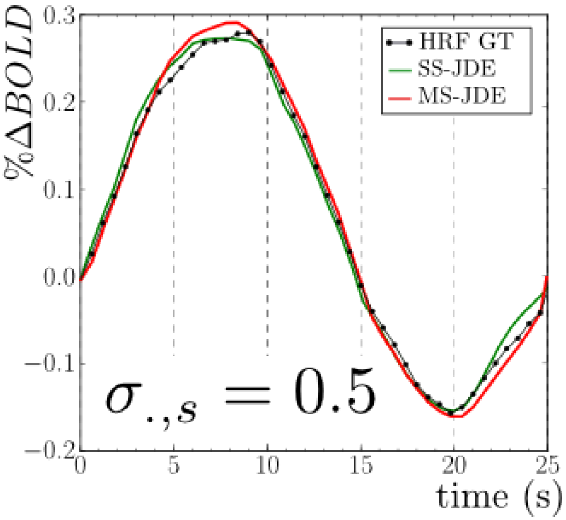
$a_j^{m,s} \sim \mathcal{N}(3.2, 0.25)$



- Drift: $\boldsymbol{\ell}_j^s \sim \mathcal{N}(0, 3.2\boldsymbol{I}_4)$
- Noise: $\boldsymbol{b}_j^s \sim \mathcal{N}(0, \sigma_{j,s}^2)$

Validation on simulations

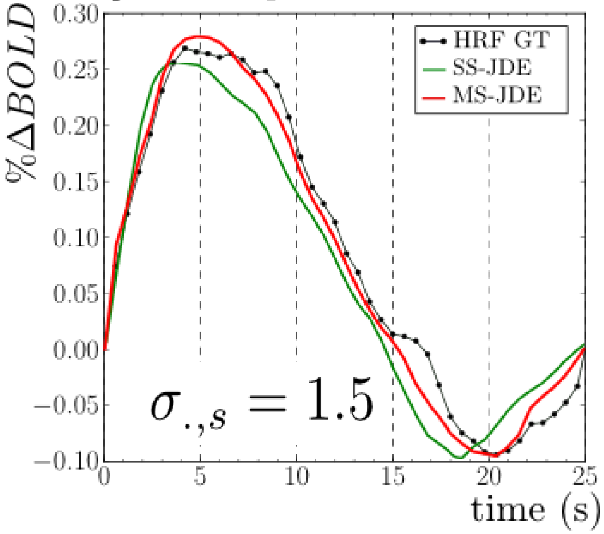
subject-specific HRF



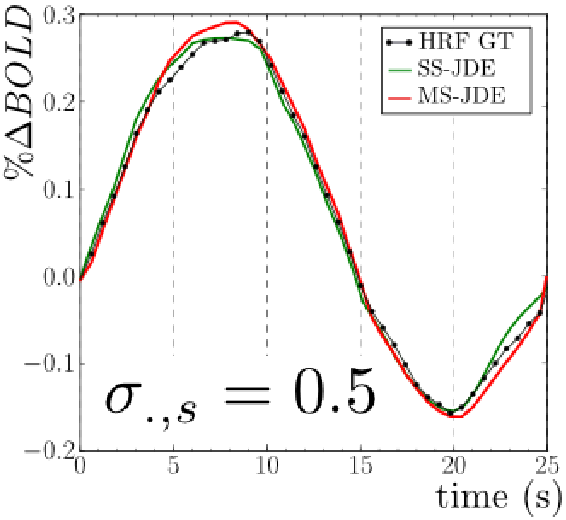
GT: Ground Truth
SS-JDE: Single-subject JDE
MS-JDE: Multi-subject JDE

Validation on simulations

subject-specific HRF



subject-specific HRF



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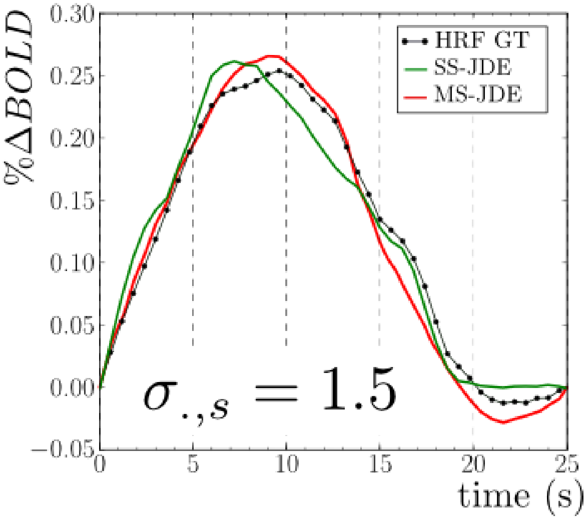

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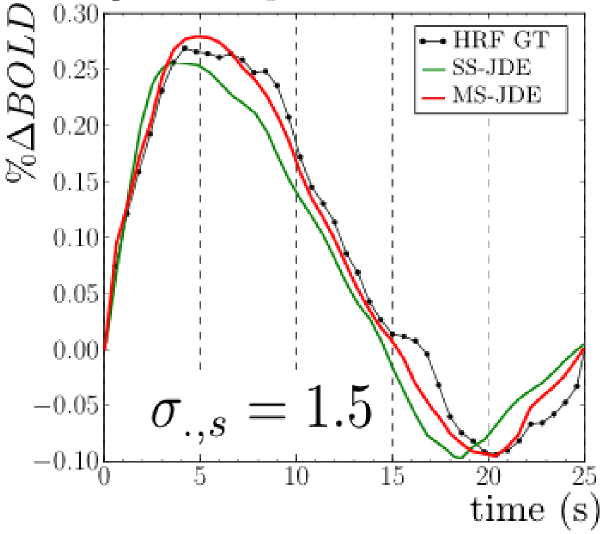
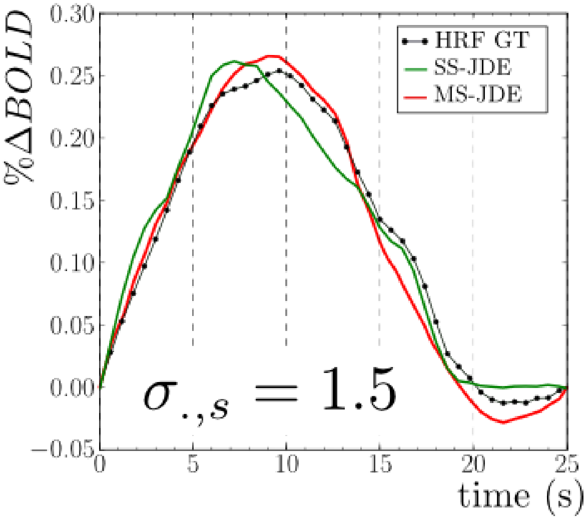
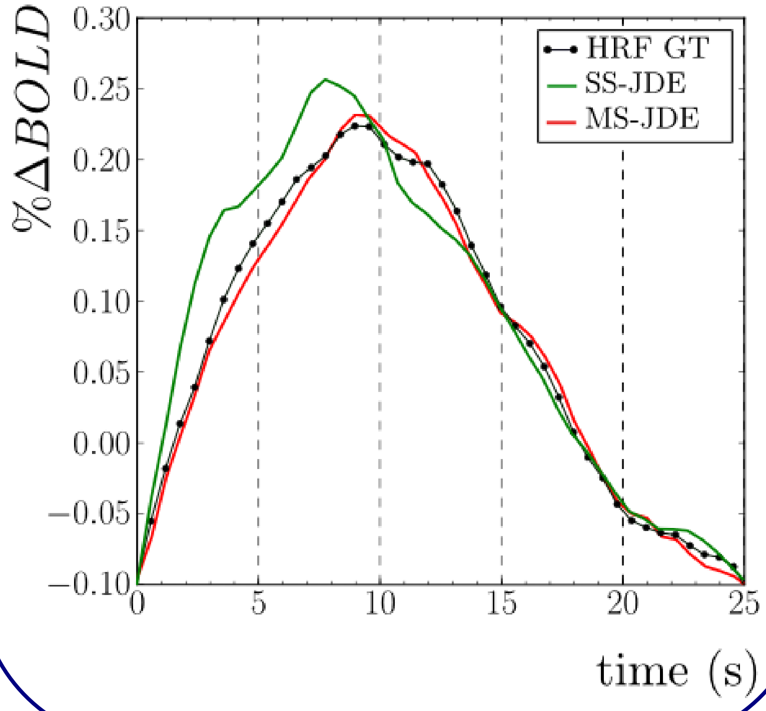


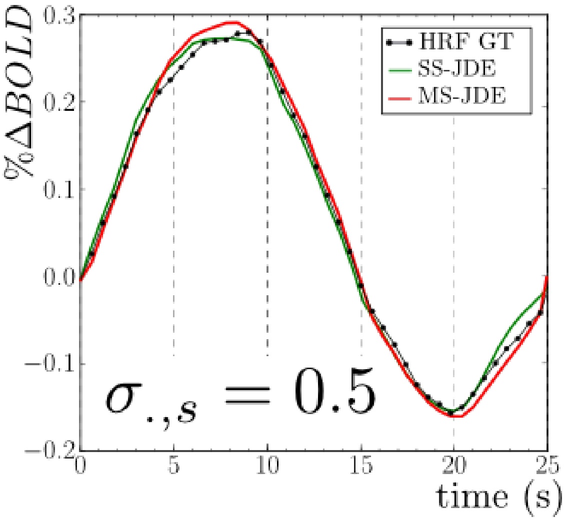
subject-specific HRF



group-level HRF



subject-specific HRF

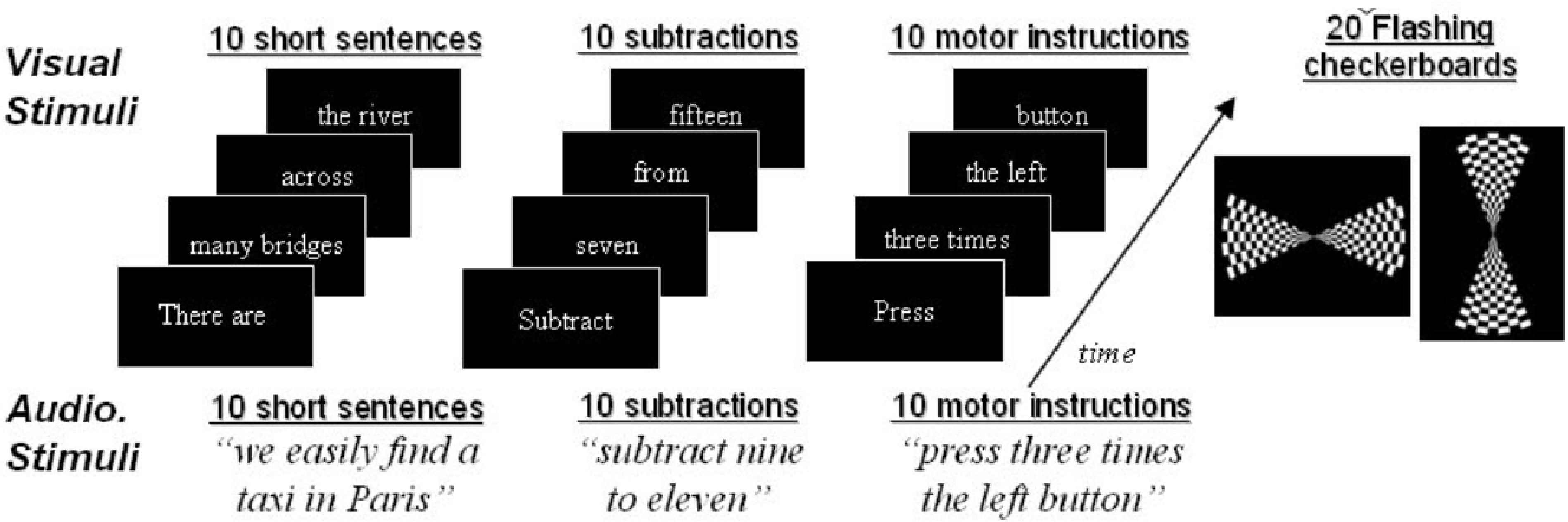


GT: Ground Truth
SS-JDE: Single-subject JDE
MS-JDE: Multi-subject JDE

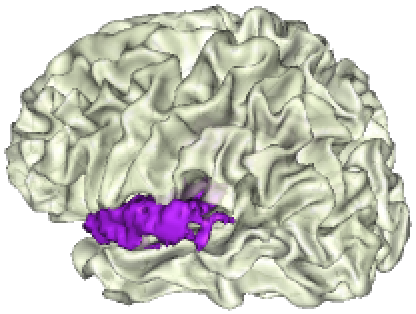
Localizer Dataset

- Fast event-related paradigm, 1 run, 400 scans, TR=1s, mband-EPI sequence (CMRR, Mineapolis), mb=3, no-PI, 3x3x3 mm^3, SOA~3.6 s

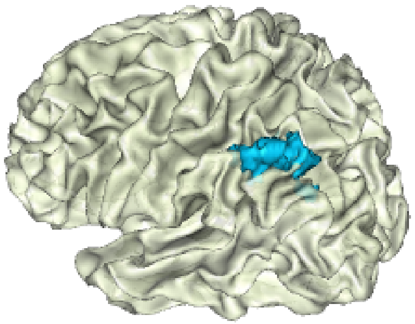
- 10 conditions, visual or auditory modality

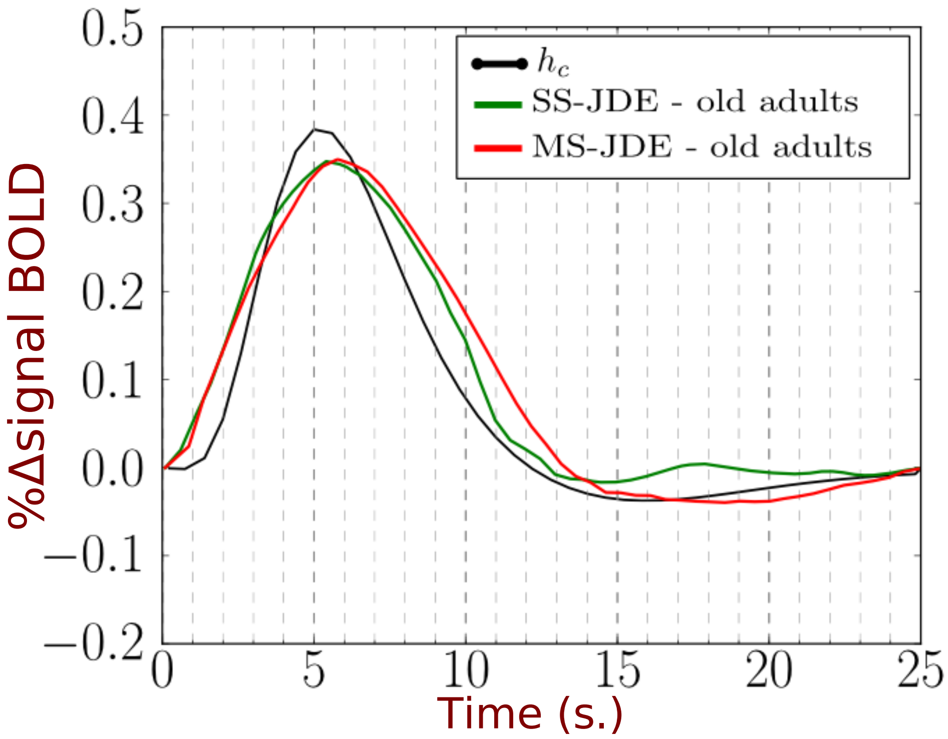


Results on Elderly Subjects



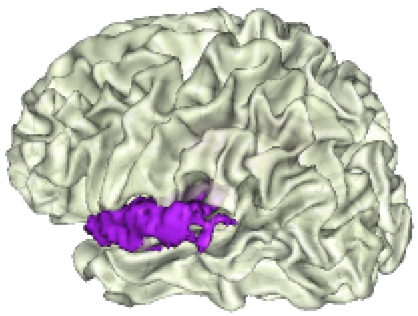
group-level HRF shape
15 elderly adults
(65 to 75 years)





elderly
- SS-JDE: TTP=6 s
  FWHM=7.2 s
- MS-JDE: TTP=5.8 s
  FWHM=7.6 s

Results on Elderly Subjects



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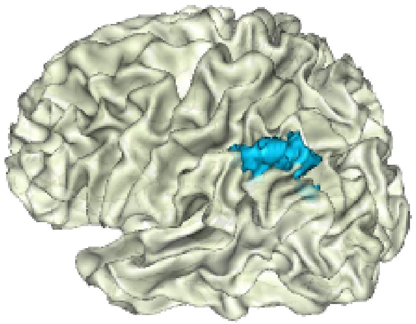
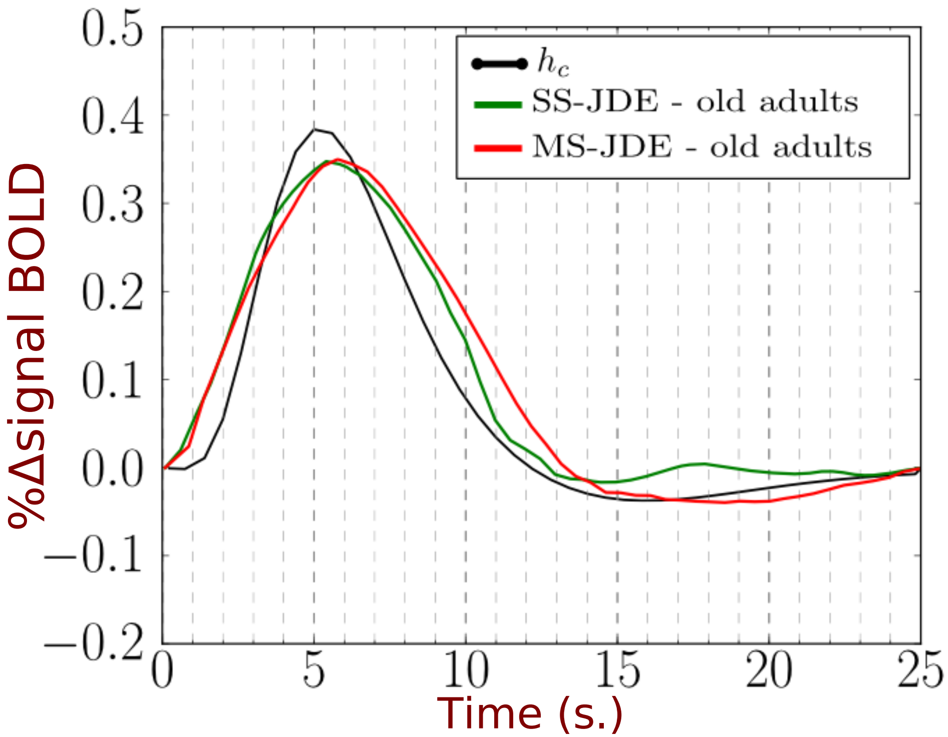
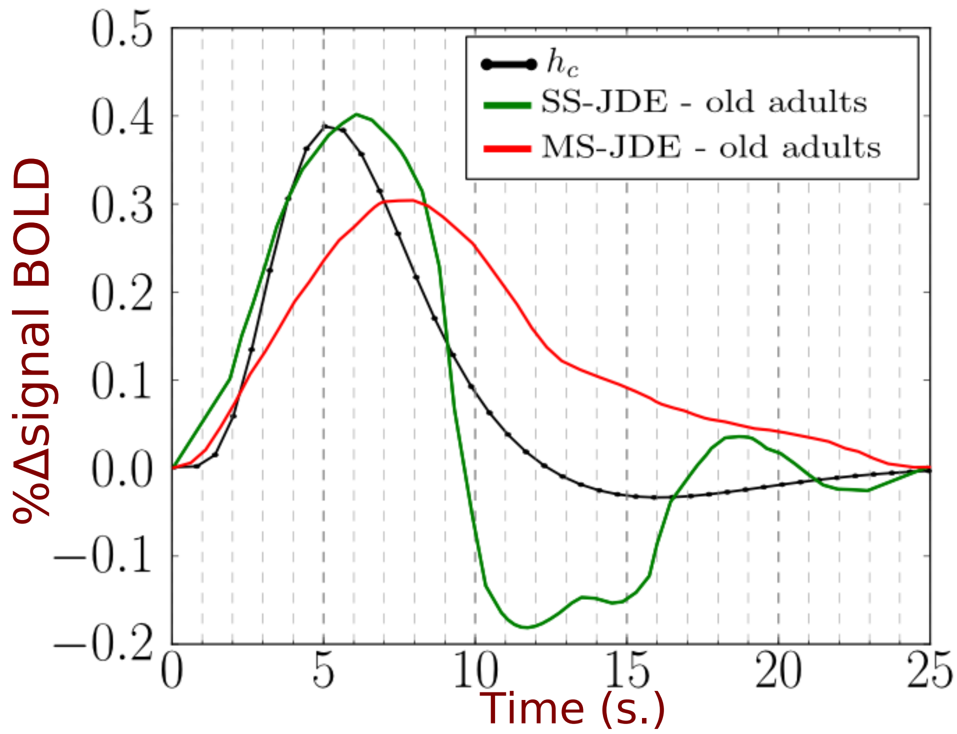


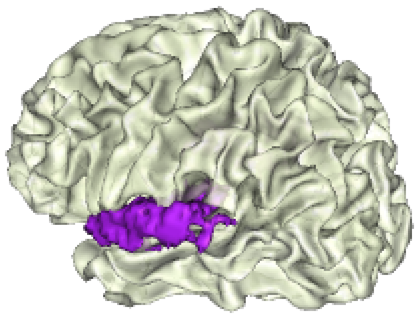




elderly
- SS-JDE: TTP=6 s, FWHM=7.2 s
- MS-JDE: TTP=5.8 s, FWHM=7.6 s

elderly
- SS-JDE: TTP=6 s, FWHM=6 s
- MS-JDE: TTP=7.5 s, FWHM=8.5 s

Results on Elderly Subjects



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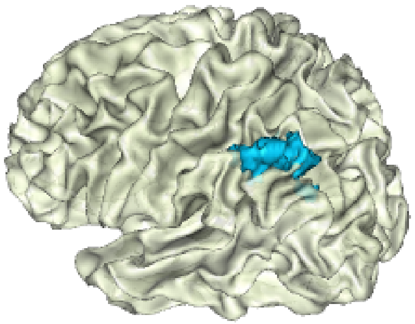
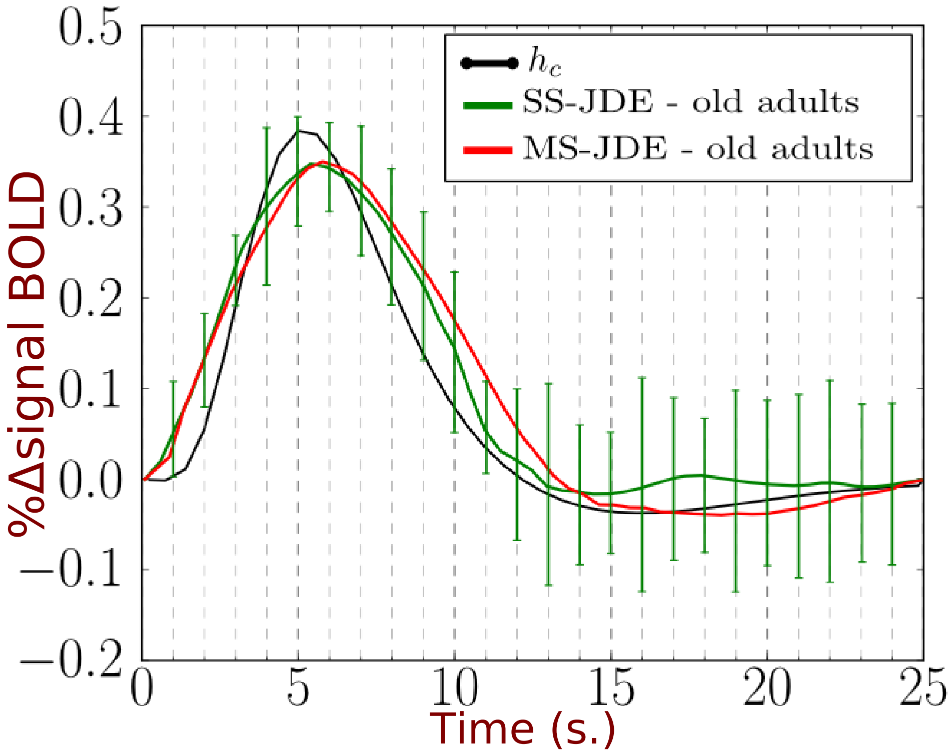
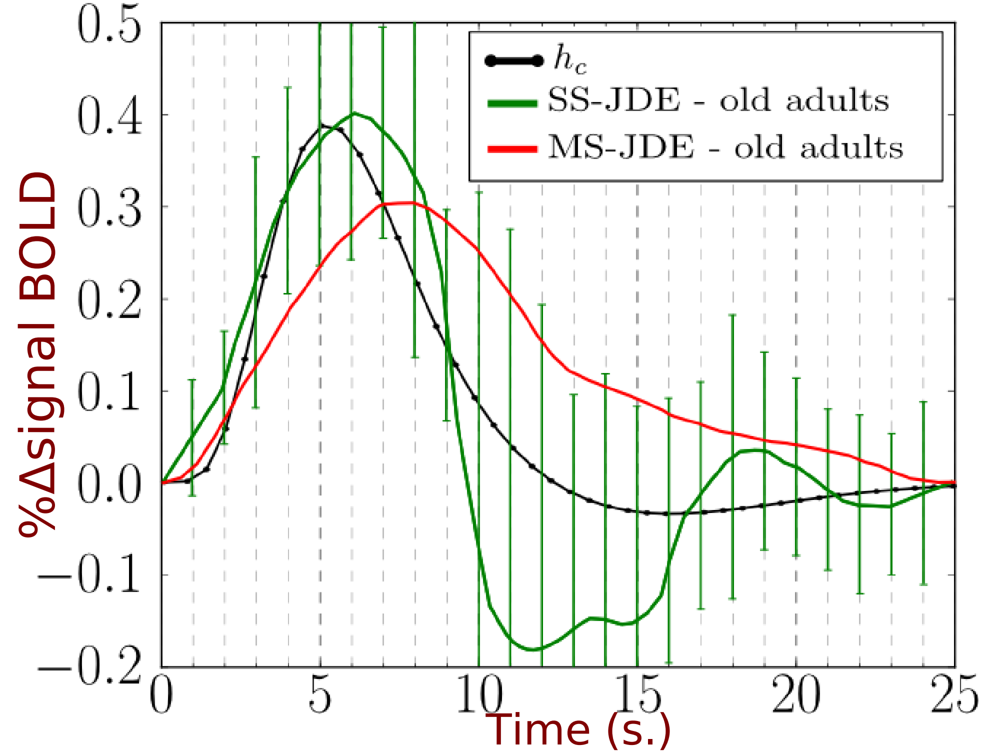
15 elderly adults
(65 to 75 years)

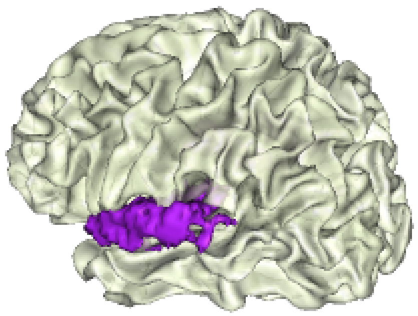






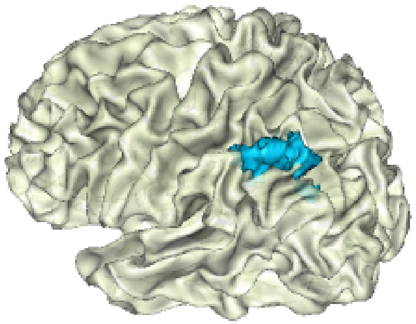
MS-JDE model captures inter-subject variability

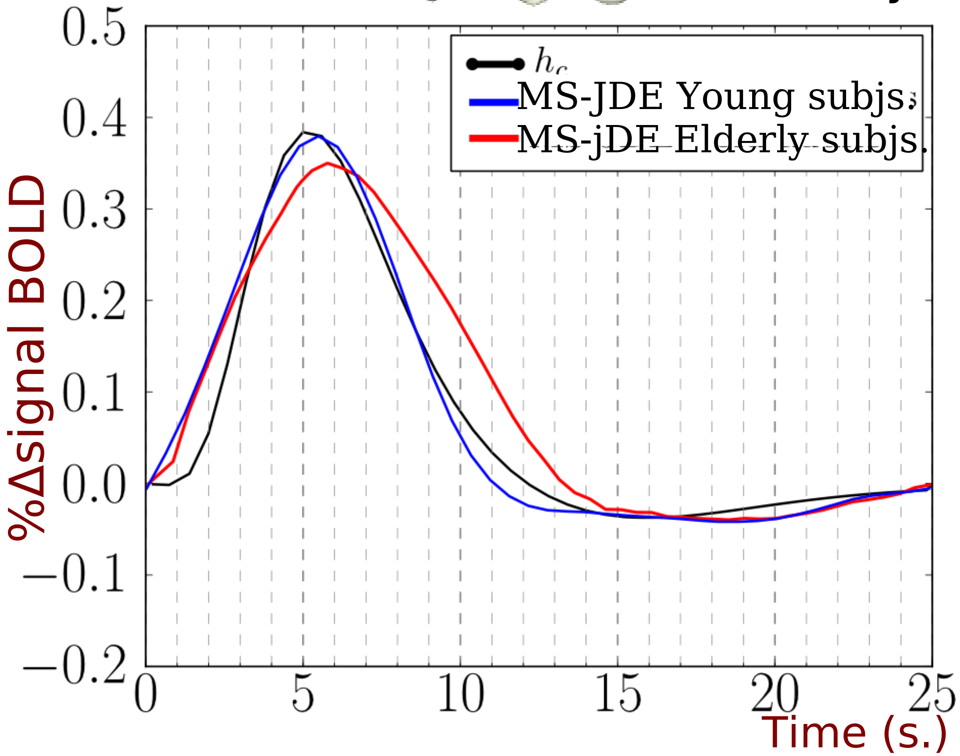
Group comparison

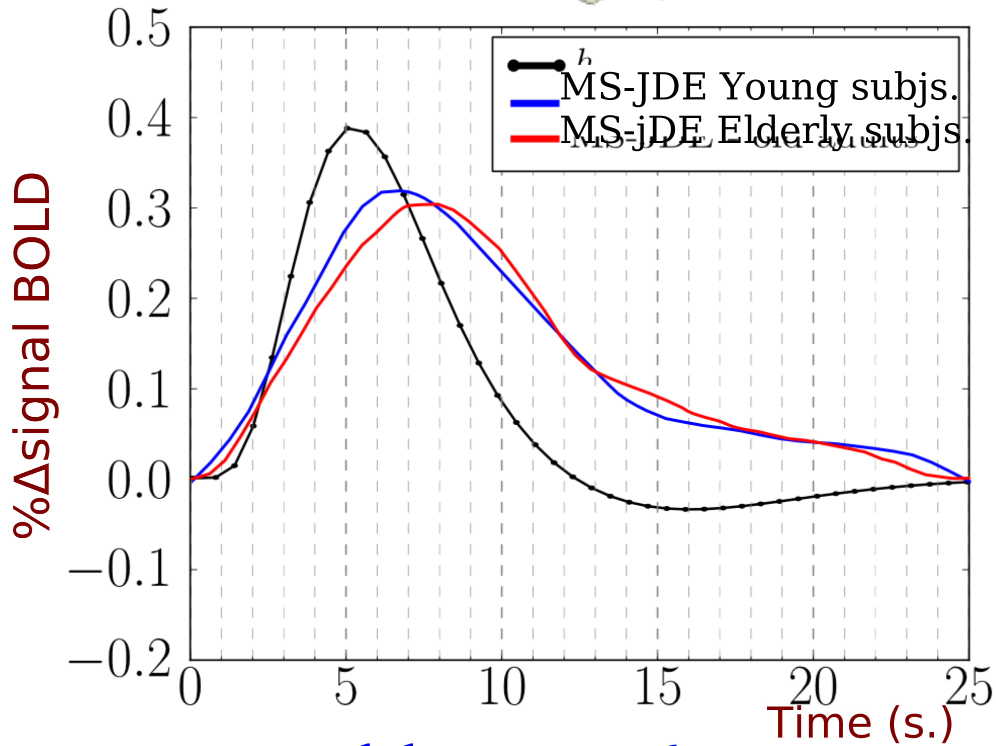


group-level HRF shapes

15 elderly adults vs 15 young adults







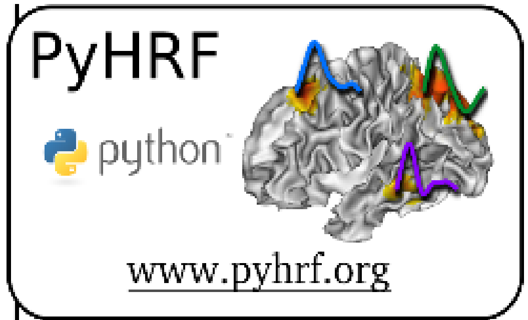
Young adults: **TTP=5.5 s**
FWHM=6 s
Elderly adults: **TTP=5.8 s**
FWHM=7.6 s

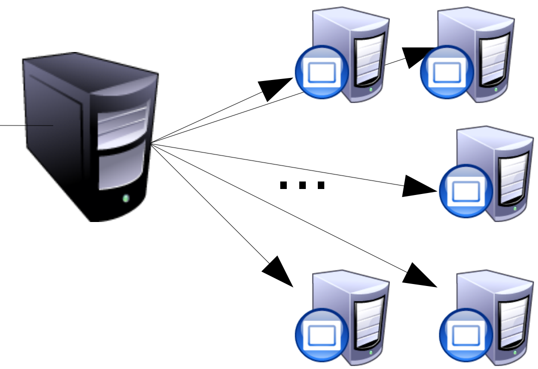
Young adults: **TTP=6.7 s**
FWHM=7.6 s
Elderly adults: **TTP=7.5 s**
FWHM=8.5 s

The PyHRF software

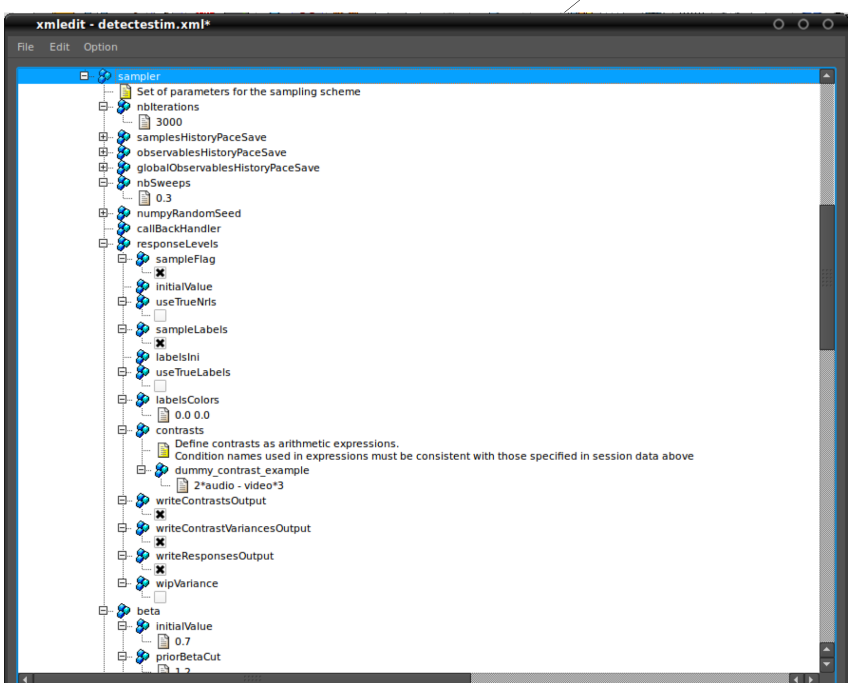
http://pyhrf.org

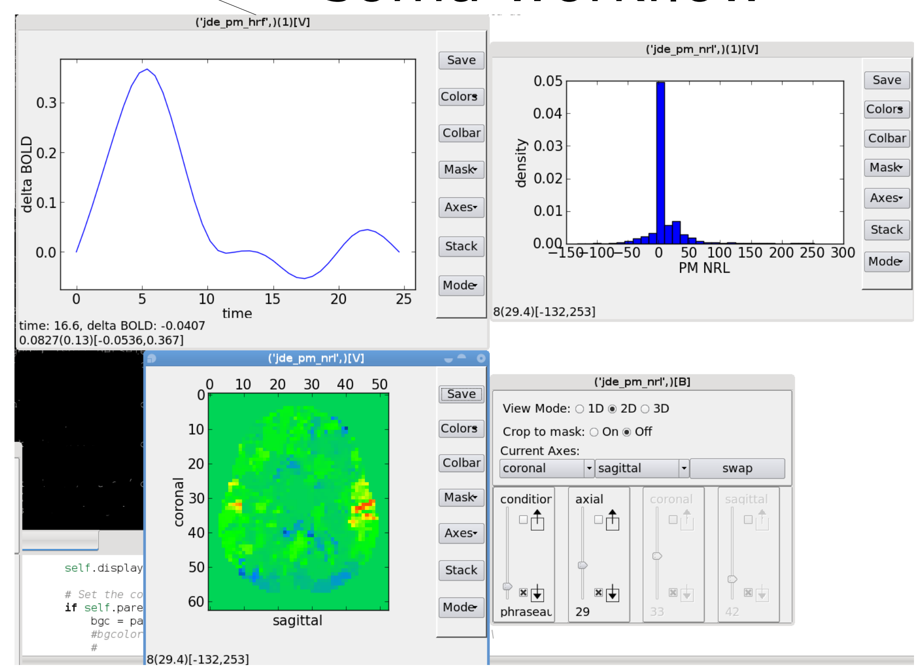
Nipy
Nibabel

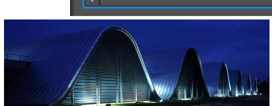




soma-workflow







XML parametrization

Visualization

Summary

- Multi-subject HRF estimation can be helpful for group comparison
- Joint detection & estimation is the right framework!
  - Neither necessarily Bayesian nor non-parametric HRF
  - But multivariate analysis of evoked activity is crucial
  - Main issue: multi-subject parcellation
- More complex random-effect models can be envisaged
- Computational bottleneck: parallelize all steps that you can!
- Perspectives :
  - Comparison with B-spline HRF decomposition
  - Multi-subject JPDE
  - Assess the relevance of hemodynamics characteristics as potential biomarkers in clinical trials (phMRI)