Preprocessing & denoising of fMRI data

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Plan

- Simple fMRI pre-processing pipeline in 2018
- Signal fluctuations or noise
- Motion related noise & denoising in GLM
- Denoising based on external physiological signals
- TAPAS Physio Toolbox
- Denoising based on PCA of noise regions signals
- Example of results
- Questions to be addressed
- Next step : Multi-Echo acquisitions
- Conclusion & references

Simple fMRI pre-processing pipeline (2018)

* Check of the data : quality, coregistration, …

* Fielmap computation → Voxel Displacements Map

* Realign & unwarp

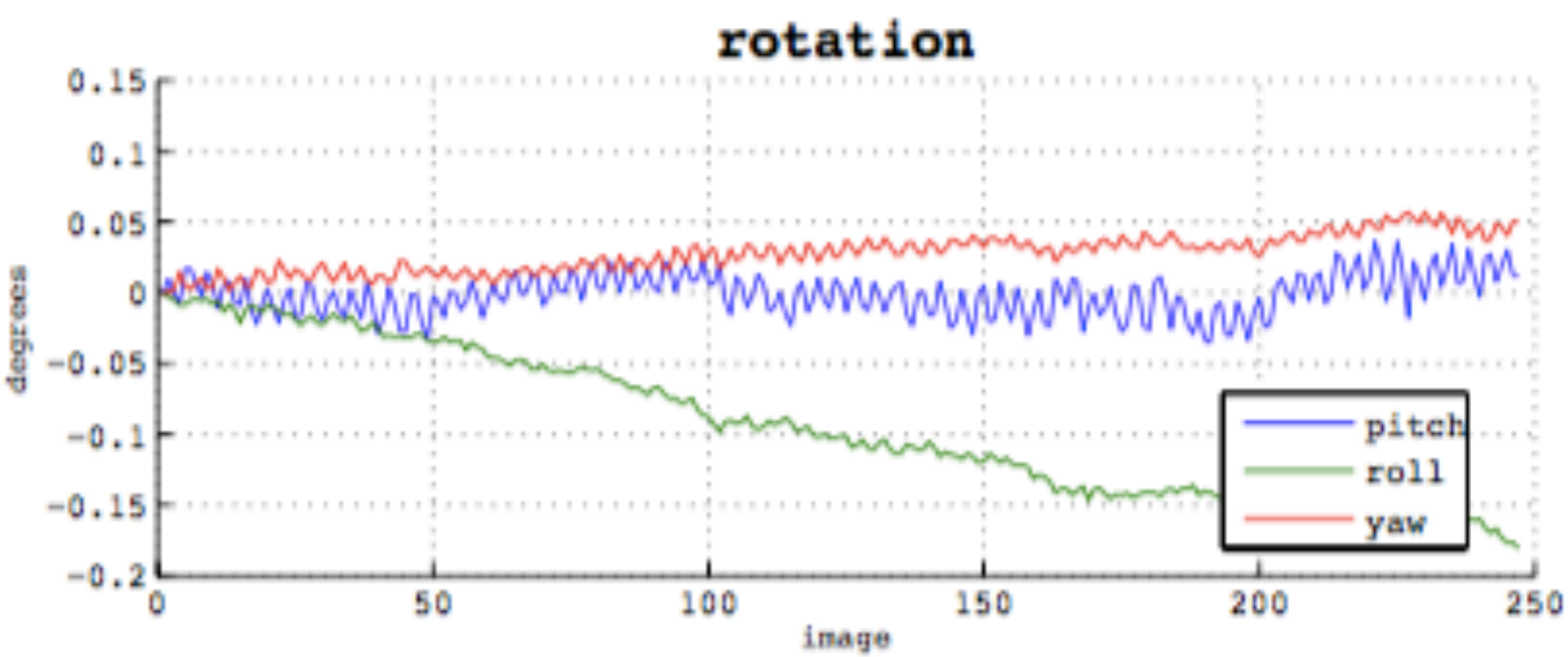
* Coregistration of anatomical data to functional data

* Spatial Normalisation to the MNI space (DARTEL)

* Spatial smoothing

Nota : the slice timing step is often skipped because of the interpolation problems and is no more really useful thanks to short TRs (≈ 1 sec)

Motion parameters estimates



→ Signal fluctuations or noise …

EPI Multi-bande sequences

→ Very short TR (≈ 1 sec)
→ Small voxels (≈ 2.5 mm iso)
→ High SNR (multi-channel receiving coils)

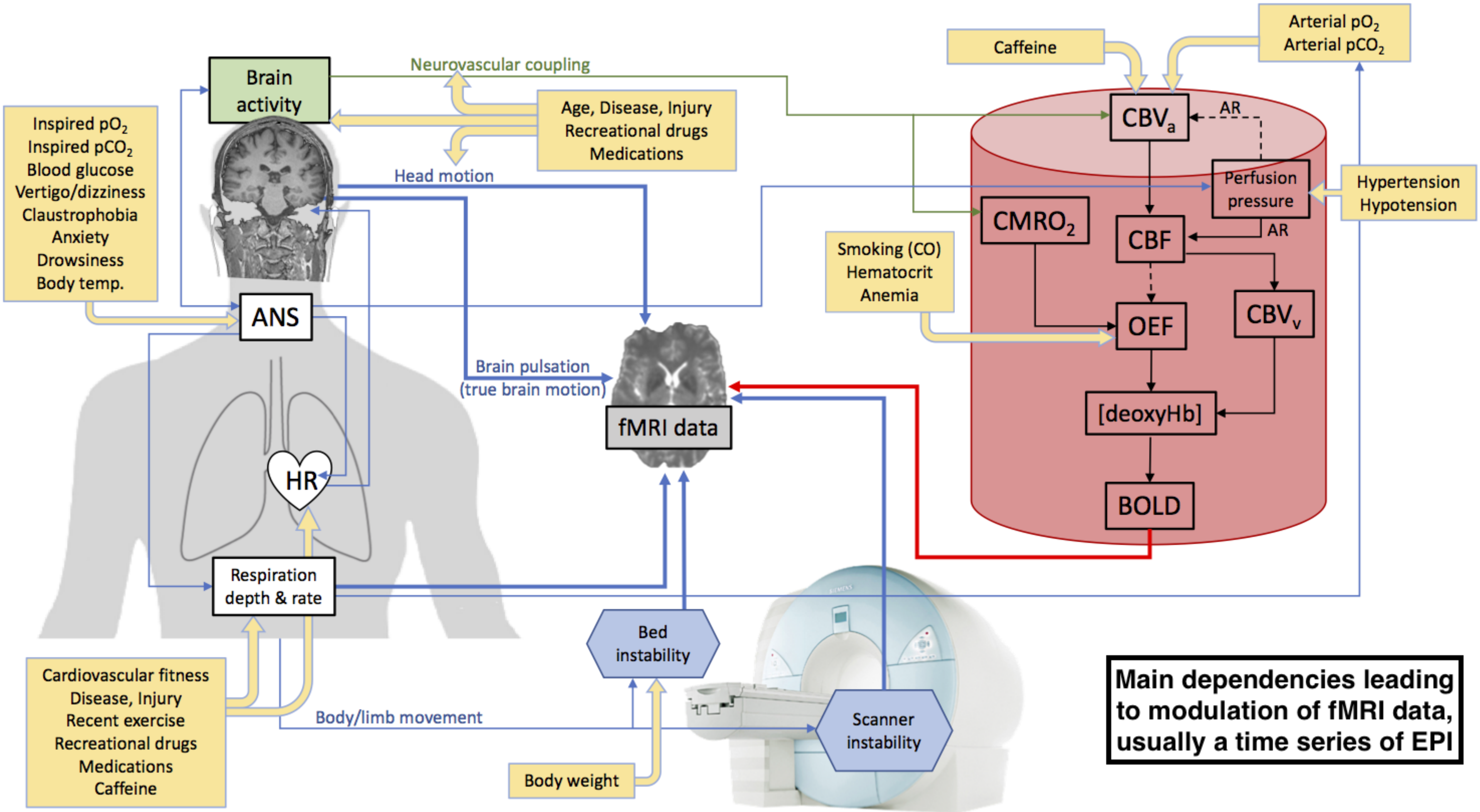
→Artefacts seem to be more visibles than with older MRI systems

→ Signal fluctuations or noise …

Different sources of noise :

- Head motion
- Cardiac pulsatility → motion (global) & inflow (local)
- Respiratory induced changes → change of B0 in the head
- Draining veins
- Slow drifts
- Hardware related instabilities

→ Signal fluctuations or noise …



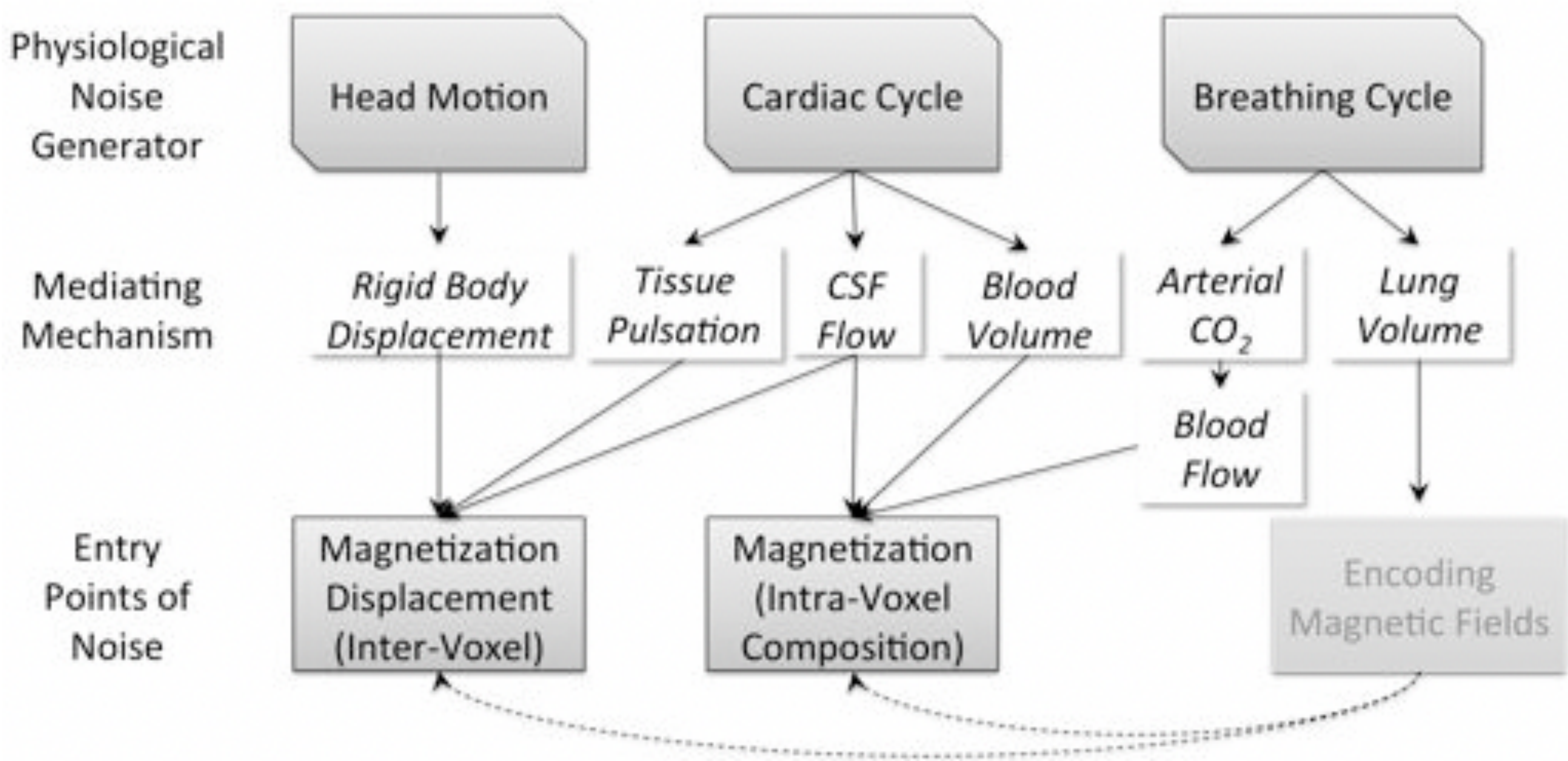
Main dependencies leading to modulation of fMRI data, usually a time series of EPI

Krainik & al, 2013

→ Signal fluctuations or noise …

<u>Different sources of noise :</u>

- Head motion
- Cardiac pulsatility → motion (global) & inflow (local)
- Respiratory induced changes → change of B0 in the head



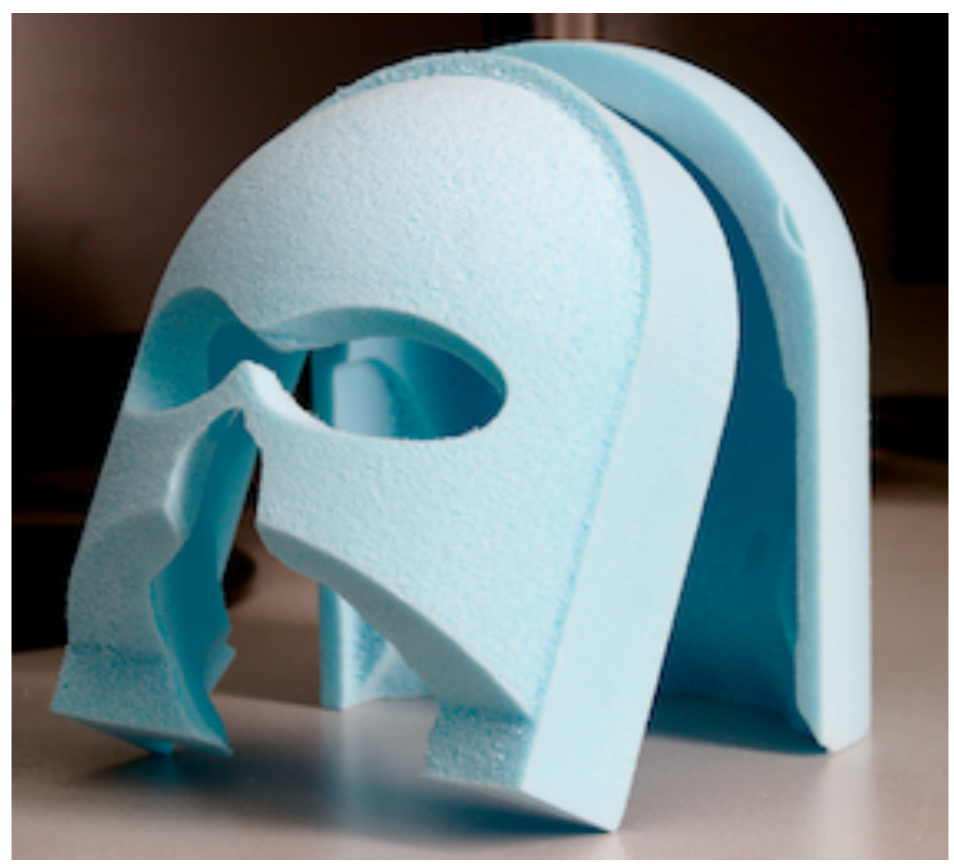
Motion-related noise

- The best solution is to limit the head motion of the subject **<u>during</u>** the data acquisition :
  - compliant & trained subjects : mock-scanner is useful !

Motion-related noise

- The best solution is to limit the head motion of the subject **<u>during</u>** the data acquisition :
  - compliant & trained subjects
  - good head restraint : inflating pads (already available)

  - or the ultimate solution : https://caseforge.co/



Motion-related noise

- The best solution is to limit the head motion of the subject **<u>during</u>** the data acquisition :
  - compliant & trained subjects
  - good head restraint

  - on-line head motion monitoring :
    - feedback to the subject in case of problematic motion
    - and/or run longer acquisitions

FIRMM : Real-time head motion analysis

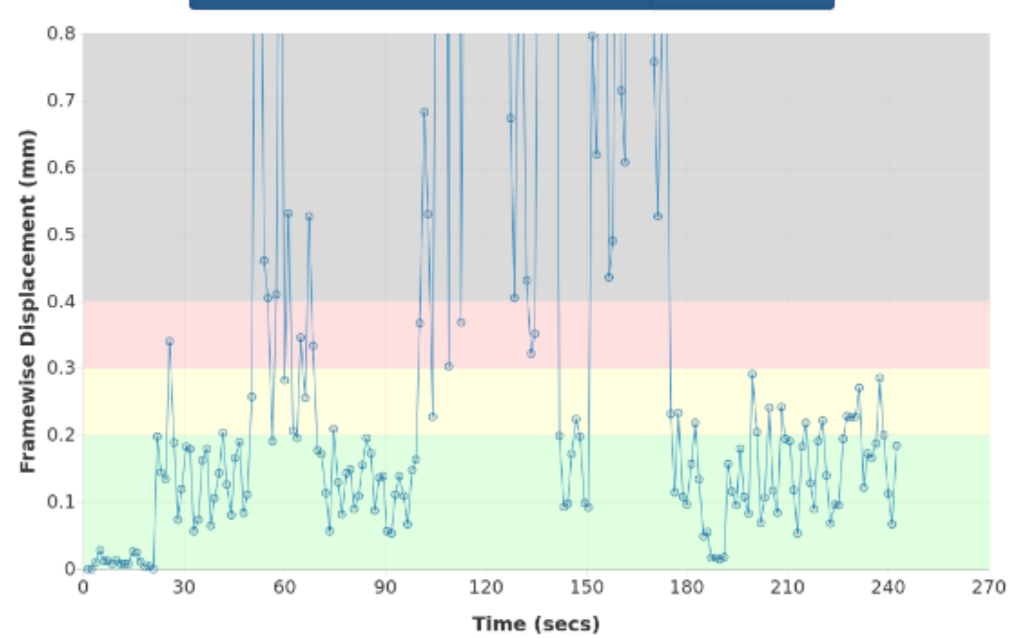
FIRMM version 2.1.3

Waiting for next DICOM...

DICOM folder being monitored	/home/firmmproc/FIRMM/incoming/20180214.JS_TOF3.18.02.14_16_45_26_STD_1.3.12.2.1107.5.2.43.66072
Patient Name	JS_TOF3
Patient ID	18.02.14-16:45:26-STD-1.3.12.2.1107.5.2.43.66072

Toggle patient info table

Display data from last 5 minutes of scanning | Display all data

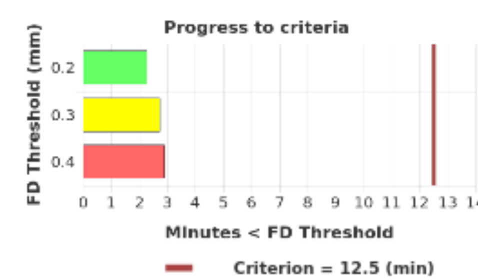


FIRMM version 2.1.3

Start | Reset

Load Previous Scan

✖ < 0.2 mm | ✖ < 0.3 mm | ✖ < 0.4 mm



Summary

Series	Description	Frames	TR (sec)	Time (min)	< 0.2 mm (min) (%)	< 0.3 mm (min) (%)	< 0.4 mm (min) (%)
15	AUDIO_RUN1_PERC	182	1.224	3:42	1:57 (52.7%)	2:25 (65.4%)	2:35 (69.8%)
10	task-rest_bold	15	1.224	0:18	0:18 (100.0%)	0:18 (100.0%)	0:18 (100.0%)
9	task-rest_bold_SBRef	1	1.224	0:01	0:01 (100.0%)	0:01 (100.0%)	0:01 (100.0%)

Collected Low Movement Frames

	< 0.2 mm	< 0.3 mm	< 0.4 mm
Good Time (min) (%)	2:17 (56.6%)	2:45 (68.2%)	2:55 (72.2%)
Good Frames	112	135	143
Bad Frames	86	63	55

Predicted Duration to Scan Criteria

	< 0.2 mm	< 0.3 mm	< 0.4 mm
Minutes to	20:53	16:47	15:14

Denoising motion-related noise

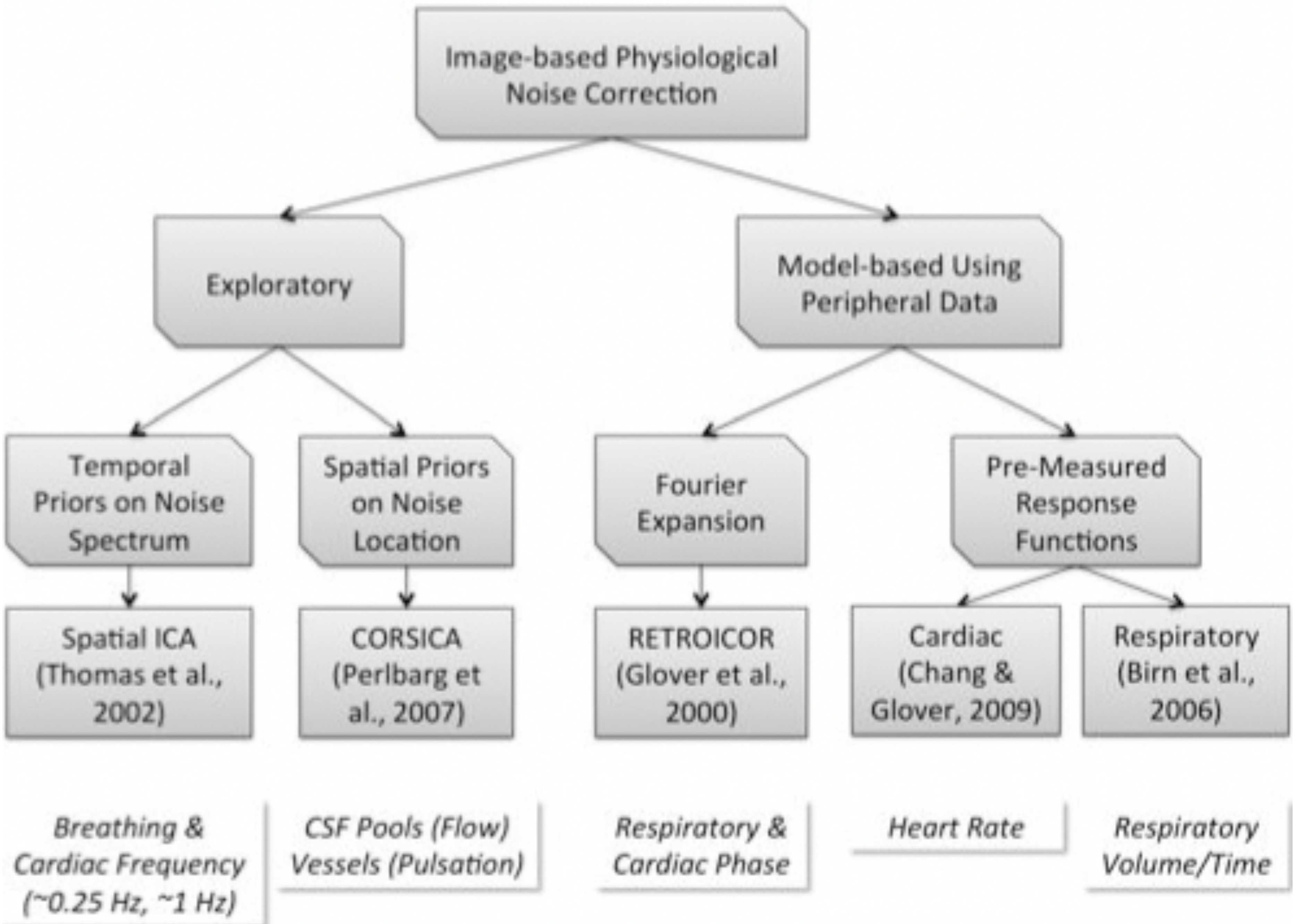
- 1/ Motion correction : Realignment pre-processing
  - classical rigid-body volume correction
  - or slice by slice : SLOMOCO (Ball & Lowe 2014), to be tested

- 2/ Modelisation of motion-reated artifacts : in GLM, 6, 12, 24 or 36 nuisance regressors : realignment parameters time series (rp(t)), their squared time series (rp^2(t)), plus one or two temporal derivatives ((rp(t-1)) (Friston & al, 1996)

- 2bis/ Modelisation of artifacted scans (head jerks, transitory problem) : censoring (1 regressor per outlier scan). See Artifact Detection Tools (ART) for example.

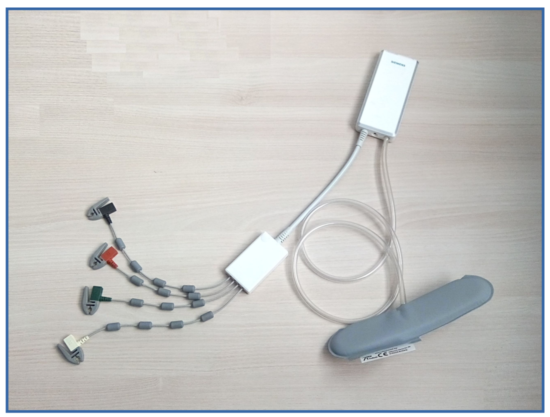
Denoising physiological-related noise

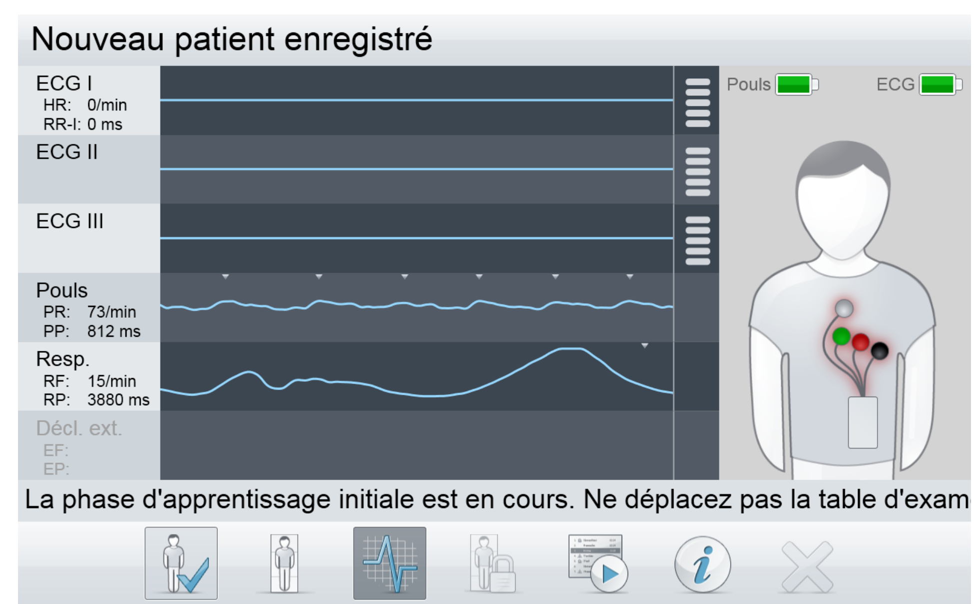
- Denoising physiological noise based on external recordings
- Data-driven denoising methods of physiological noise



Denoising physiological-related noise

- <u>Denoising physiological noise based on external recordings</u>
  - Respiration cycle : pneumatic belt
  - Cardiac pulse : Photo-Plethysmo-Graph (PPG)





Denoising physiological-related noise

- Denoising physiological noise based on external recordings

  In RETROspective Image CORrection (RETROICOR, Glover et al., 2000), the quasi-periodic physiological noise time series is modelled by means of a low-order Fourier series with time-varying cardiac and respiratory phases, which are fit to the data as nuisance regressors and removed.

Denoising physiological-related noise

- <u>Denoising physiological noise based on external recordings</u>

  The same physiological recordings can also be employed to reduce low-frequency BOLD fluctuations related to varying cardiac and respiratory rates
  - Heart Rate Variability (HRV)
  - Respiration Volume Time series (RVT)

- Assuming that the relationship between the HRV and RVT fluctuations and the BOLD signal follows a linear model
  → nuisance regressors obtained by convolving the HRV and RVT time series with a respiratory response function (Birn et al., 2008) and cardiac response function (Chang et al., 2009)

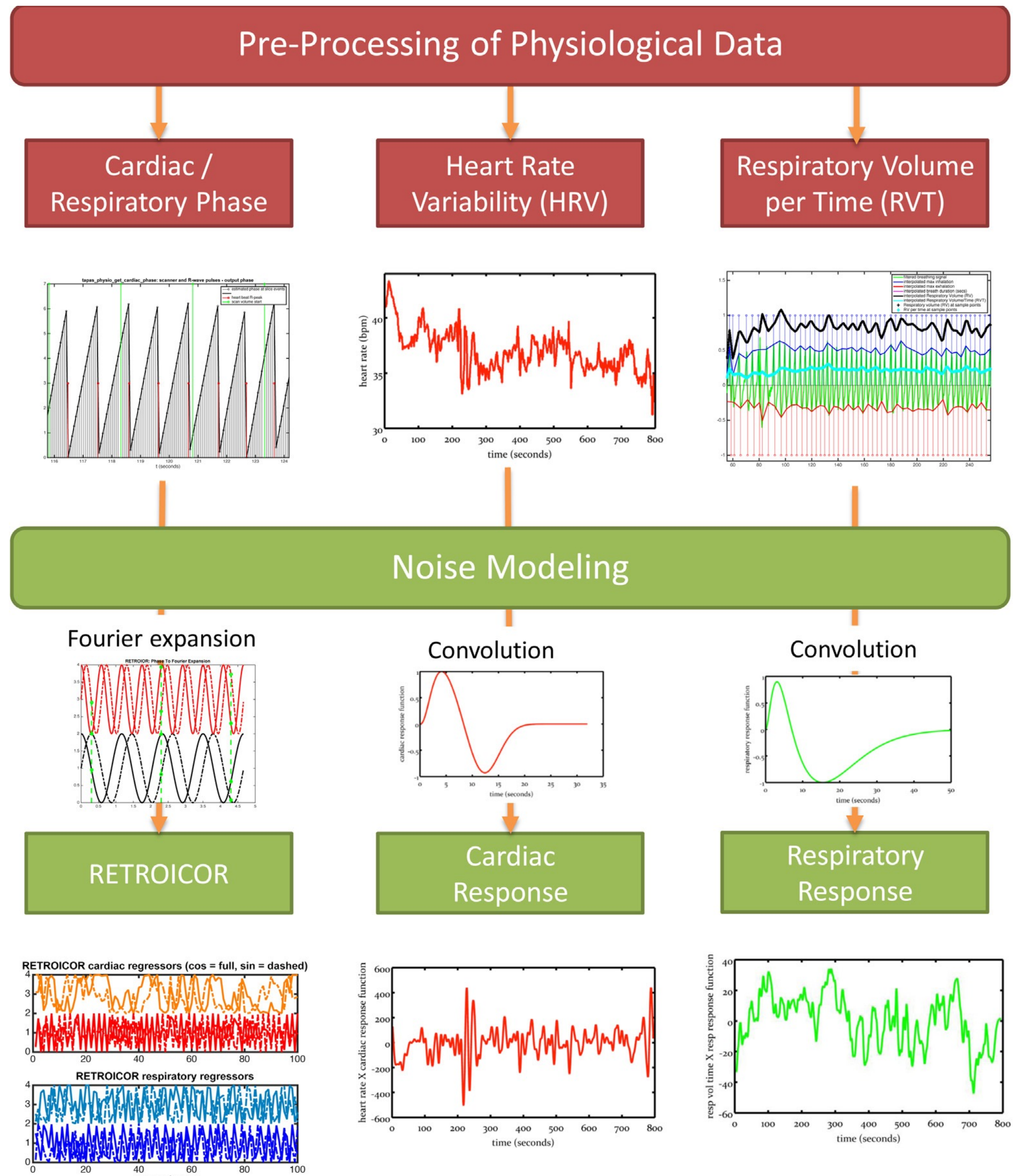
Denoising physiological-related noise

- Denoising physiological noise based on external recordings

2/ Nuisance regressors (RETROICOR, HRV, RVT)

TAPAS Physio Toolbox

The PhysIO Toolbox for Modeling Physiological Noise in fMRI Data
Kasper & al.
J of Neuroscience Methods 276 (2017) 56–72



Denoising physiological-related noise

- <u>Denoising physiological noise based on external recordings</u>

1/ Physiological Peak Detection Algorithm

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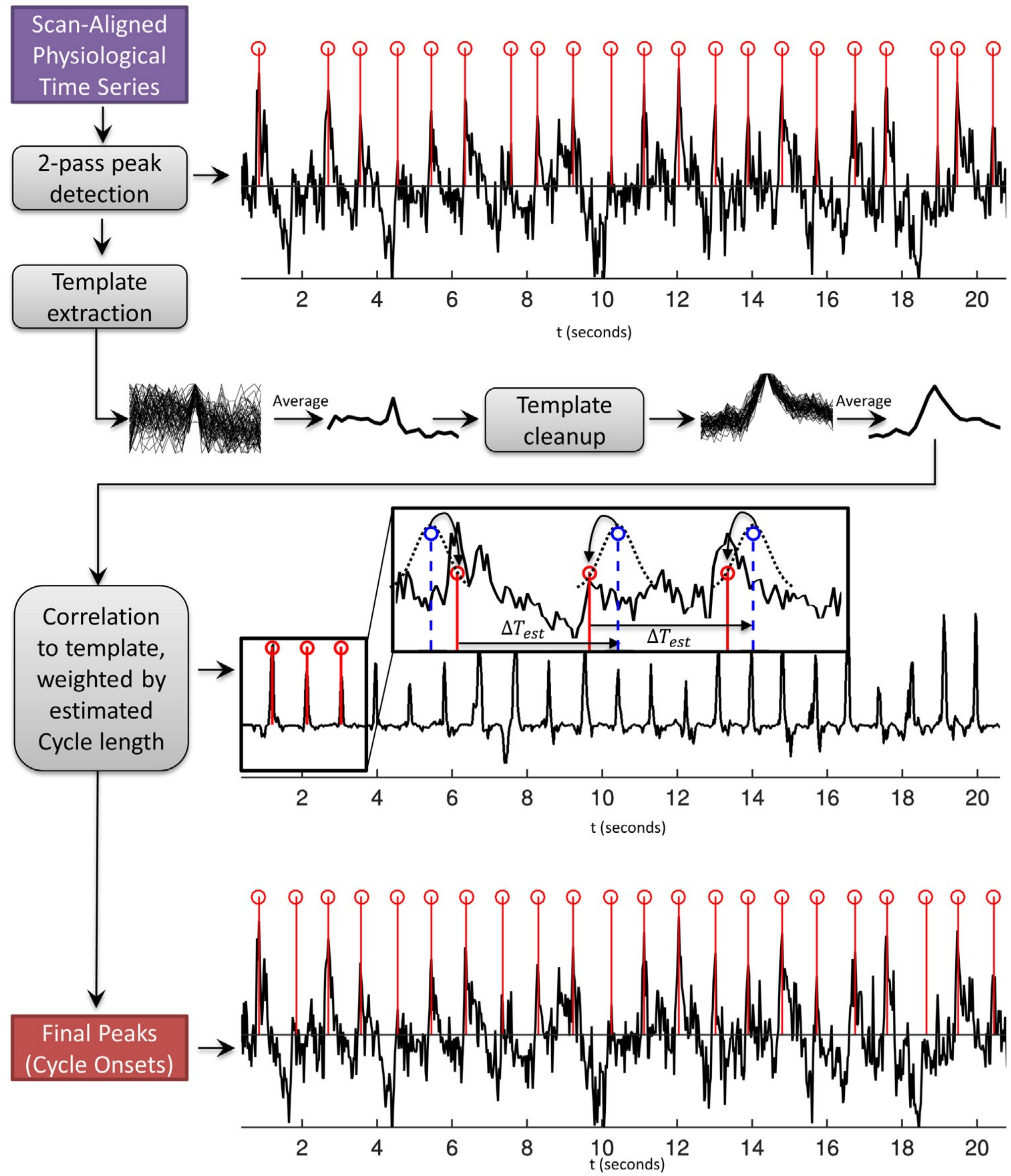
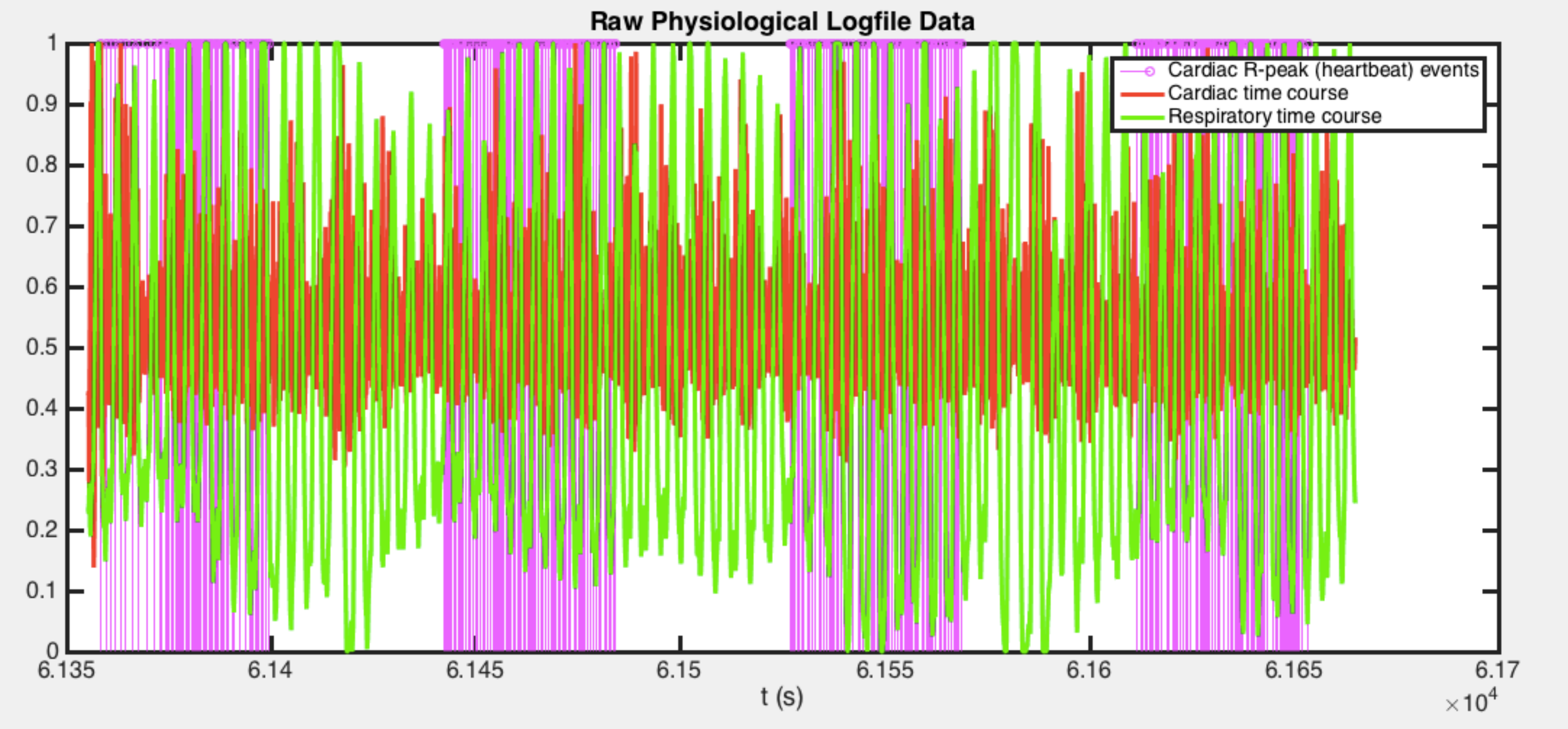


Denoising physiological-related noise

- <u>Denoising physiological noise based on external recordings</u>

1/ Preprocessing of physiological data



Denoising physiological-related noise

- <u>Denoising physiological noise based on external recordings</u>

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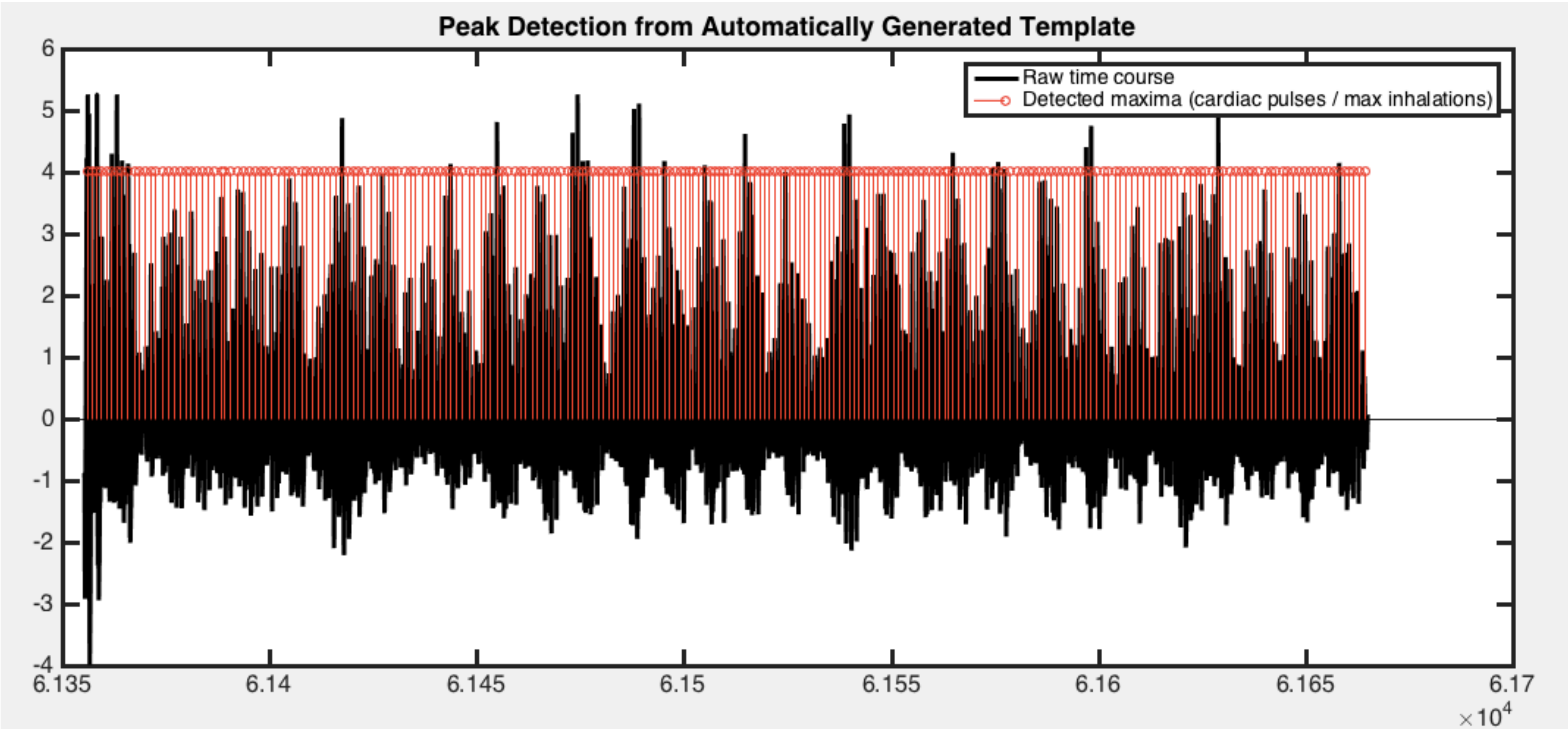
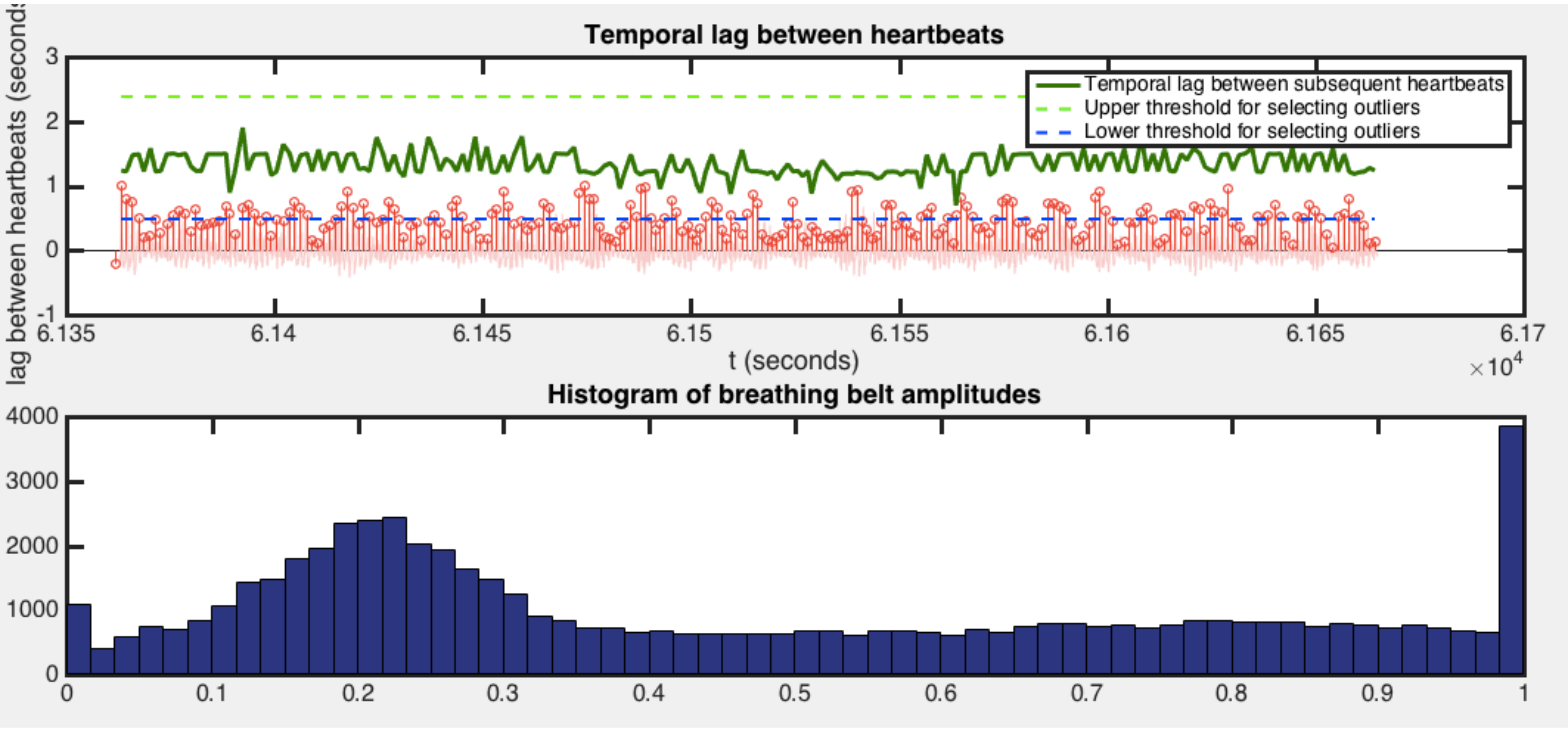


Denoising physiological-related noise

- <u>Denoising physiological noise based on external recordings</u>

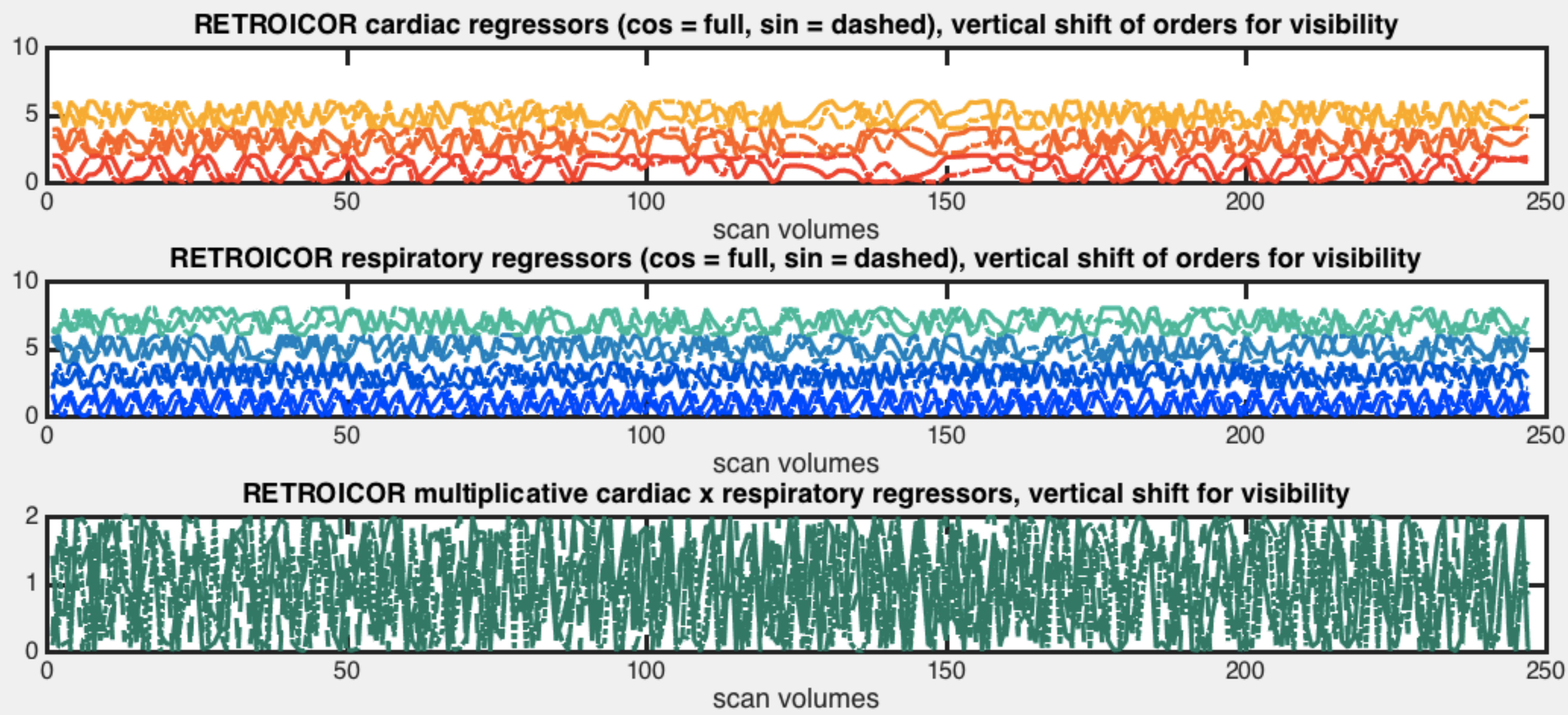
  1/ Preprocessing of physiological data



Denoising physiological-related noise

- Denoising physiological noise based on external recordings

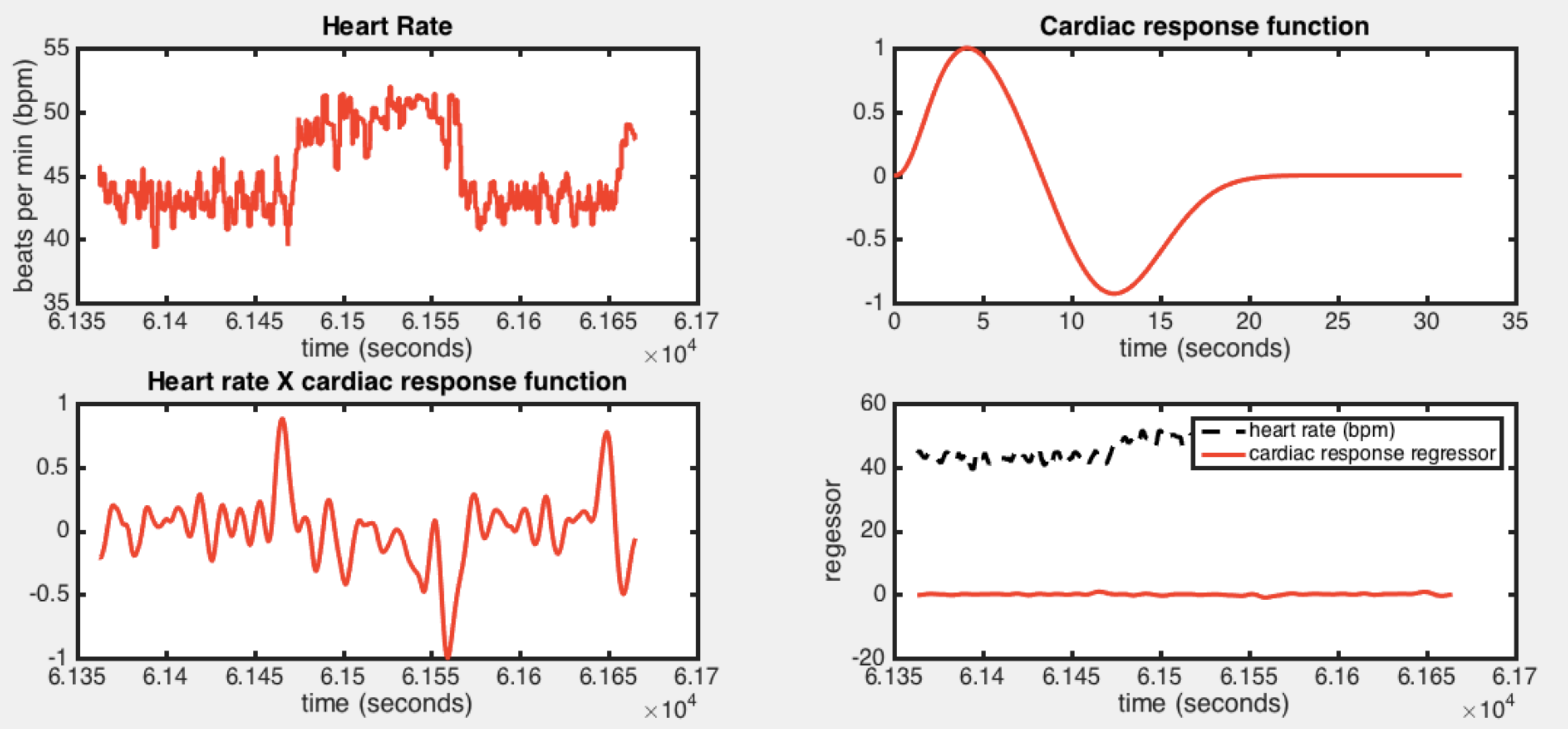
2/ Nuisance regressors : RETROICOR



Denoising physiological-related noise

- Denoising physiological noise based on external recordings

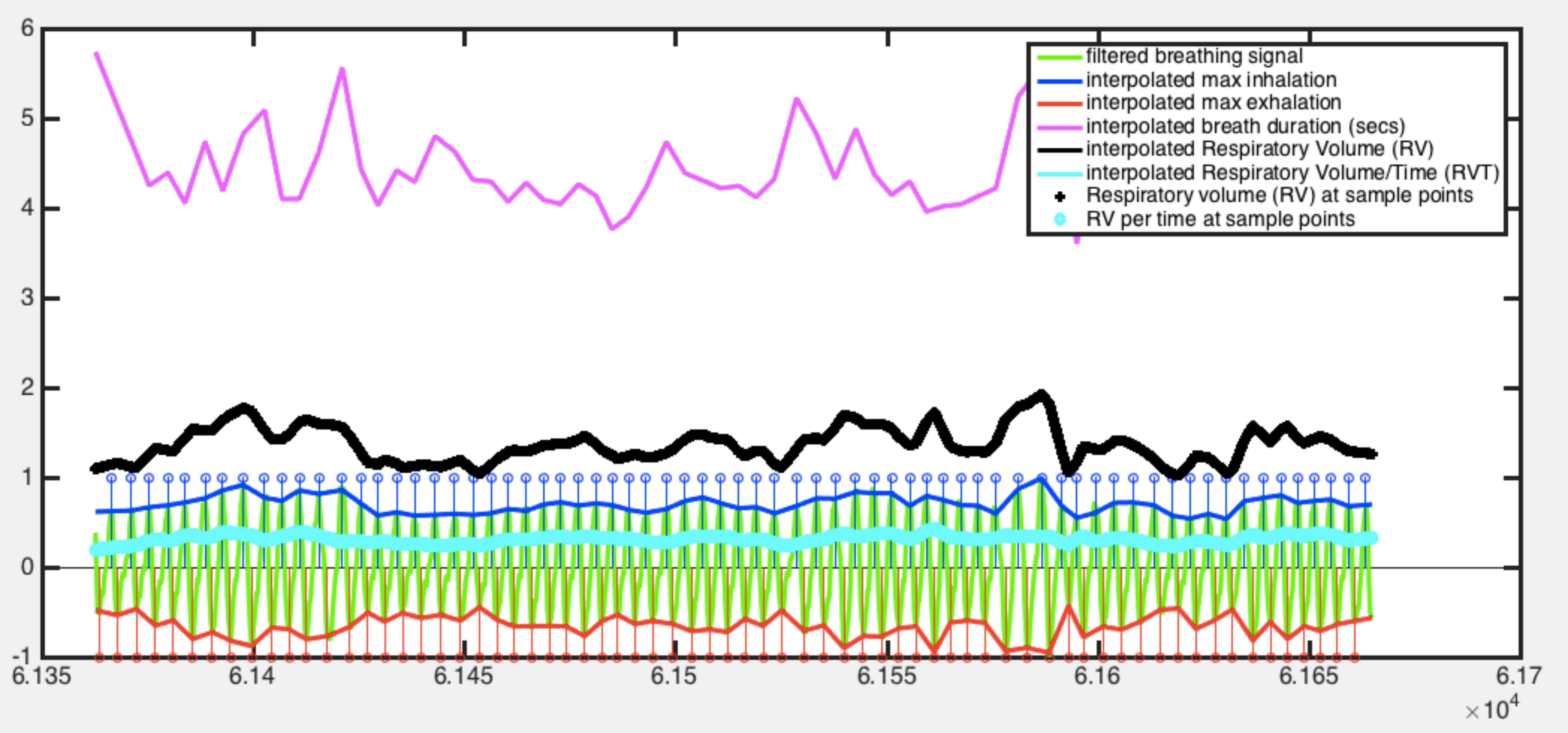
  2/ Nuisance regressors : HRV x CRF



Denoising physiological-related noise

- Denoising physiological noise based on external recordings

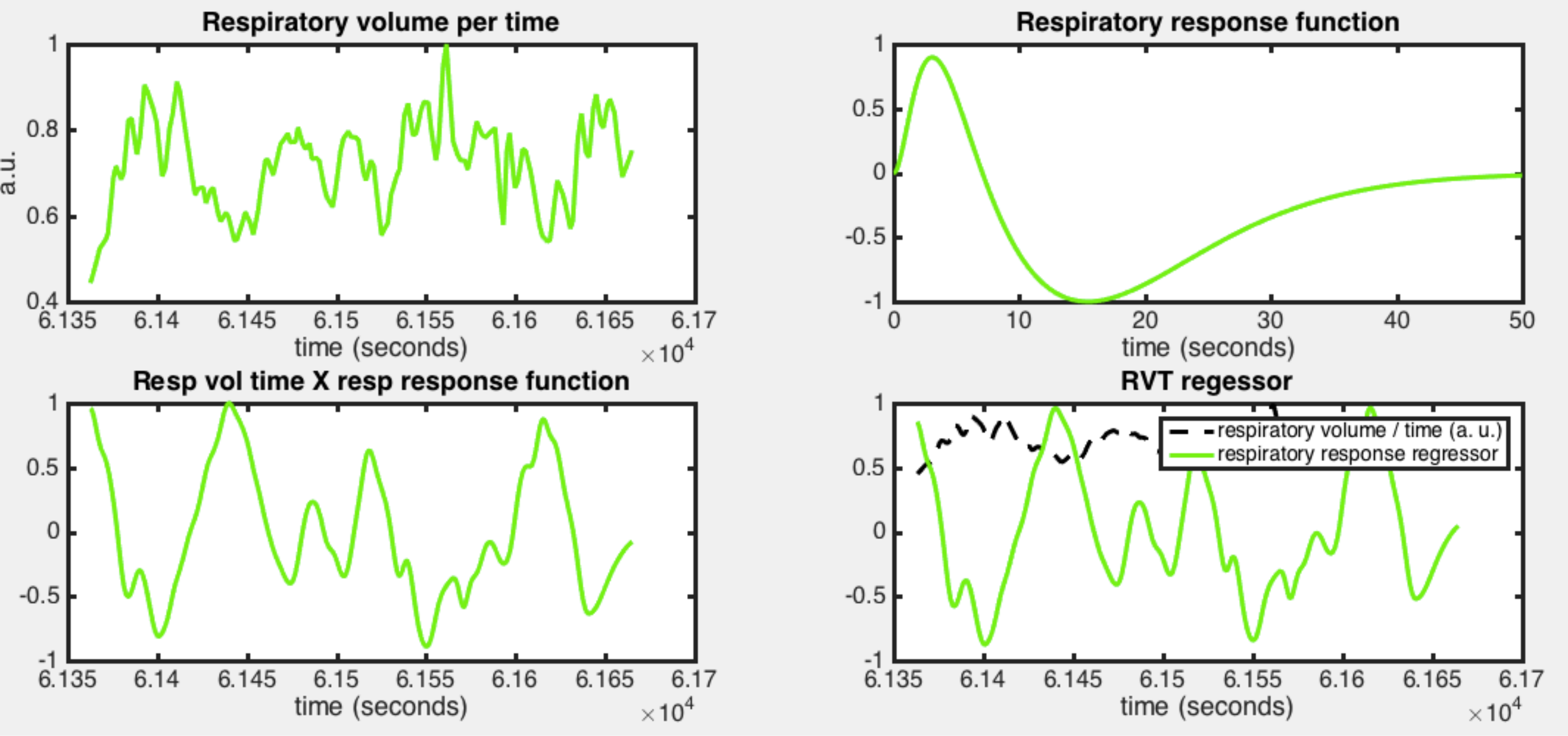
2/ Respiratory Volume per Time (RVT)



Denoising physiological-related noise

- <u>Denoising physiological noise based on external recordings</u>

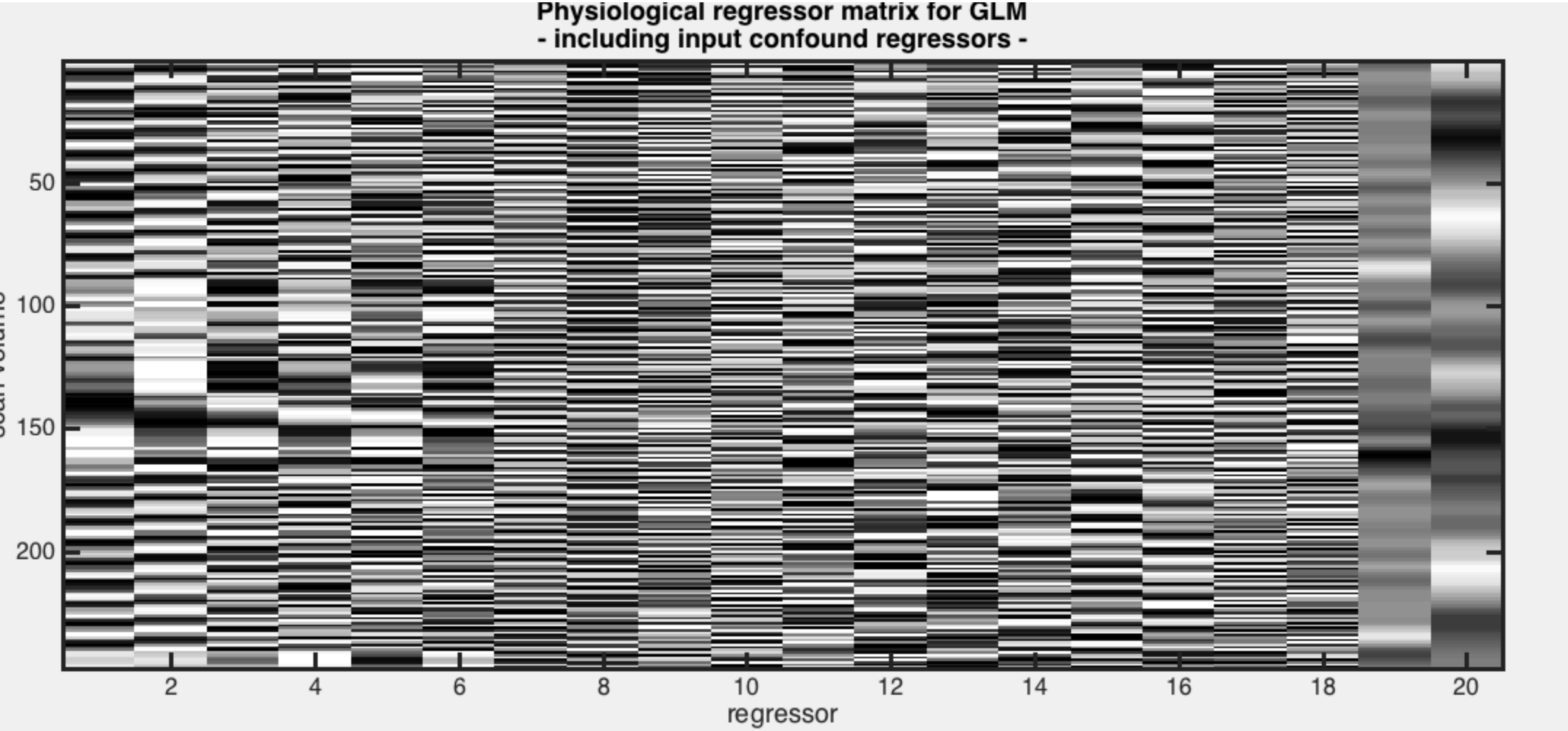
  2/ Nuisance regressors : RVT x RRF



Denoising physiological-related noise

- Denoising physiological noise based on external recordings

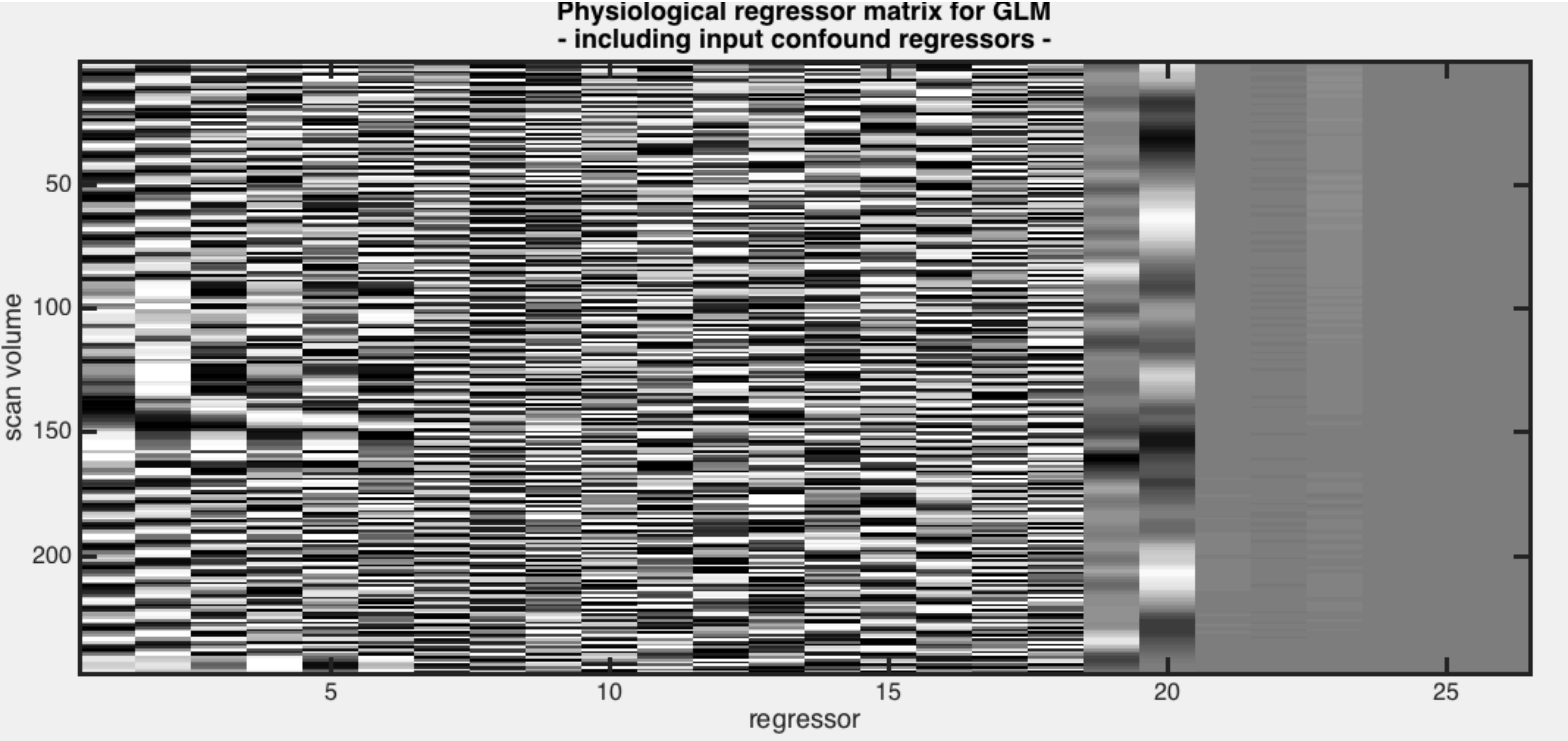
2/ Nuisance regressors (RETROICOR, HRV, RVT)



Denoising physiological-related noise

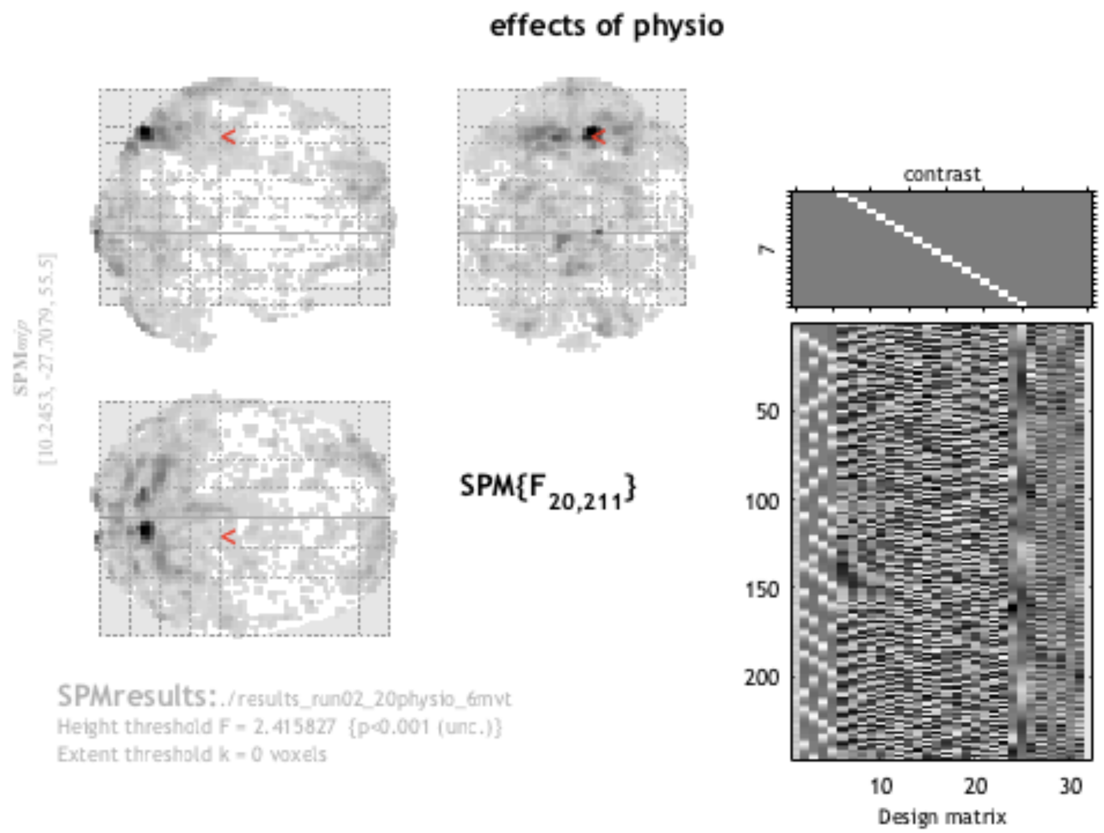
- Denoising physiological noise based on external recordings

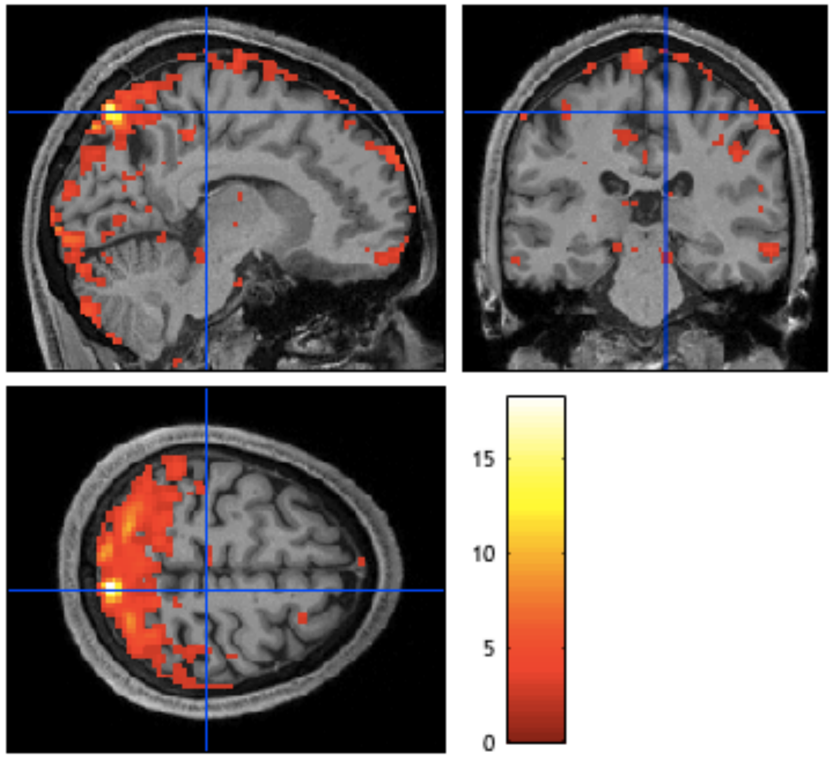
  2/ Nuisance regressors (RETROICOR, HRV, RVT) + 6 mvts



Denoising physiological-related noise

- Denoising physiological noise based on external recordings

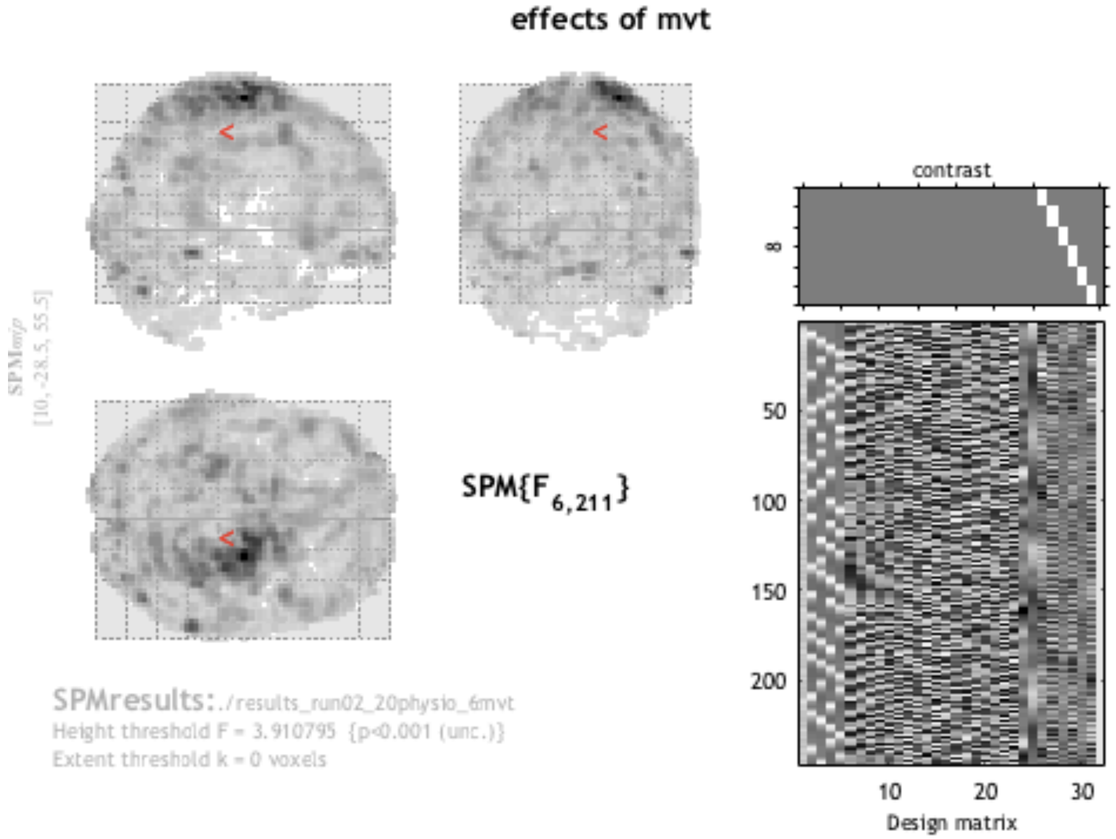


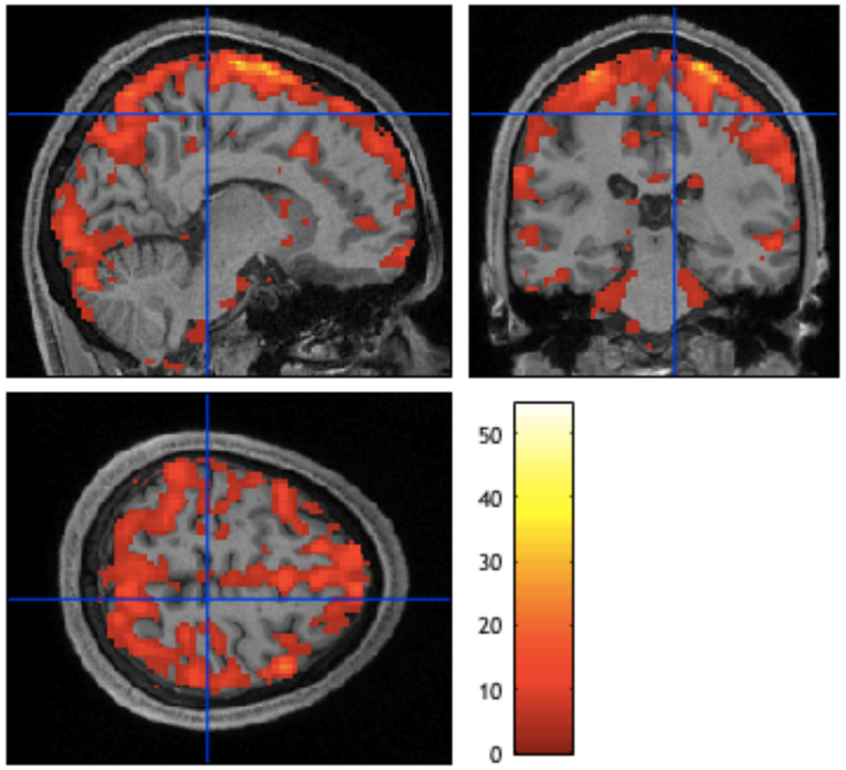


Effects of physio nuisance regressors

Denoising physiological-related noise

- Denoising physiological noise based on external recordings

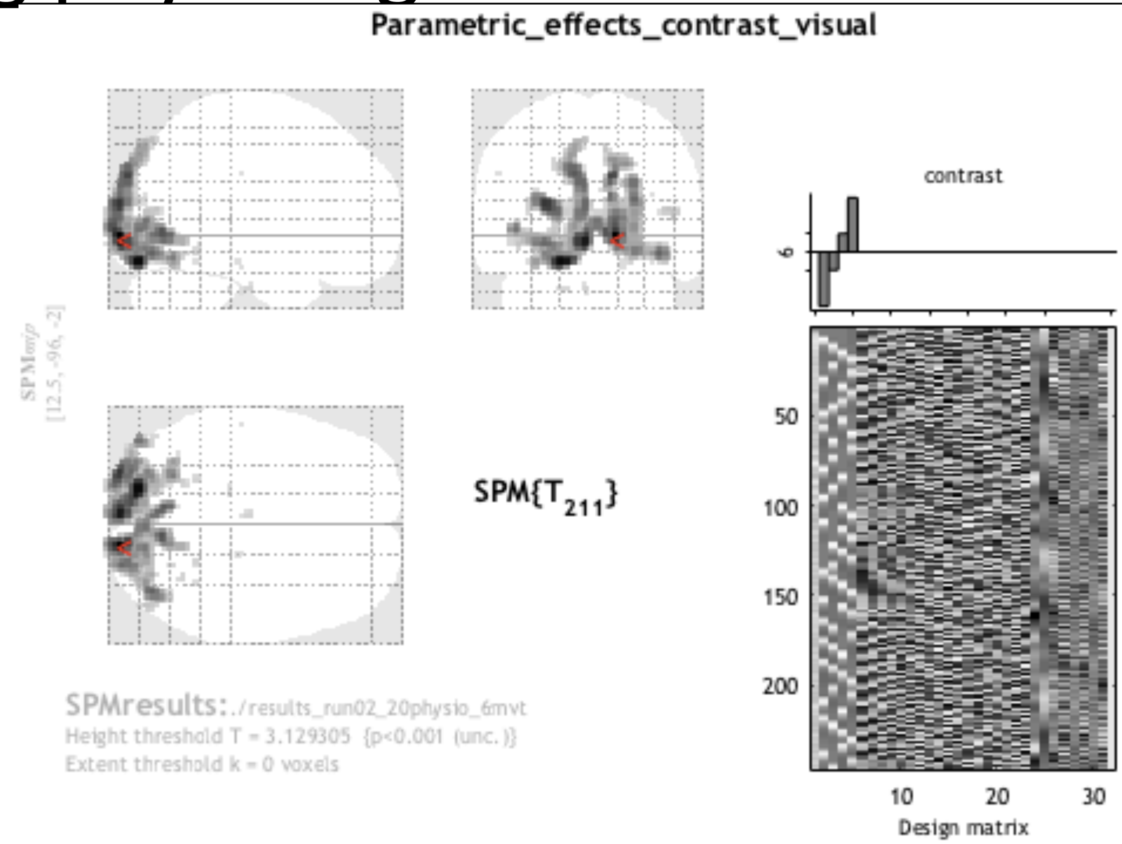


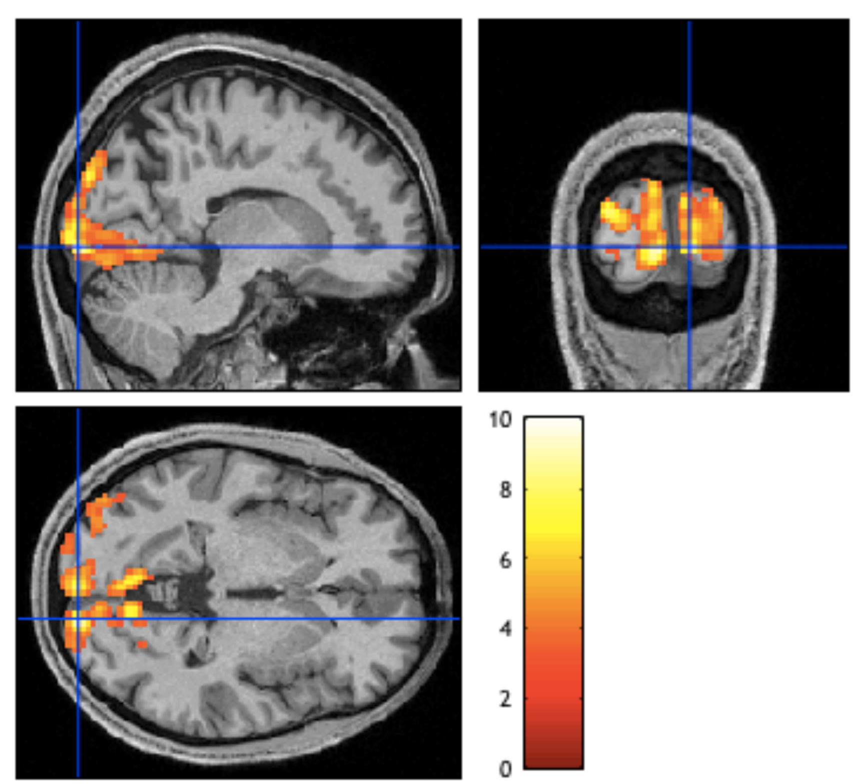


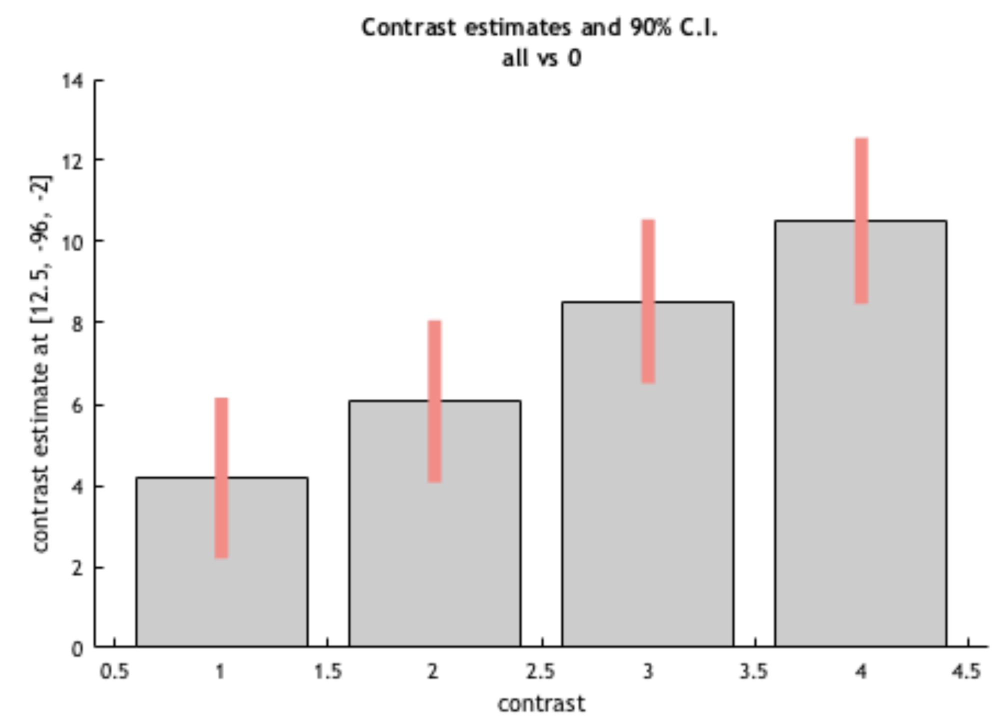
Effects of movement parameters

Denoising physiological-related noise

- Denoising physiological noise based on external recordings

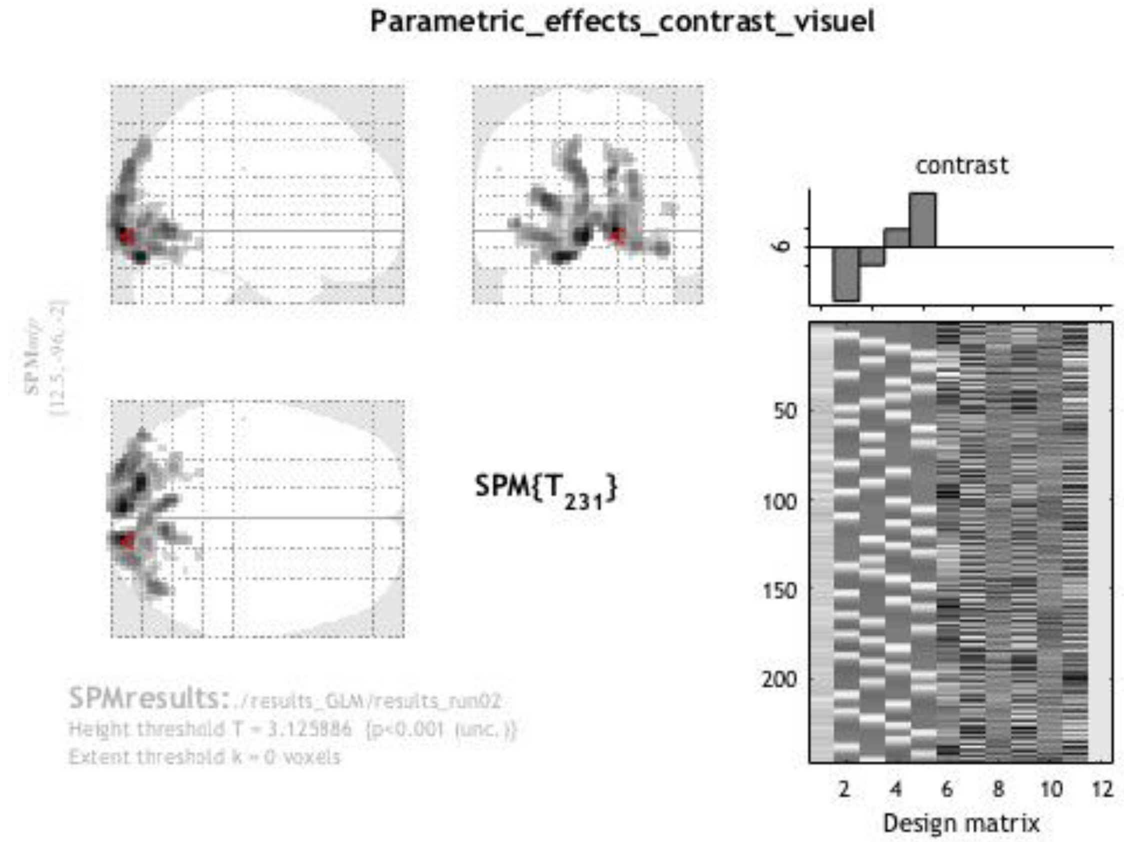


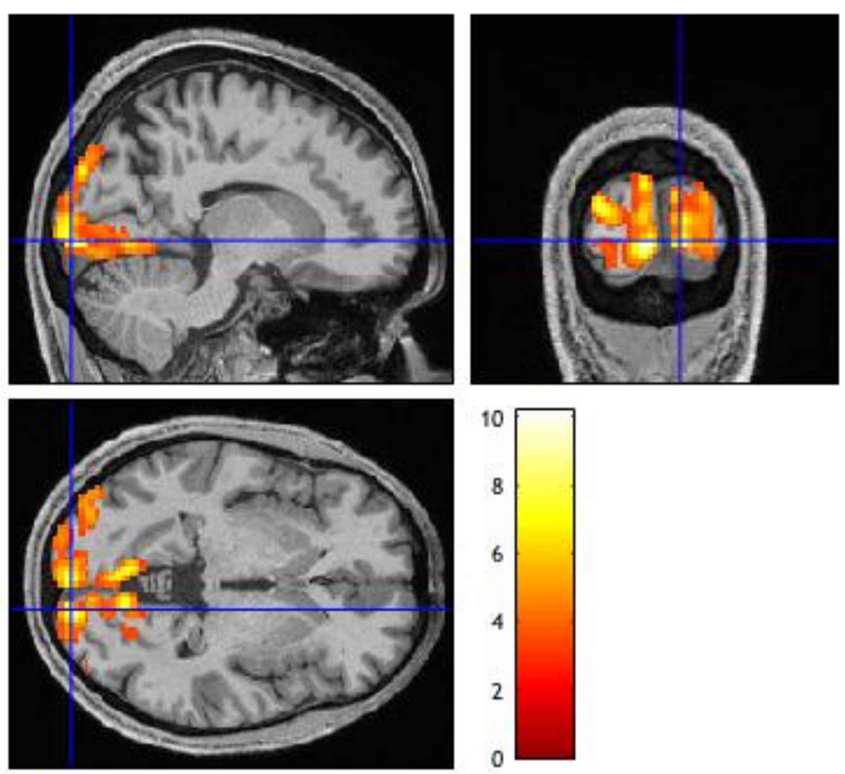


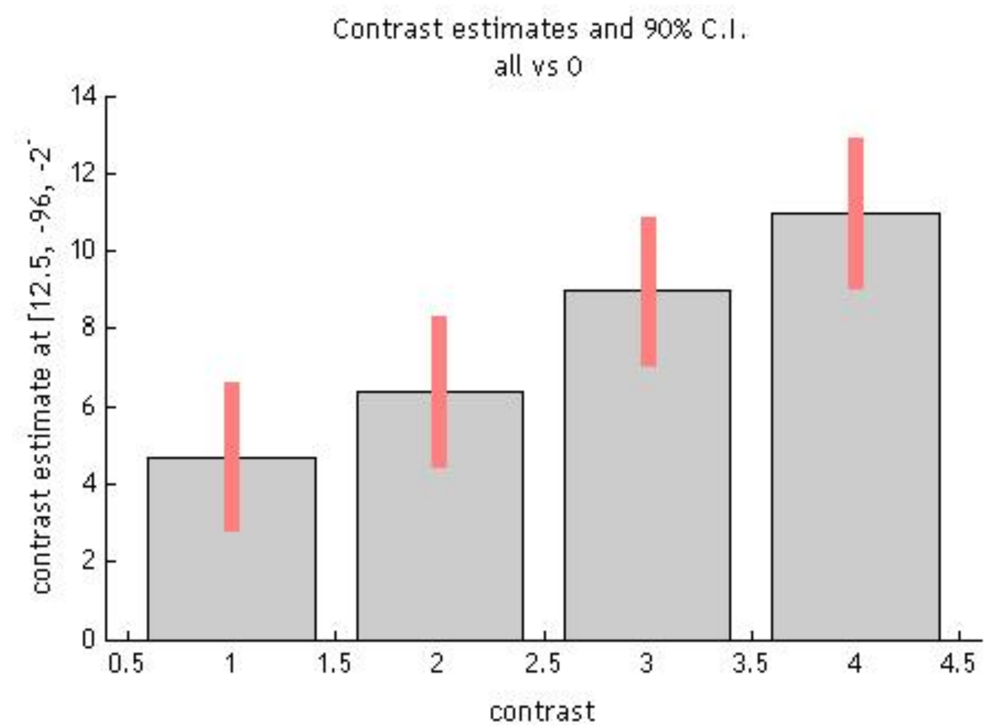


Denoising physiological-related noise

- « Good » subject ≈ identical than without physio denoising

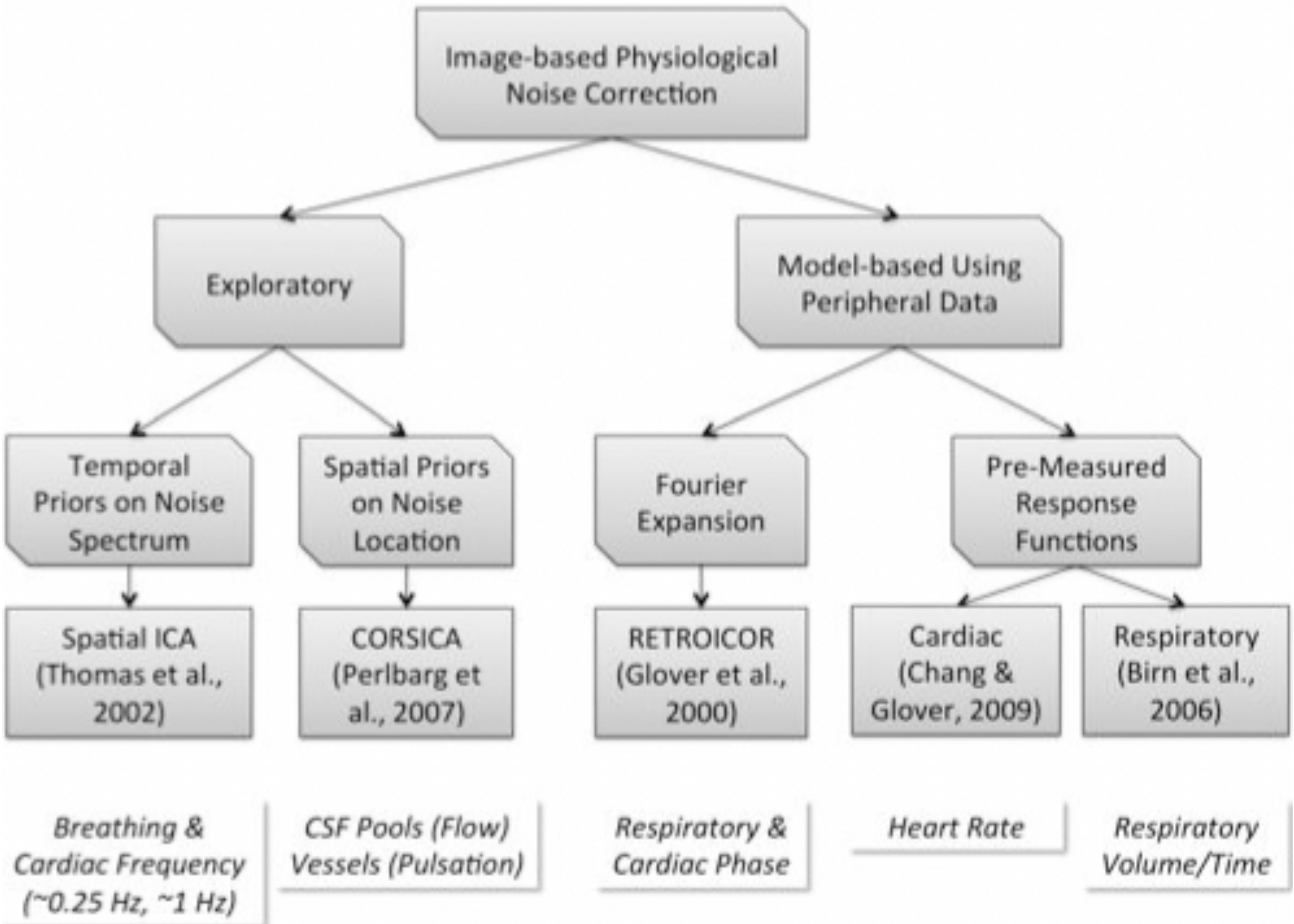






Denoising physiological-related noise

- Denoising physiological noise based on external recordings
- Data-driven denoising methods of physiological noise



Denoising physiological-related noise

- Data-driven denoising methods of physiological noise
  - based on **Principal Component Analysis (PCA)** of noise regions signals : white matter (WM) & Cerebro-Spinal Fluid (CSF)
    - CompCor (Behzadi et al., 2007)
  - based on **Independent Component Analysis (ICA)**
    - temporal ICA : PESTICA (Beall and Lowe, 2007)
    - spatial ICA : CORSICA (Perlbarg & al, 2007)
    - spatial ICA : ICA-AROMA (Pruim & al, 2015) & FIX-ICA (Salimi-Khorshidi & al, 2014) : available in FSL

→ **Determine nuisance regressors for the GLM analysis**

Denoising physiological-related noise

- Data-driven denoising methods of physiological noise
  Based on Principal Component Analysis (PCA)

  - Selection of noise regions signals :
    - Thresholding the tissues volume fraction map (at 0.99)
    - Performing a map erosion by two pixels
      → minimizing the effect of partial voluming with other tissue types.

  - Extraction of EPI non-smoothed data in the noise regions

  - Principal Component Analysis (PCA) on these EPI data

Denoising motion & physiological-related noise

TAPAS Physio Toolbox

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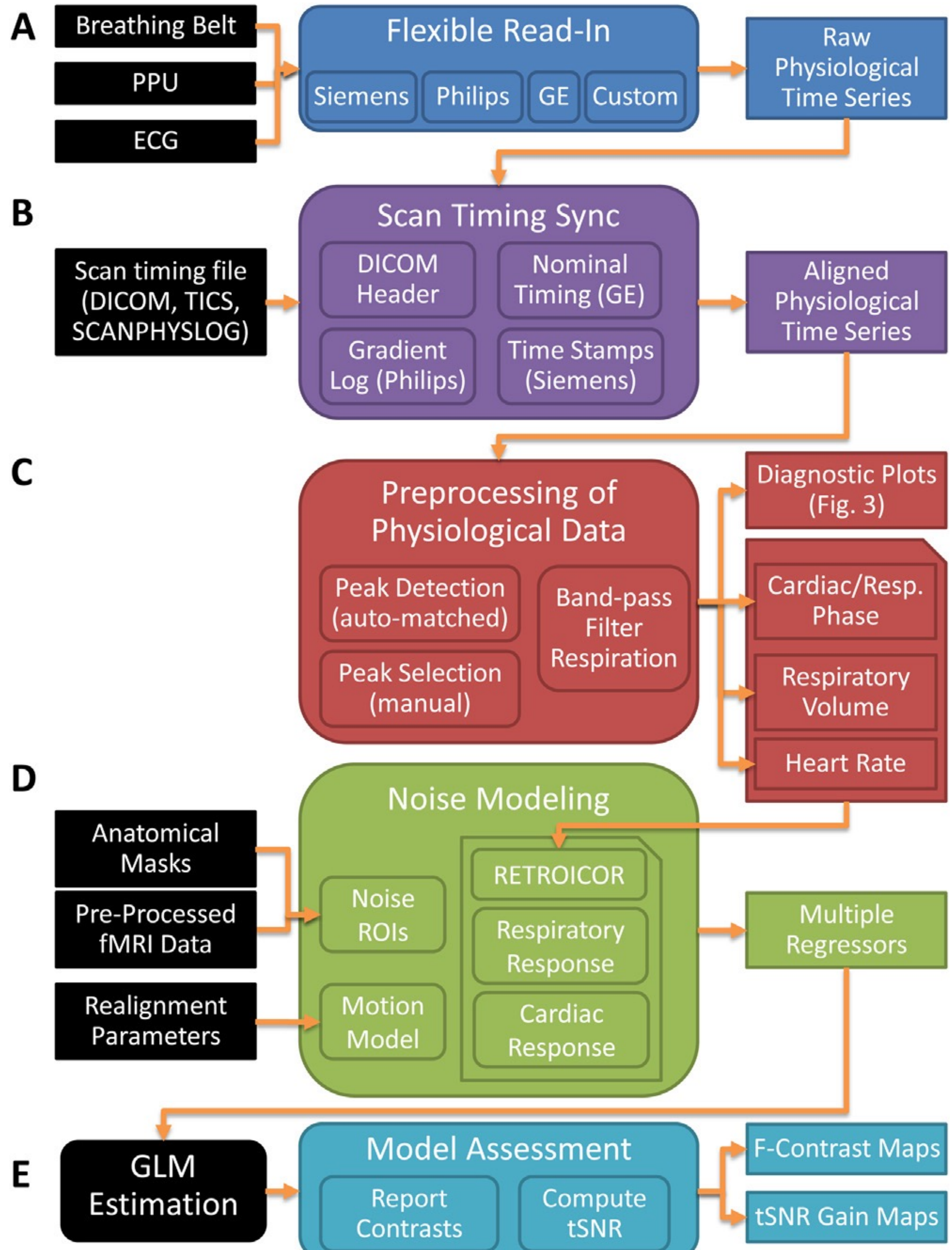
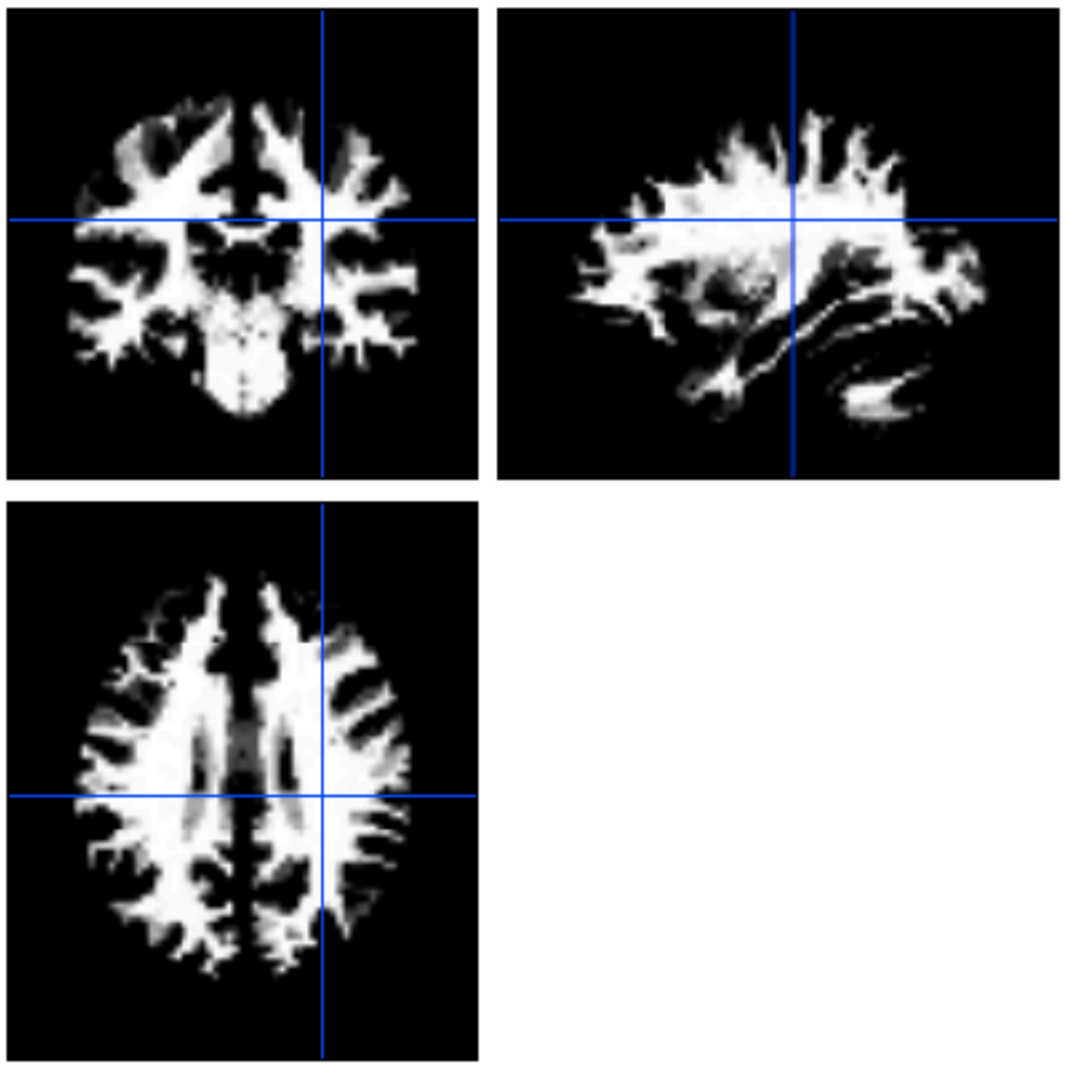


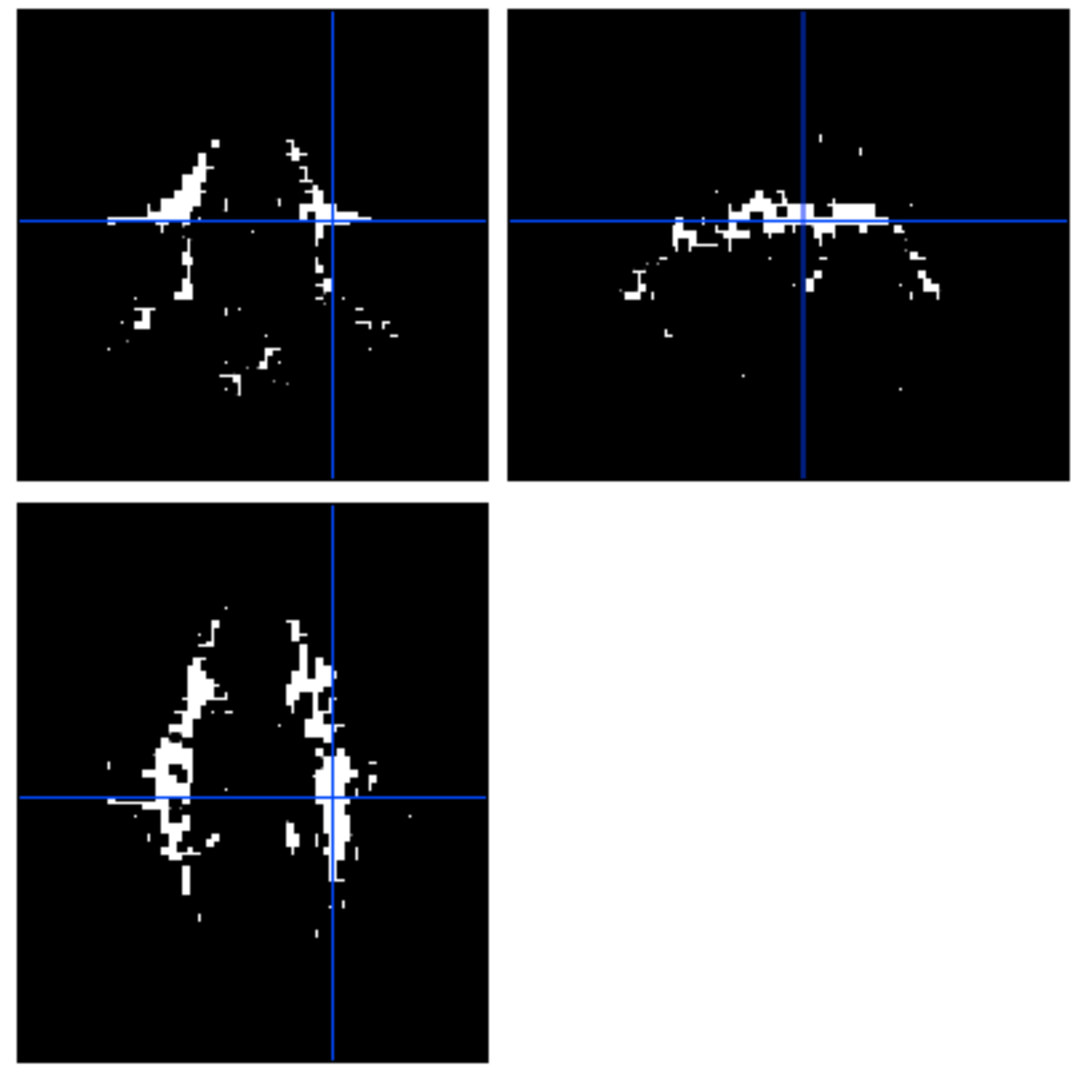
Denoising motion & physiological-related noise

- Masks/tissue probability maps characterizing where noise resides : ROI 1

White Matter



White Matter (thresholded & cropped)

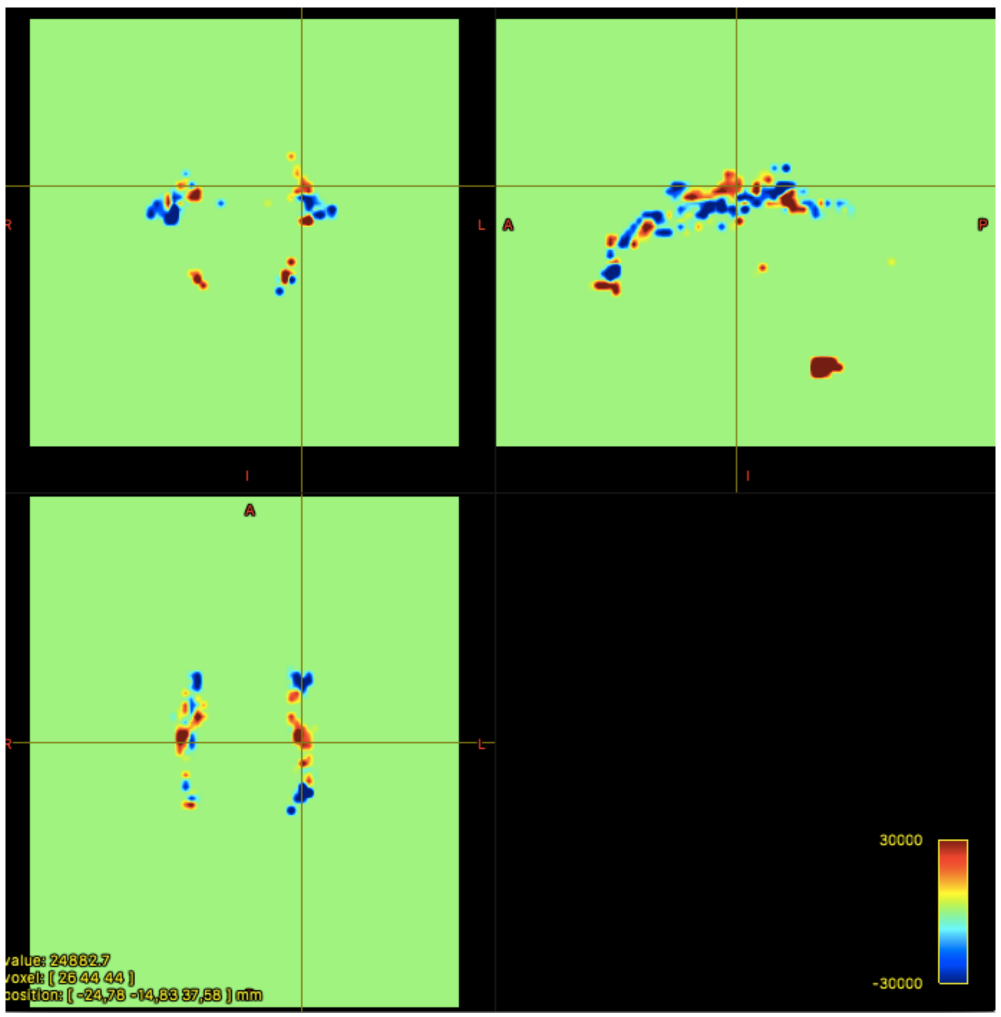


Denoising motion & physiological-related noise

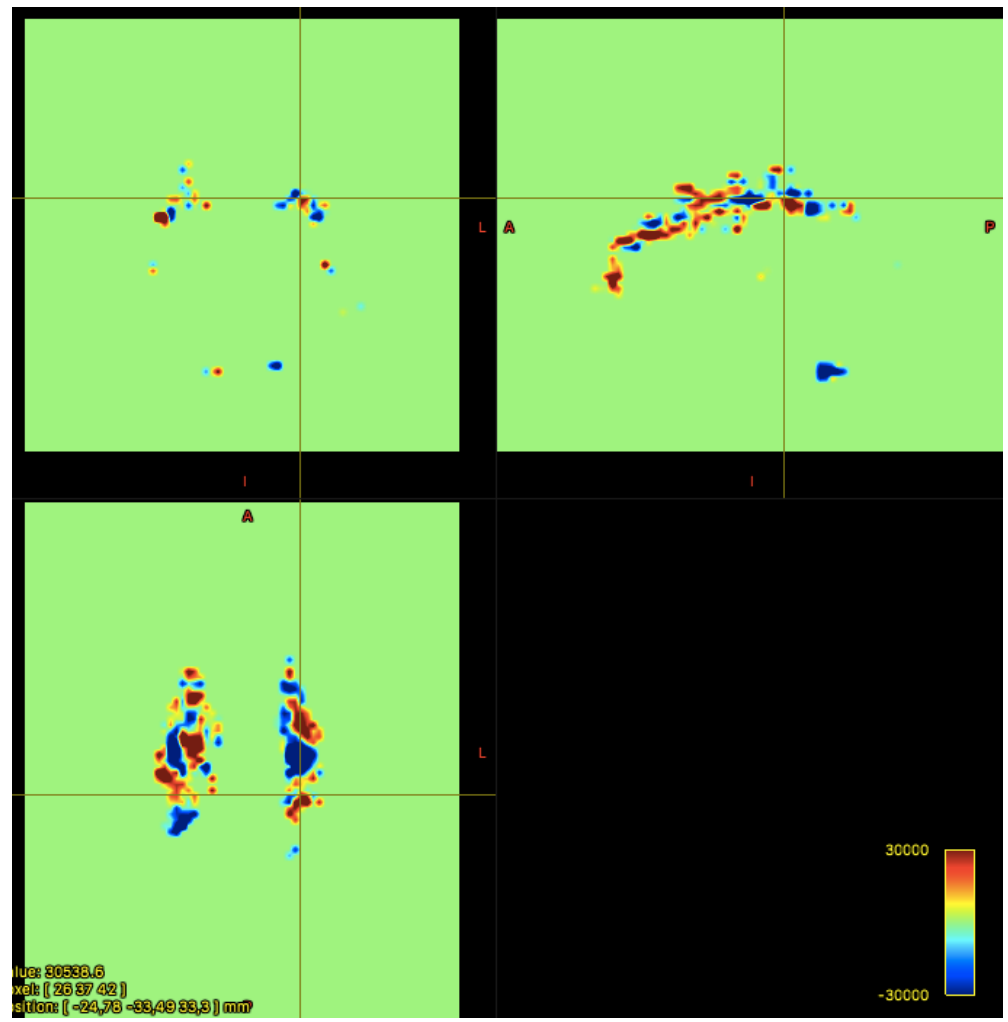
- **Principal Component Analysis (PCA) of <u>non-smoothed EPI data</u> in WM (thresholded & cropped)**

  → N Principal Spatial Components in WM

PC 1



PC 2



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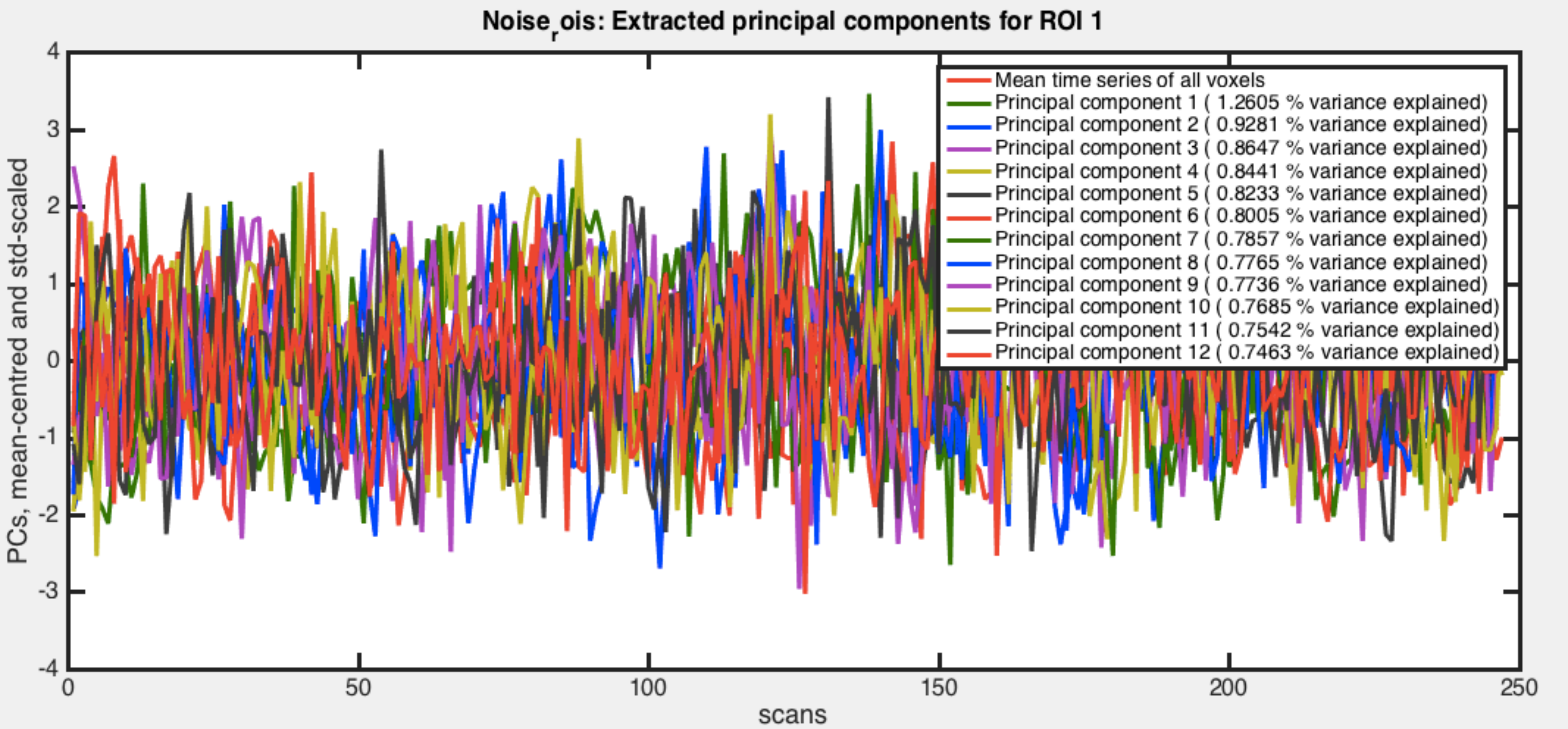
Denoising motion & physiological-related noise

- **Principal Component Analysis (PCA) of <u>non-smoothed EPI data</u> in WM (thresholded & cropped)**

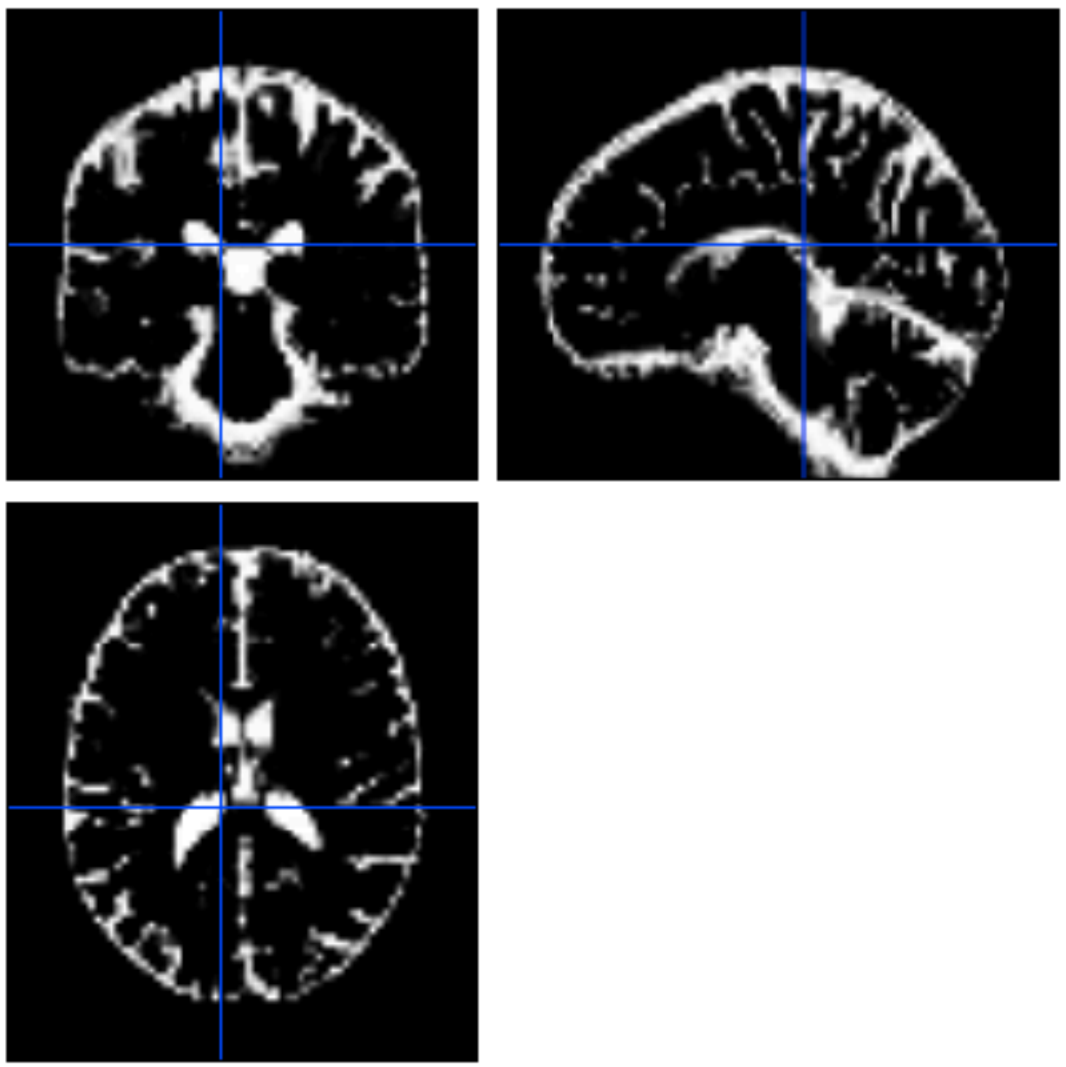
  → N Temporal Components : nuisance regressors



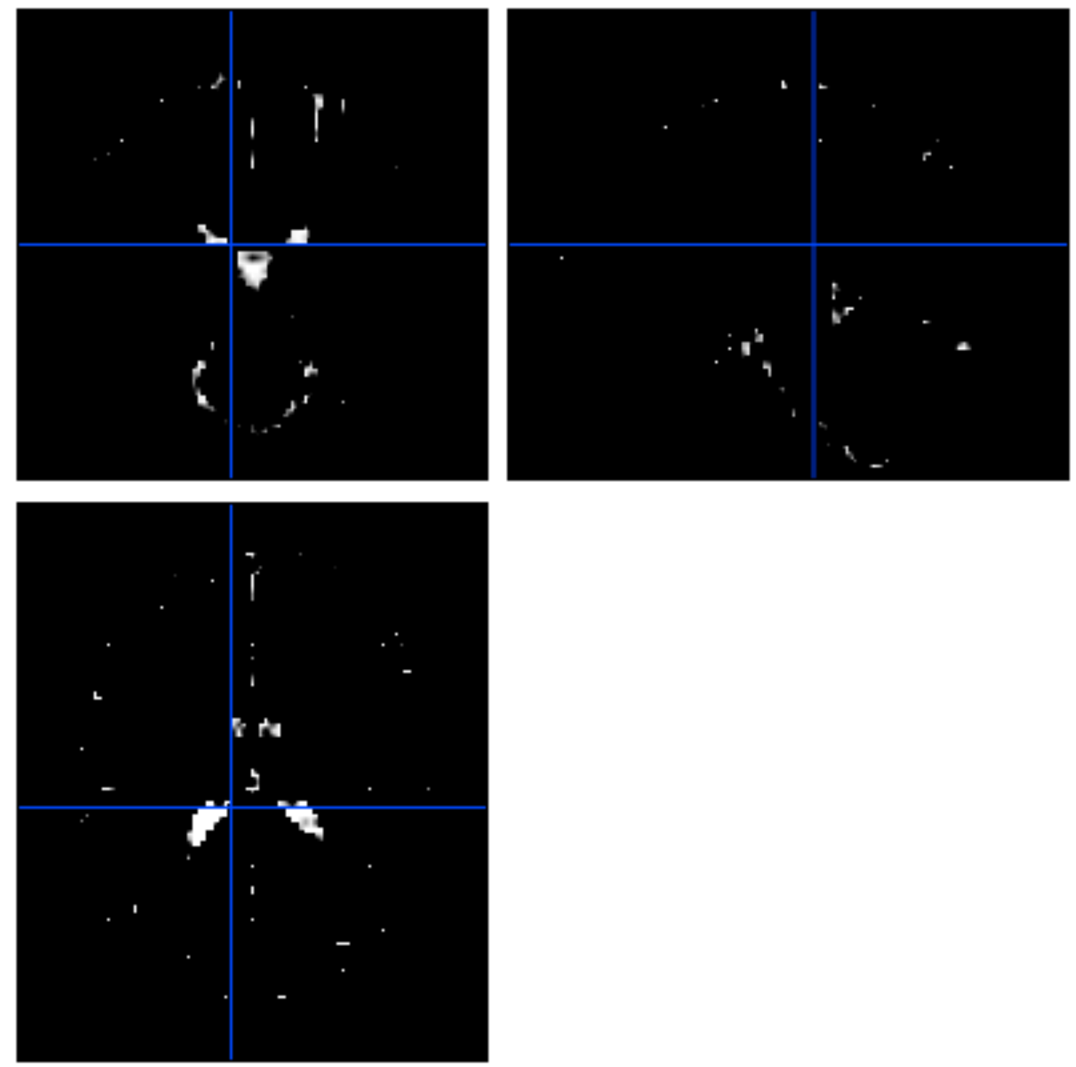
Denoising motion & physiological-related noise

- **Masks/tissue probability maps characterizing where noise resides : ROI 2**

Cerebro-Spinal Fluid (CSF)



CSF (thresholded)

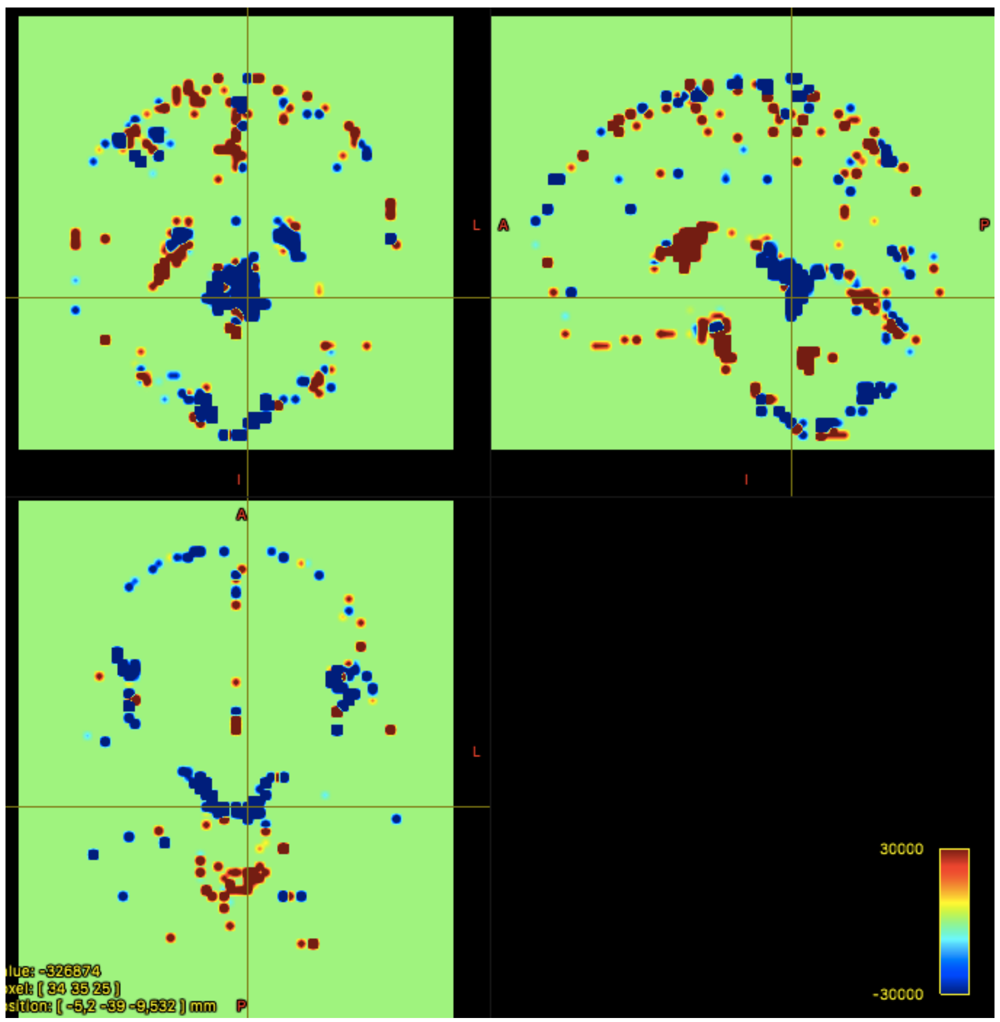


Denoising motion & physiological-related noise

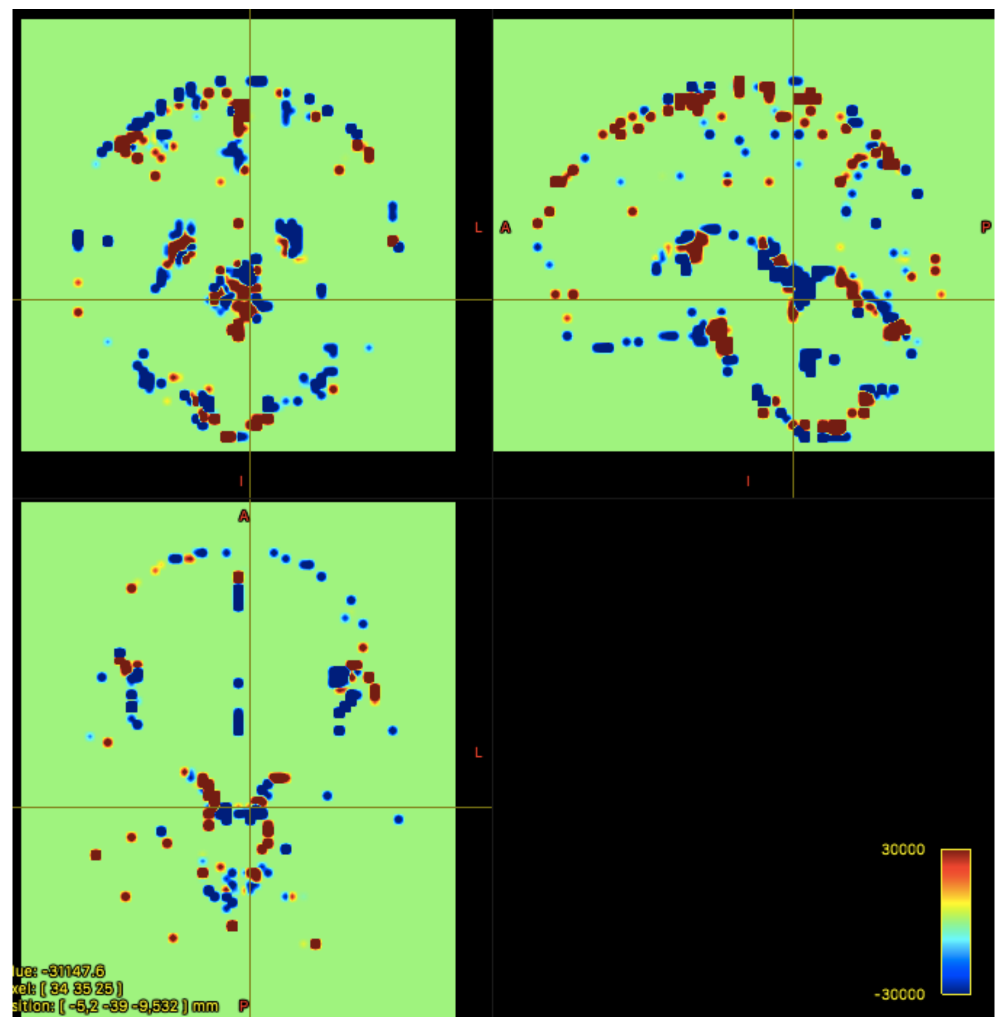
- Principal Component Analysis (PCA) of <u>non-smoothed EPI data</u> in CSF
-

→ N Principal Spatial Components in CSF

PC 1



PC 2



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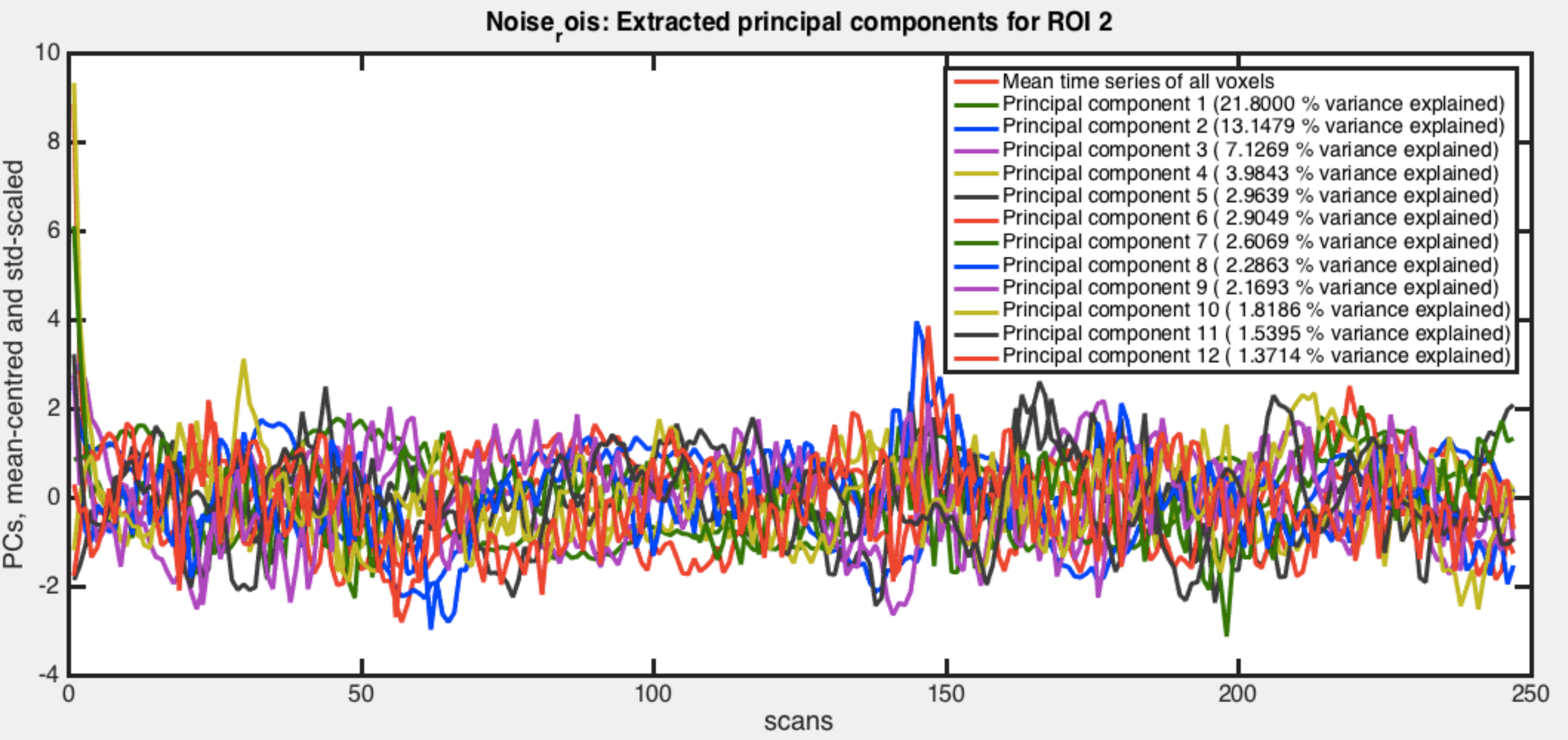
Denoising motion & physiological-related noise

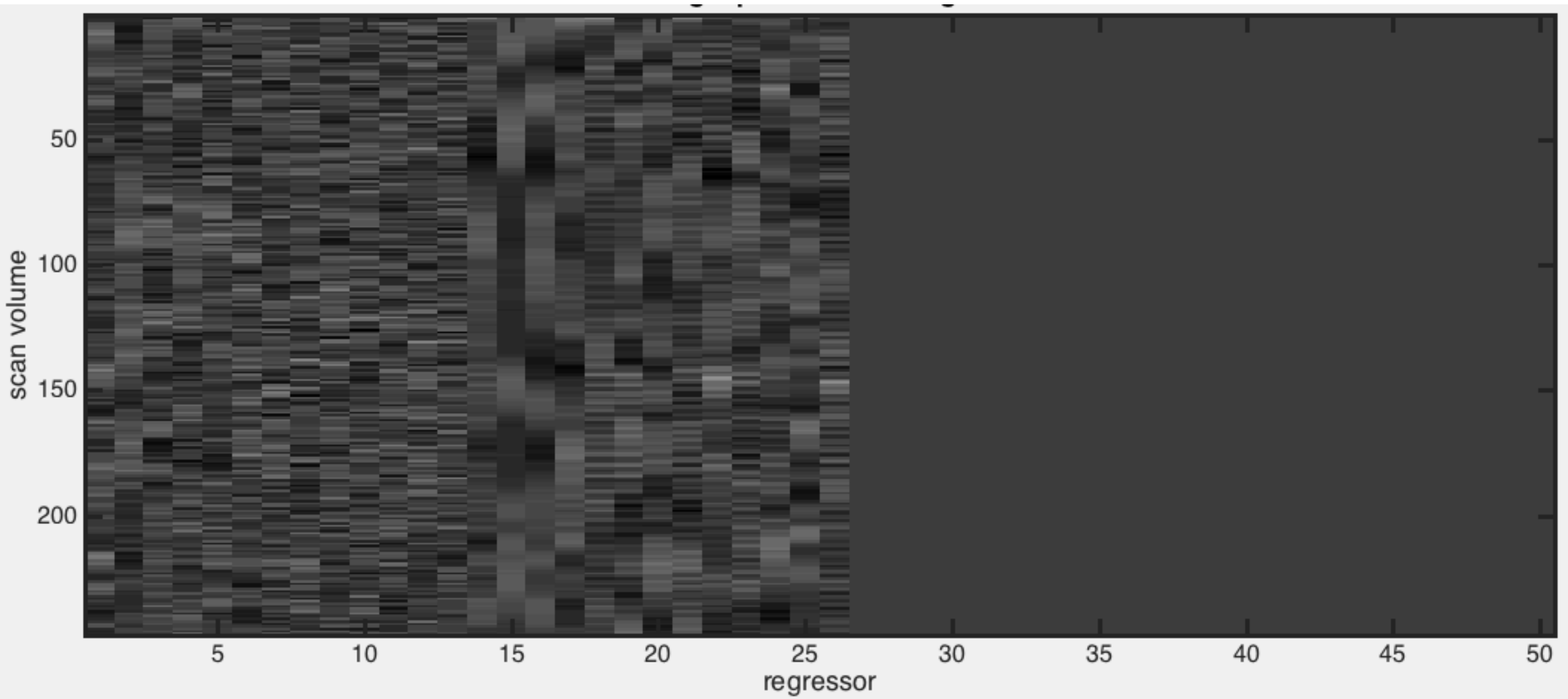
- **Principal Component Analysis (PCA) of <u>non-smoothed EPI data</u> in CSF**

→ N Temporal Components : nuisance regressors



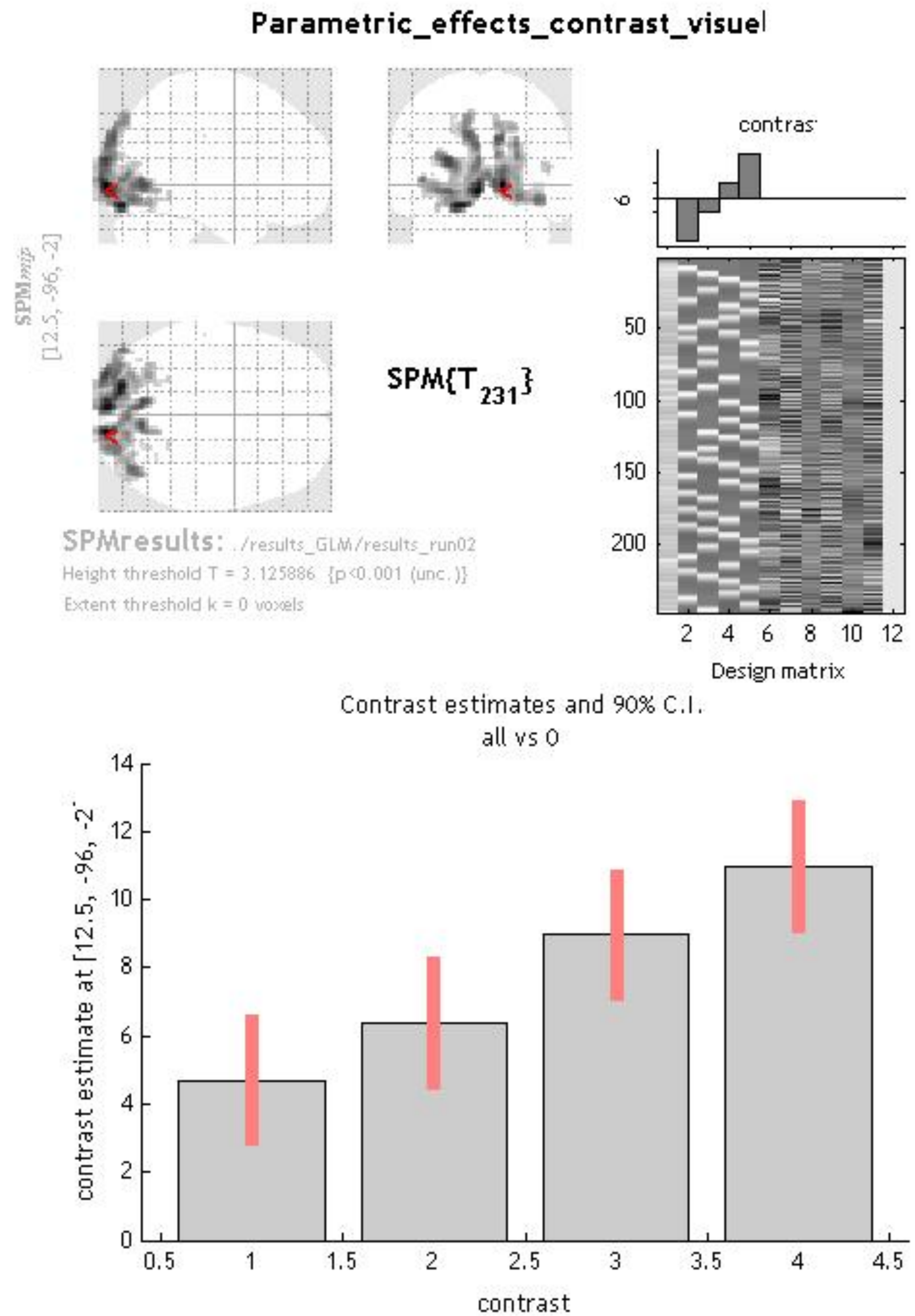
Denoising motion & physiological-related noise

- **12 PCs + 1 mean for WM, 12 PCs + 1 mean for CSF, 24 movement parameters**



Denoising motion & physiological-related noise

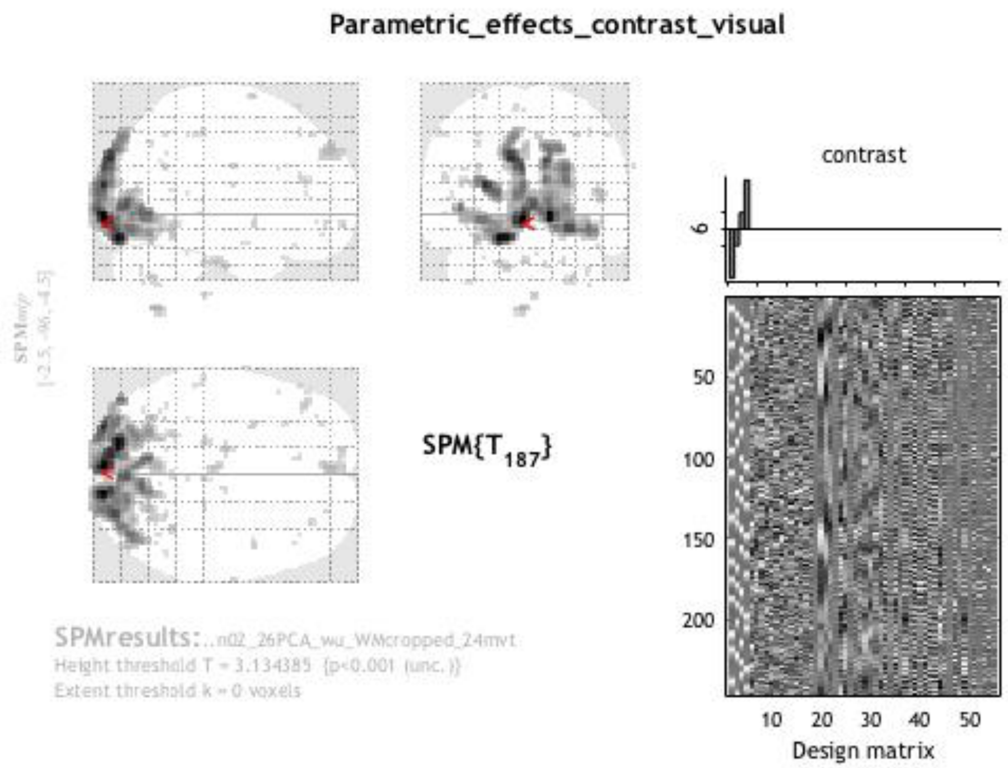
- **Only 6 realign parameters**

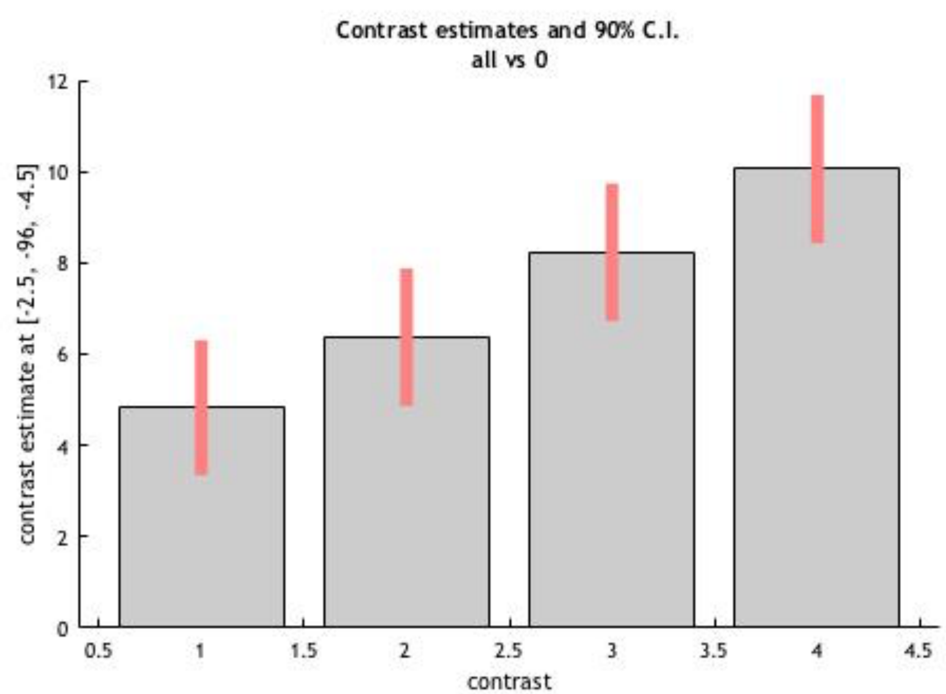


→ T max = 10.18

Denoising motion & physiological-related noise

- **12 PCs + 1 mean for WM, 12 PCs + 1 mean for CSF, 24 movement parameters**

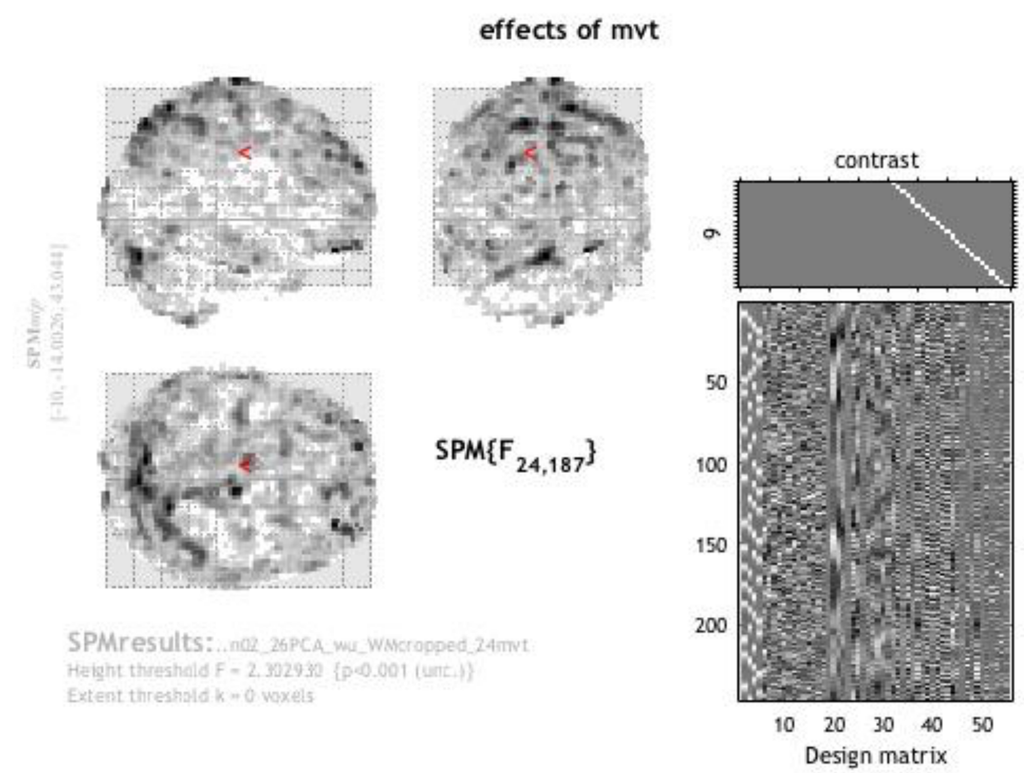


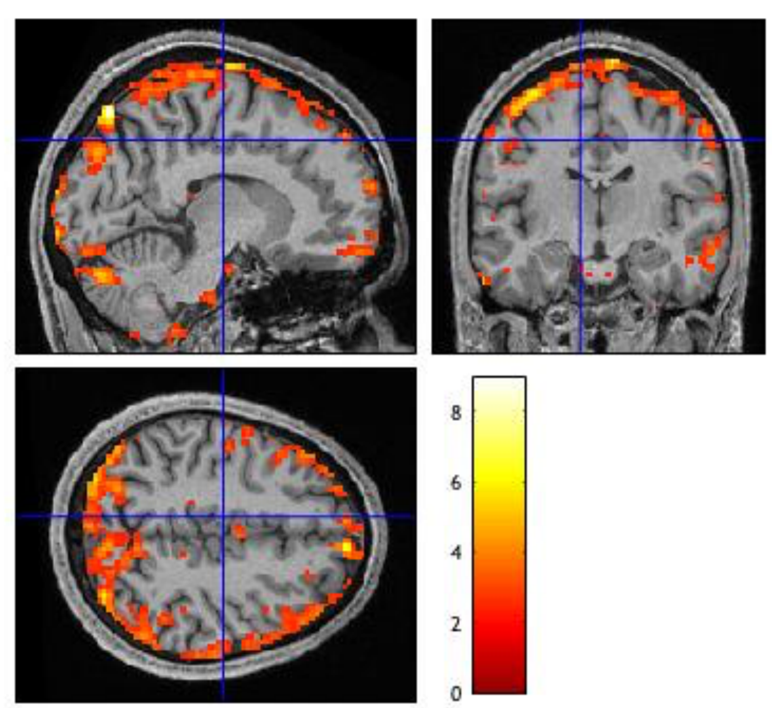


→ **T max = 11.65**

Denoising motion & physiological-related noise

- 12 PCs + 1 mean for WM, 12 PCs + 1 mean for CSF, 24 movement parameters

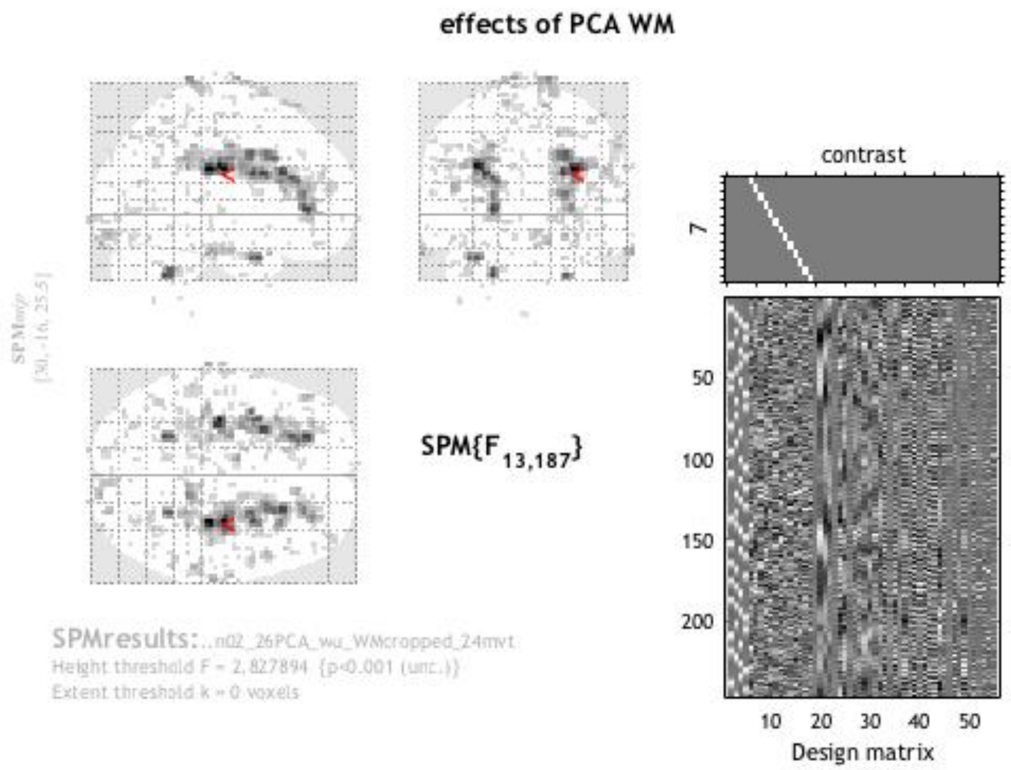


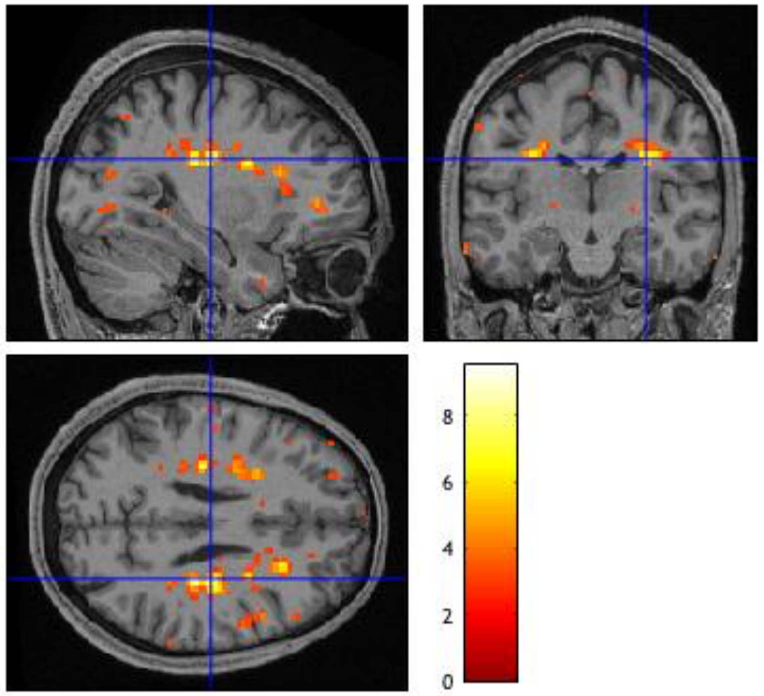


Effects of movement parameters

Denoising motion & physiological-related noise

- **12 PCs + 1 mean for WM, 12 PCs + 1 mean for CSF, 24 movement parameters**

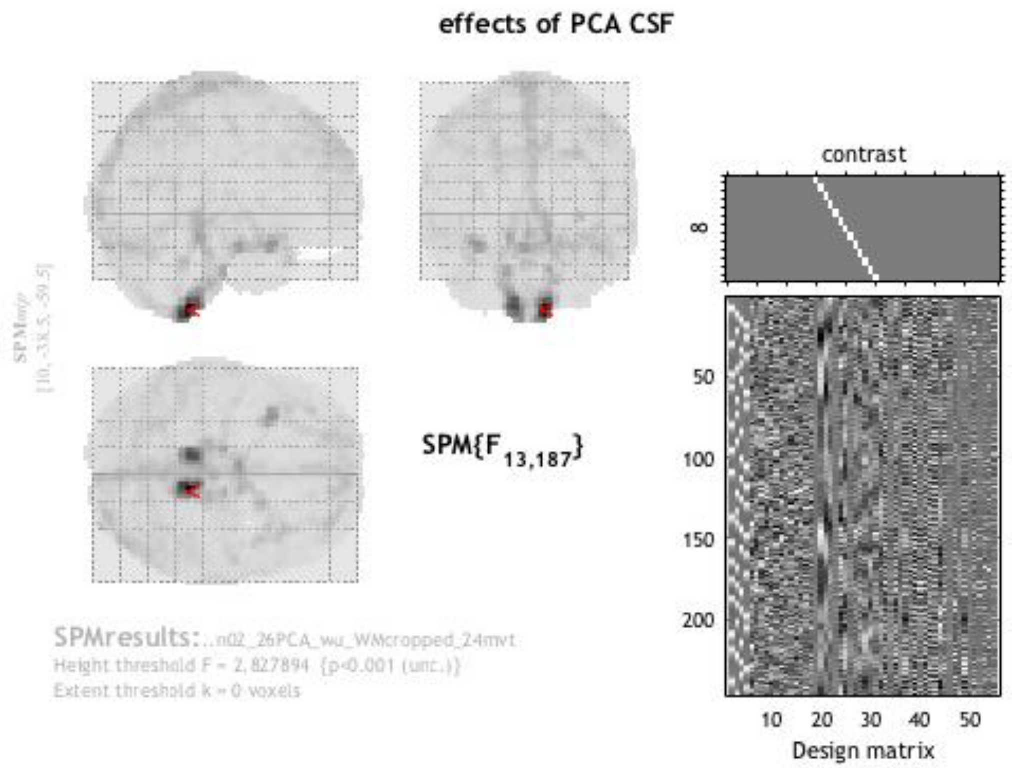


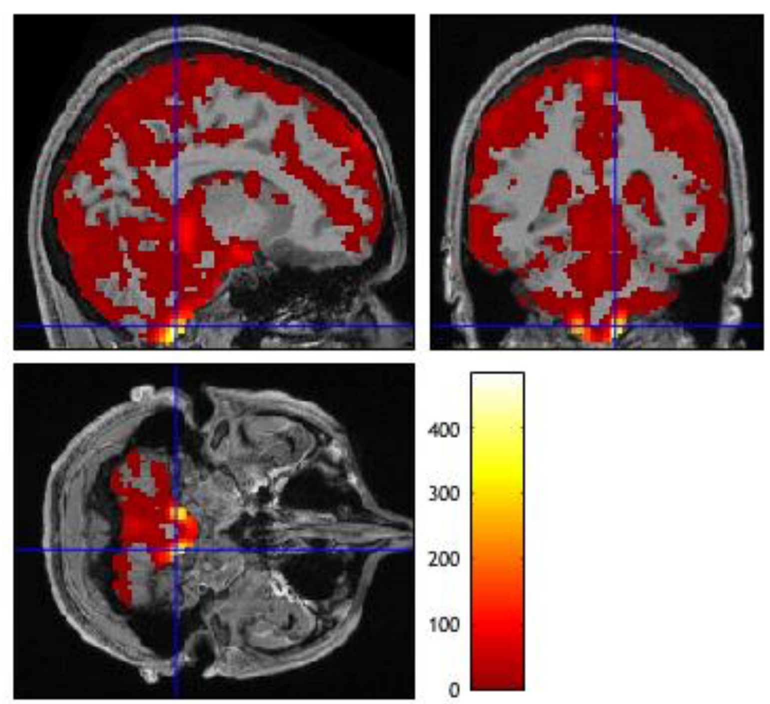


Effects of WM nuisance regressors

Denoising motion & physiological-related noise

- 12 PCs + 1 mean for WM, 12 PCs + 1 mean for CSF, 24 movement parameters



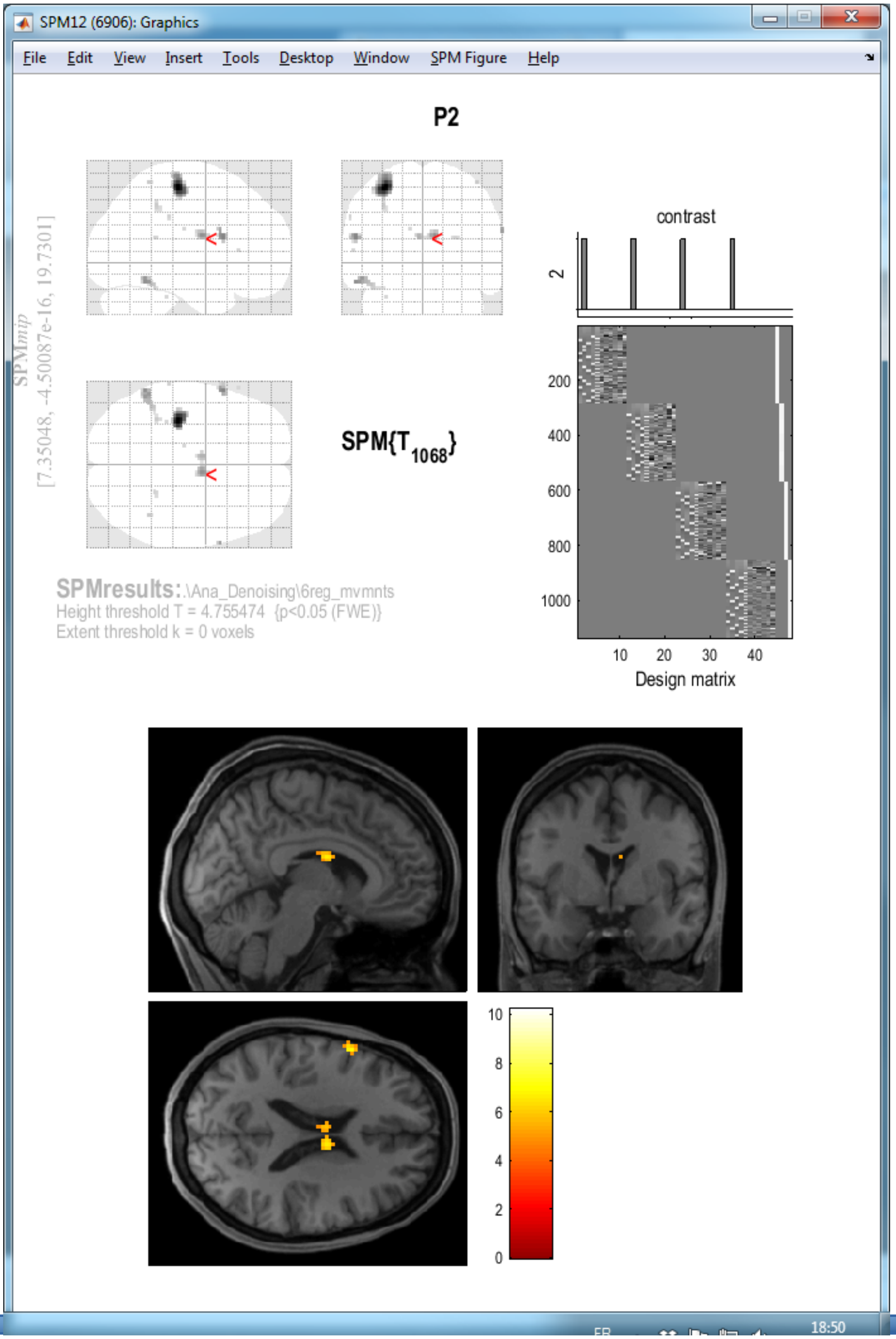


Effects of CSF nuisance regressors

Denoising motion & physiological-related noise

- Other example : **non-null contrast [1 0 0 …], old subject**, right hand stimulation

6 nuisance regressors : realign parameters rp(t)

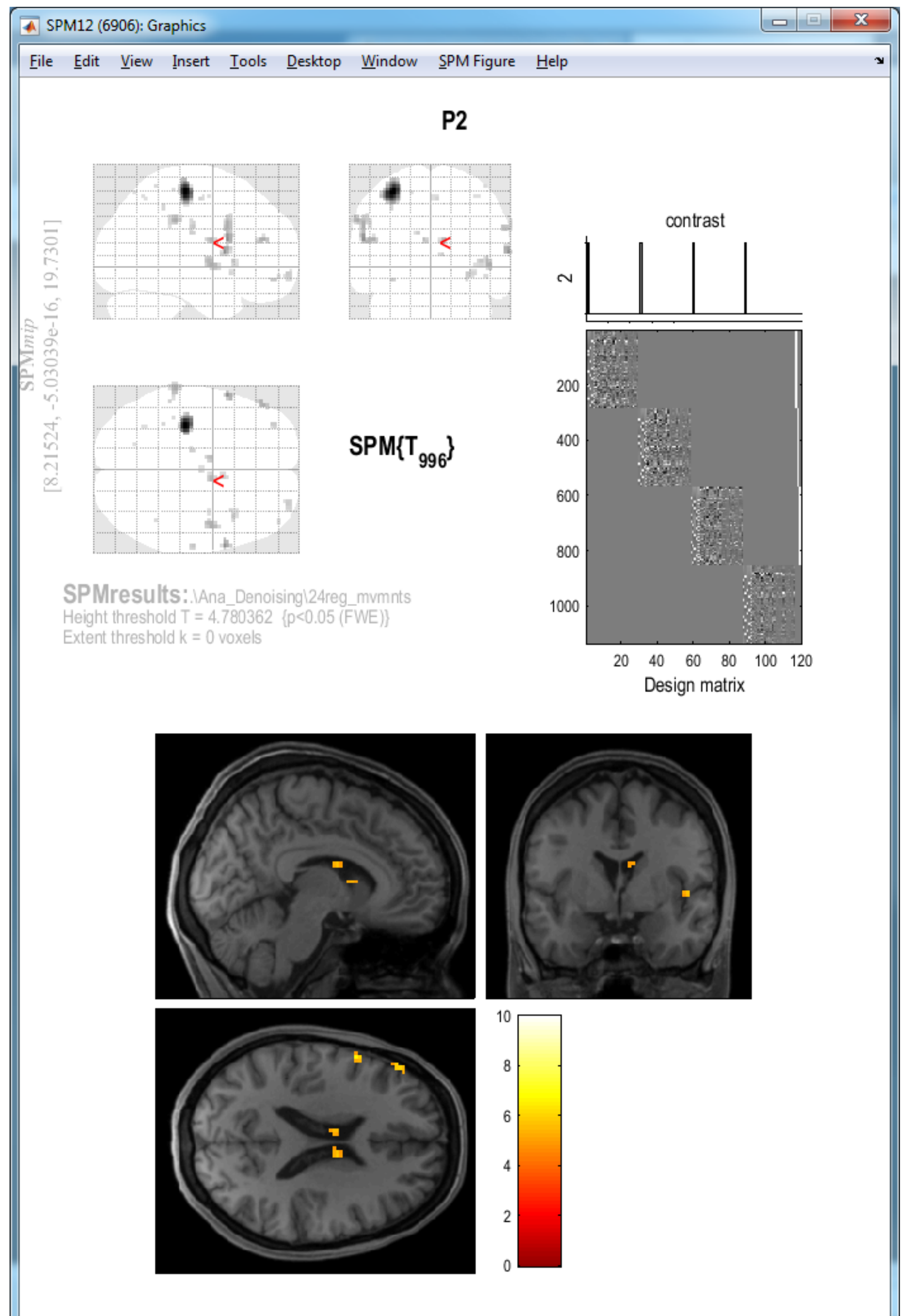


Thanks to Caroline Landelle

Denoising motion & physiological-related noise

- Other example : **non-null contrast [1 0 0 …], old subject**, right hand stimulation

24 nuisance regressors : rp(t), rp^2(t), rp(t-1), rp^2(t-1)

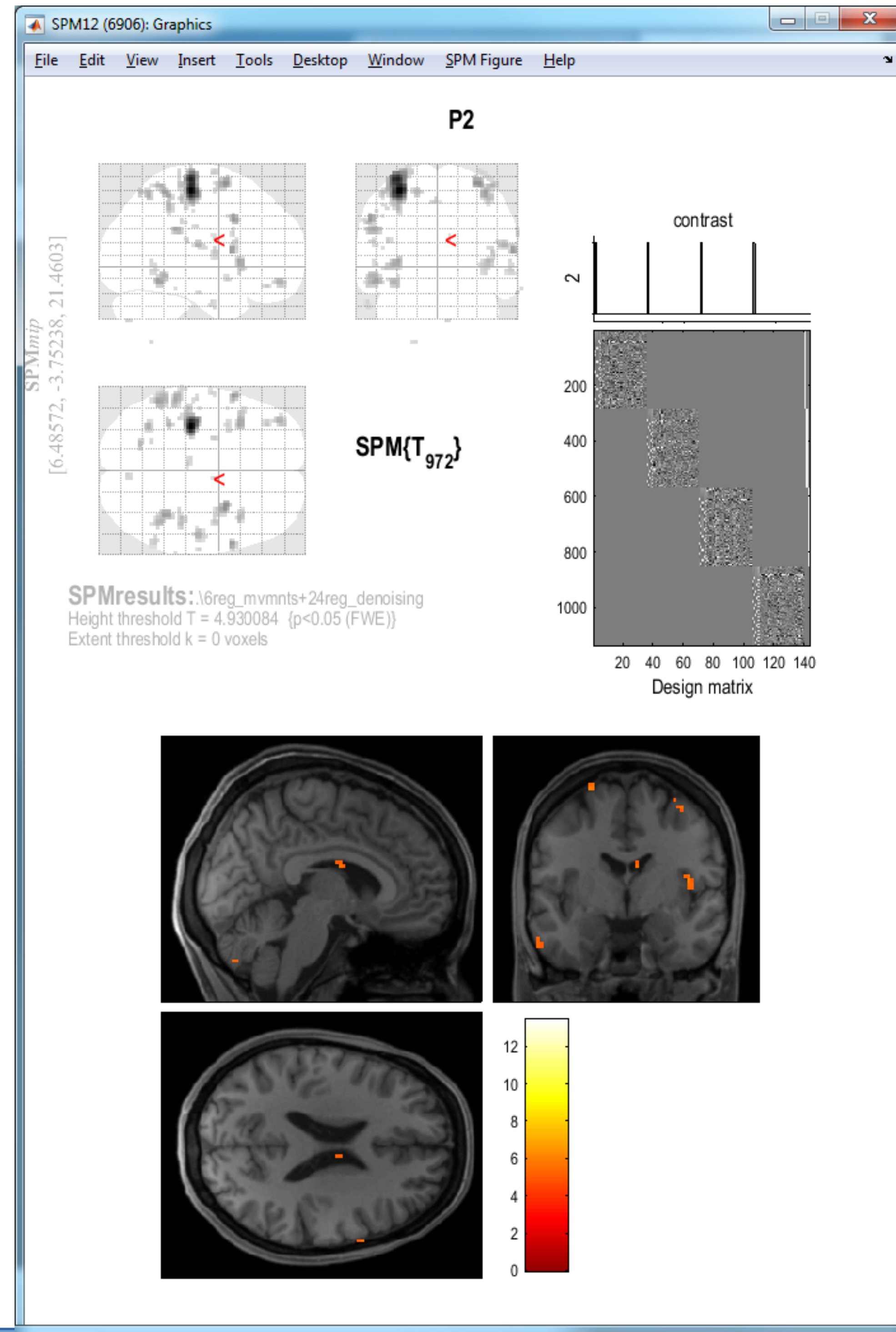


Thanks to Caroline Landelle

Denoising motion & physiological-related noise

- Other example : **non-null contrast [1 0 0 …], old subject**, right hand stimulation

30 nuisance reg : 6 realign parameters rp(t) + 12 PCA WM + 12 PCA CSF

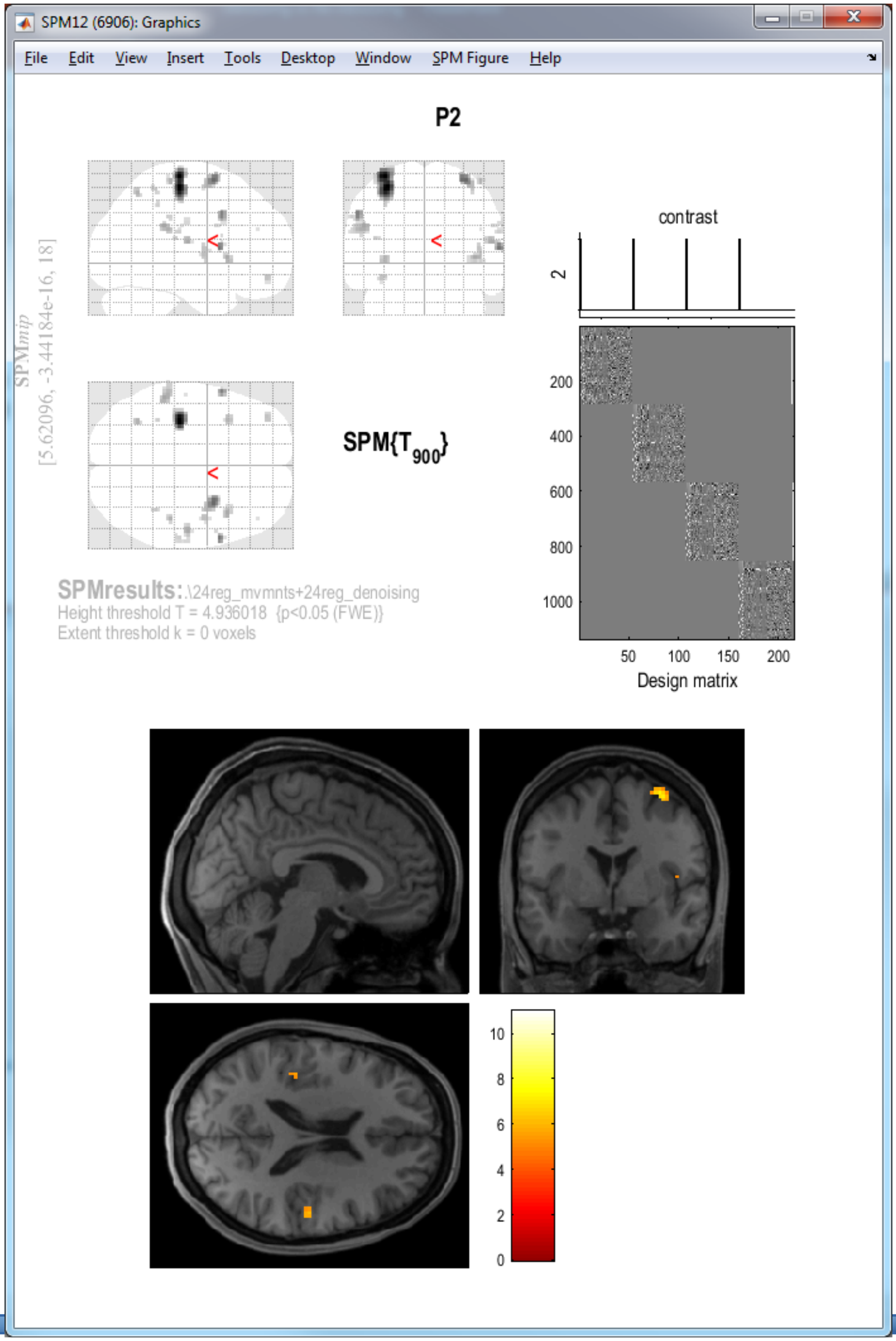


Thanks to Caroline Landelle

Denoising motion & physiological-related noise

- Other example : **non-null contrast [1 0 0 …], old subject**, right hand stimulation

48 nuisance reg : rp(t), rp^2(t), rp(t-1), rp^2(t-1) + 12 PCA WM + 12 PCA CSF



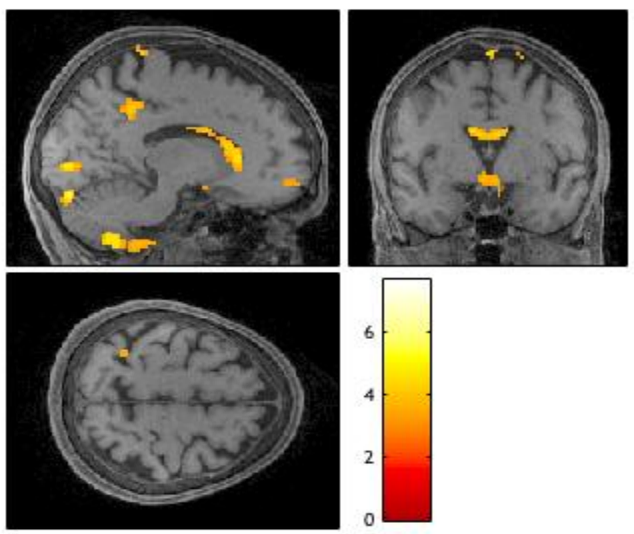
Thanks to Caroline Landelle

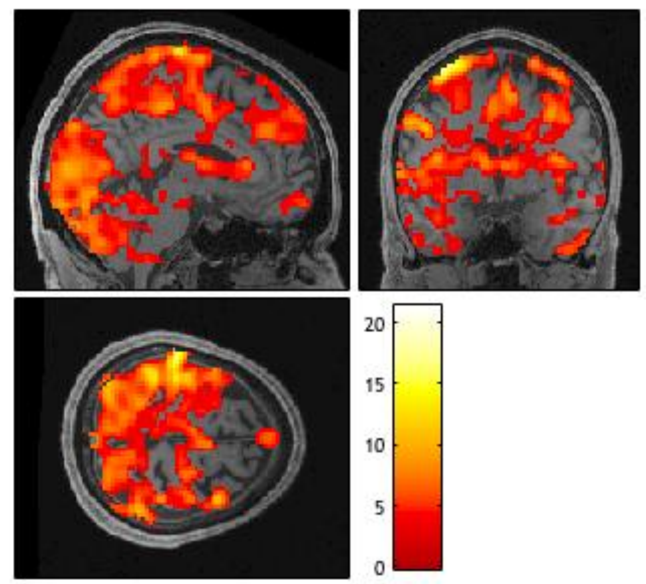
Denoising motion & physiological-related noise

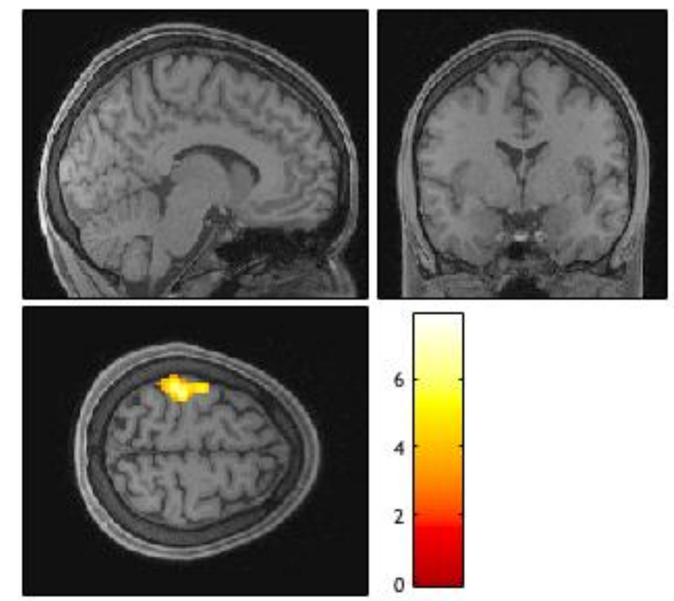
- → **For some subjects, the denoising with 48 nuisance regressors (rp(t), rp^2(t), rp(t-1), rp^2(t-1), 12 PCA WM, 12 PCA CSF) is very efficient**

Loss of ventricular noising activity	Loss of all brain noising activity	Greater statistical values

Before

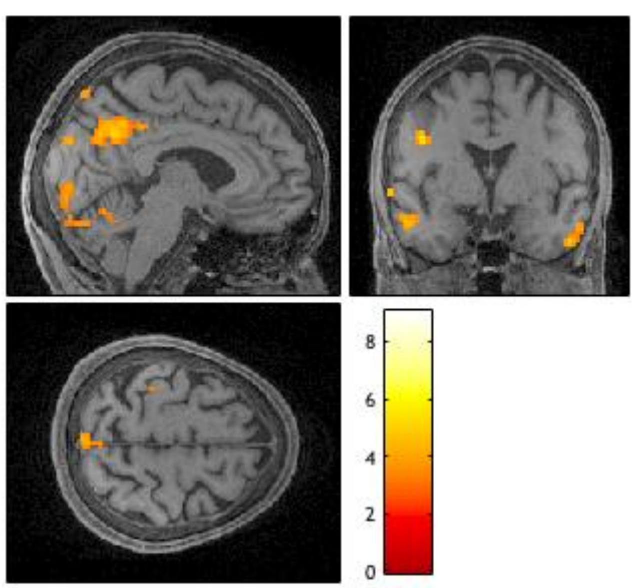


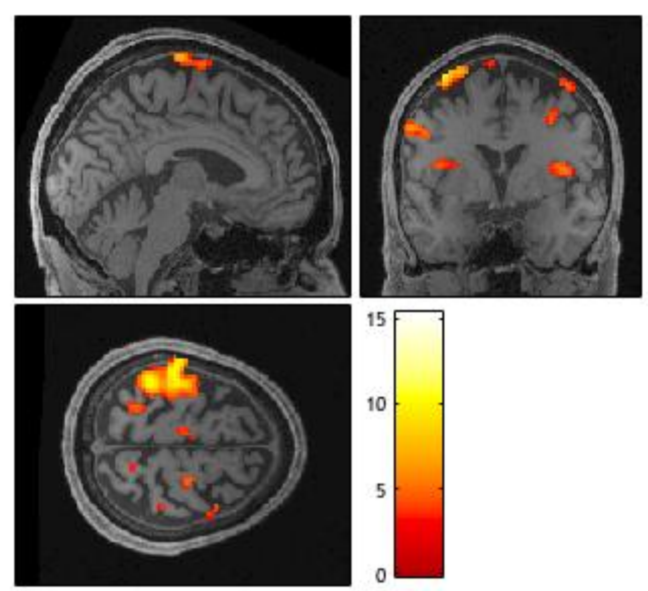


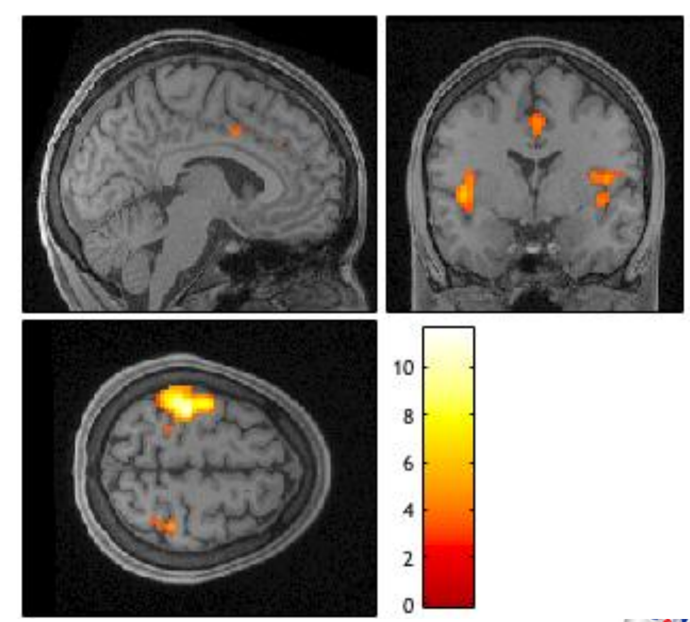


Denoising

After



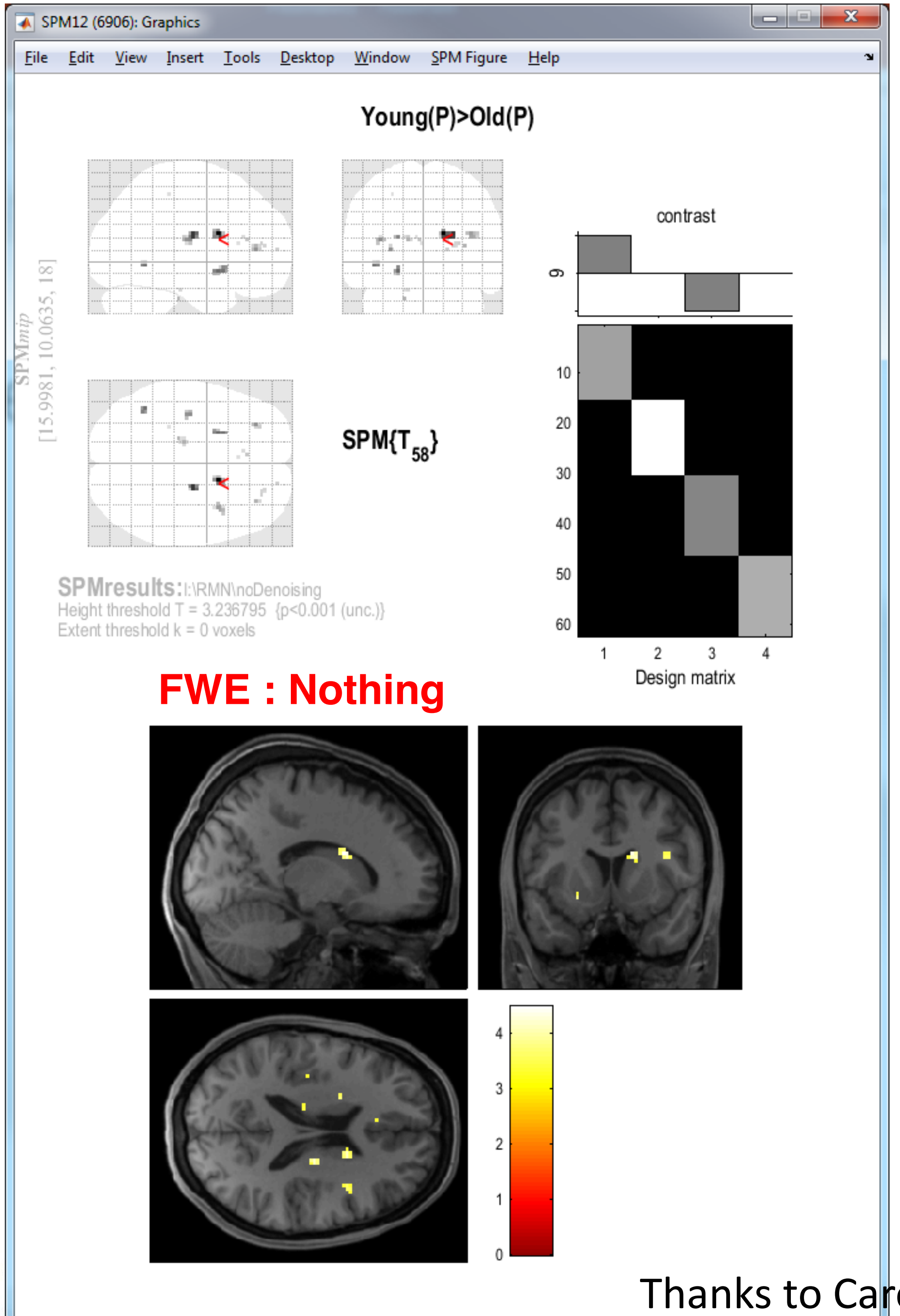


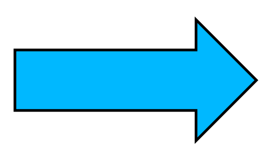


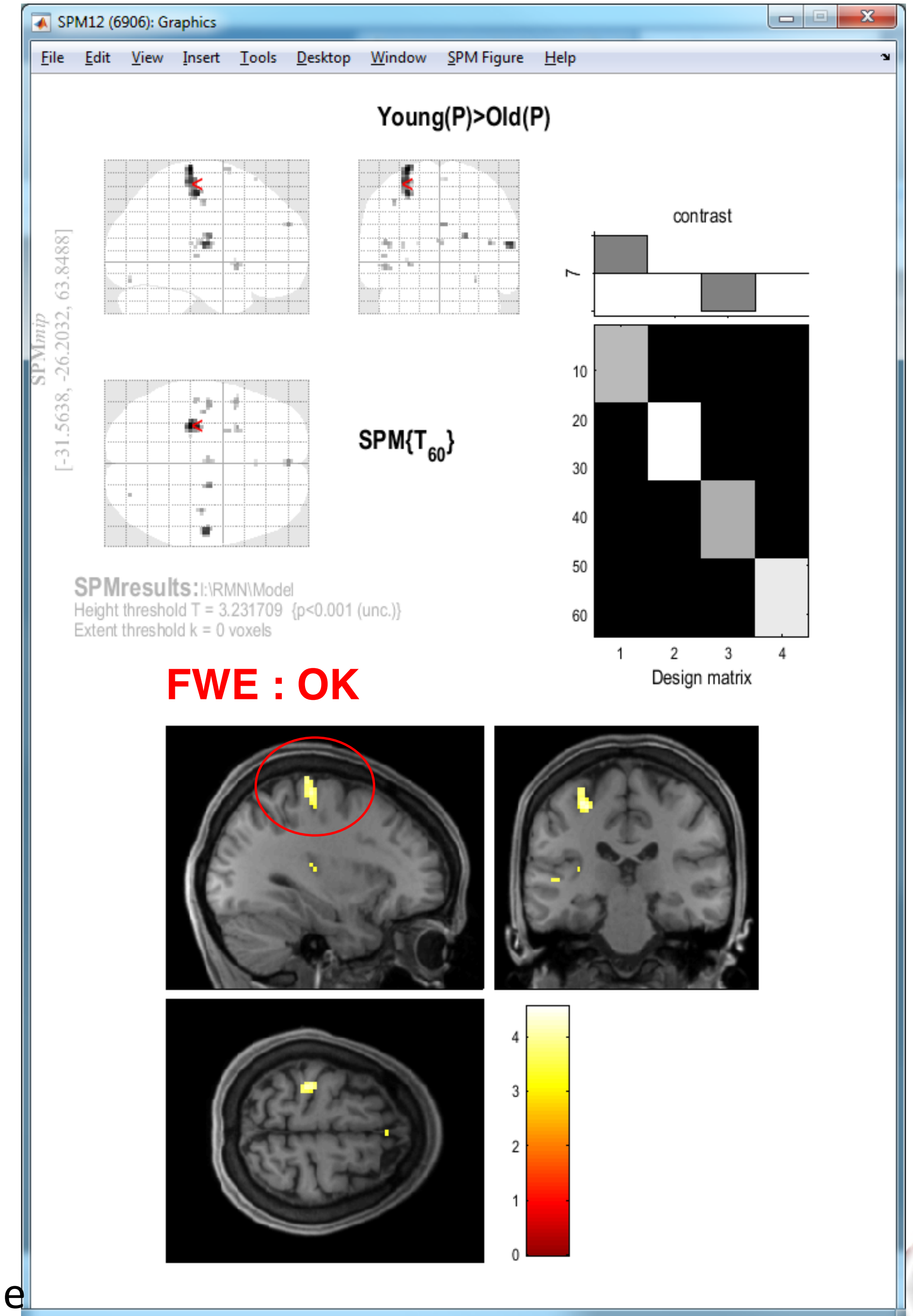
Thanks to Caroline Landelle

Denoising motion & physiological-related noise

- For inter-group comparison, the denoising with 48 nuisance regressors (rp(t), rp^2(t), rp(t-1), rp^2(t-1), 12 PCA WM, 12 PCA CSF) is very efficient







Thanks to Caroline Landelle

Denoising physiological-related noise

- Data-driven denoising methods of physiological noise

Based on Principal Component Analysis (PCA) of noise regions signals : white matter (WM) & Cerebro-Spinal Fluid (CSF)

→ Questions :

- Precise definition of noise region signals (minimizing the effect of partial voluming with other tissue types)
- PCA to be performed on non-smoothed EPI data
- Number of PCs for each tissue ? % of variance explained ?
- **Need to orthogonalize the nuisance regressors from the task-related regressors**

Denoising physiological-related noise

- <u>Data-driven denoising methods of physiological noise</u>

Based on Independent Component Analysis (ICA)

- temporal ICA : PESTICA (Beall and Lowe, 2007)
- spatial ICA : CORSICA (Perlbarg & al, 2007)
- spatial ICA : ICA-AROMA (Pruim & al, 2015) & FIX-ICA (Salimi-Khorshidi & al, 2014) : available in FSL

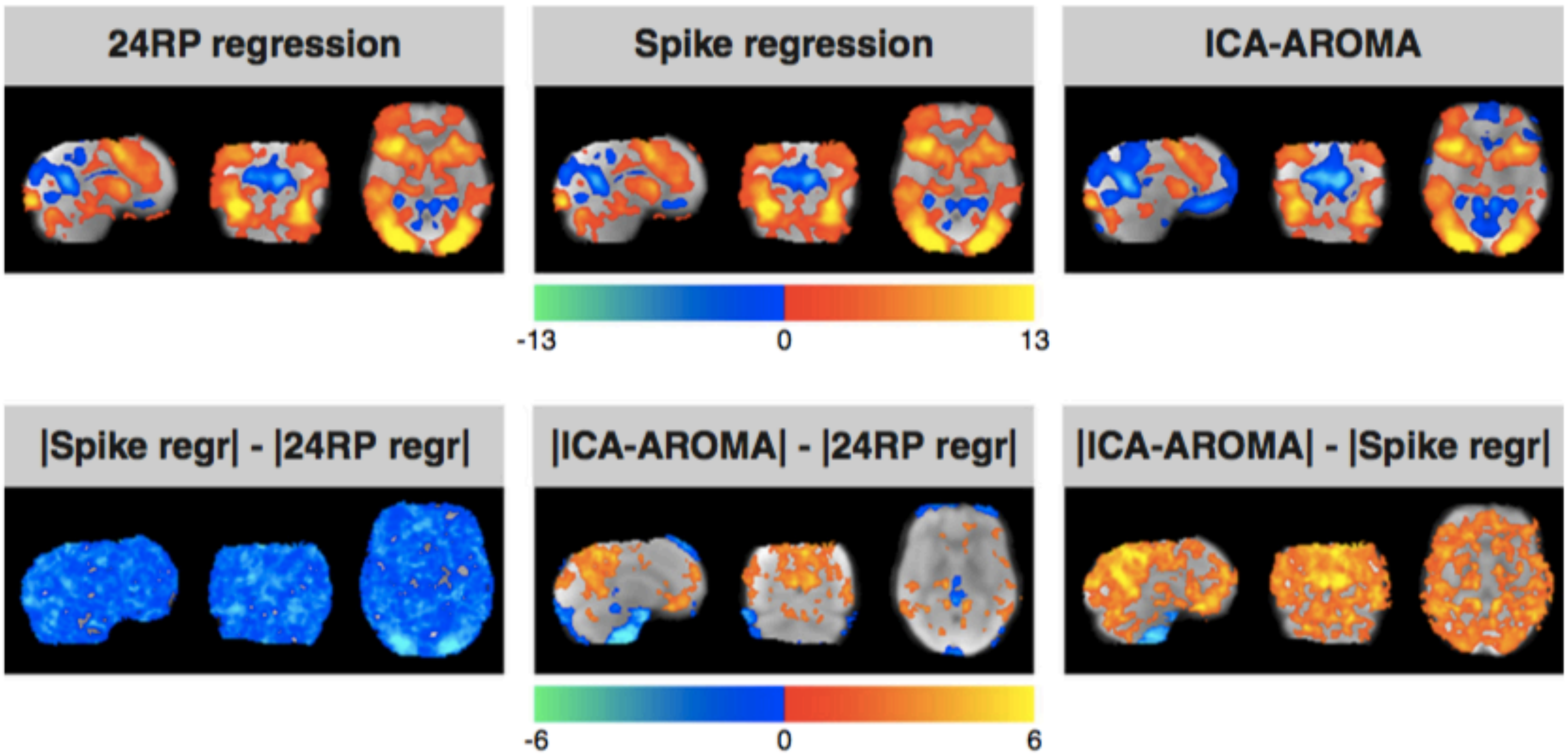
→ Question :
Choice of the components to be removed to the EPI data ?

Denoising physiological-related noise

- Data-driven denoising methods of physiological noise

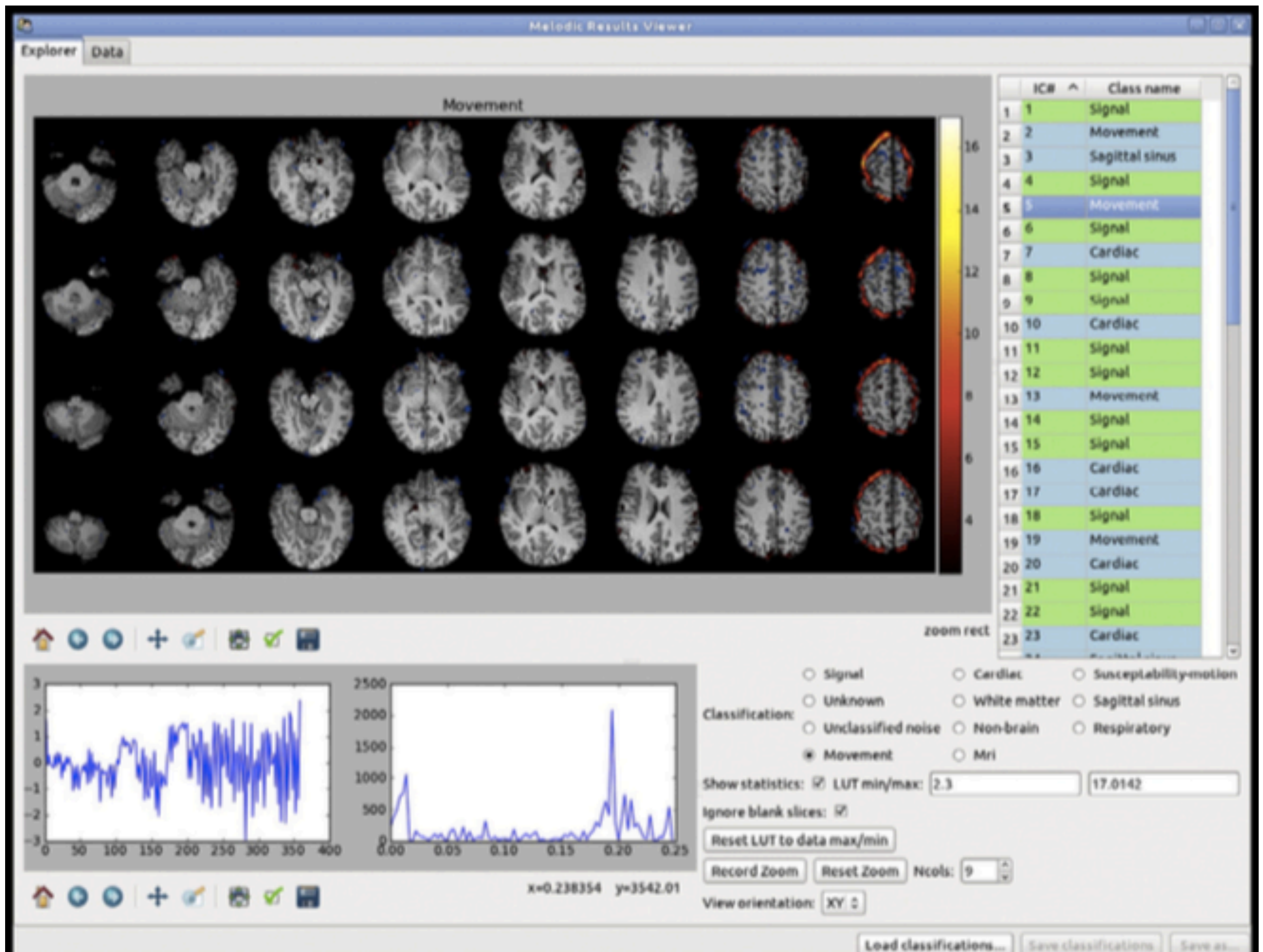
  Based on Independent Component Analysis (ICA)
  - ICA-AROMA (Pruim & al, 2015) : available in FSL

    → remove motion-related ICA components from FMRI data



Denoising physiological-related noise

- <u>Data-driven denoising methods of physiological noise</u>
  Based on Independent Component Analysis (ICA)
- FIX-ICA (Salimi-Khorshidi & al, 2014) : available in FSL
  → aims to auto-classify ICs into "good" vs "bad" components



Denoising physiological-related noise

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  Based on Independent Component Analysis (ICA)
- FIX-ICA (Salimi-Khorshidi & al, 2014) : available in FSL
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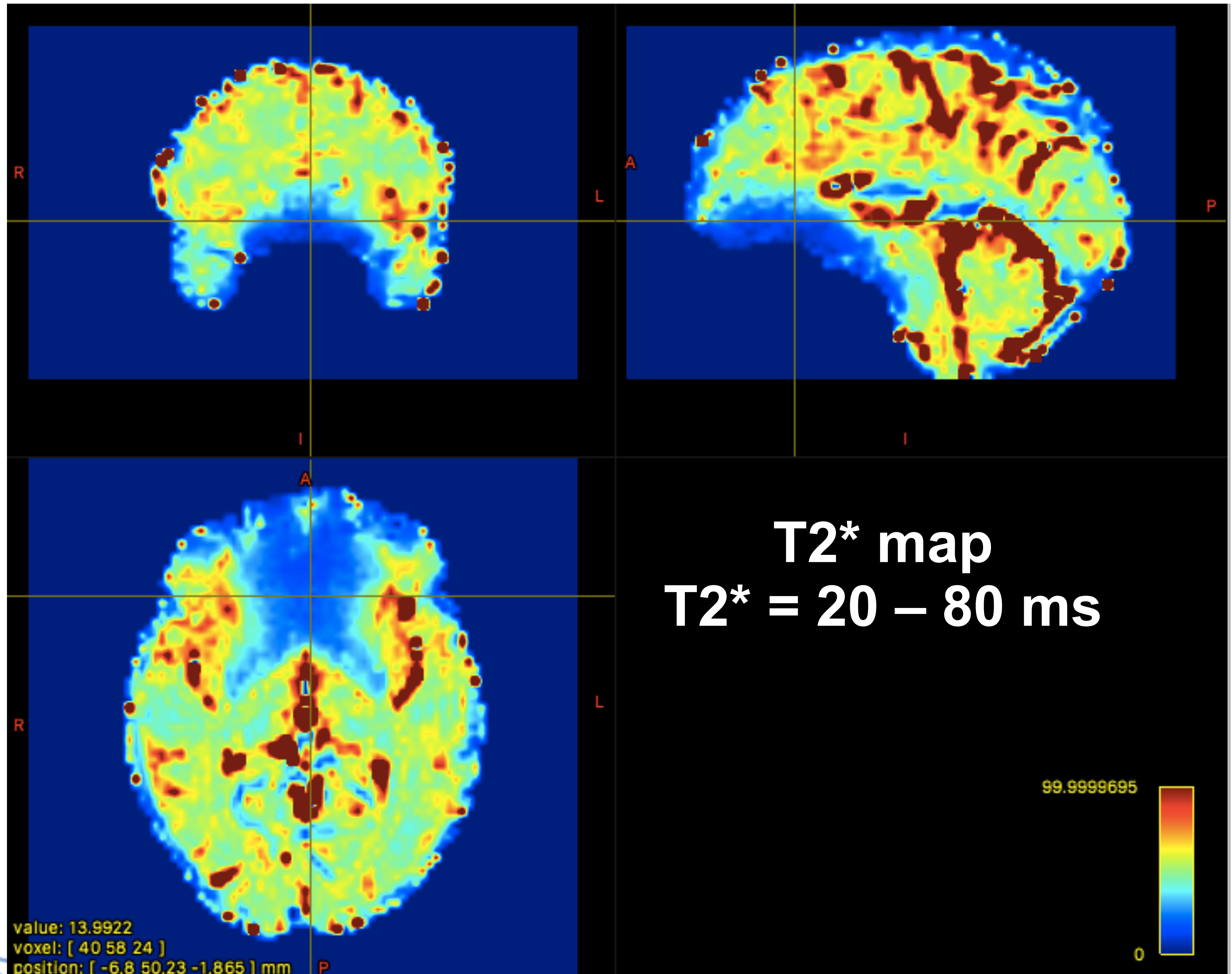
- Example : FMRIB's ICA-based Xnoiseifier – FIX (FSL)
  http://www.fmrib.ox.ac.uk/analysis/FIX-training/fix_eg.html

Next step : Multi-Echo acquisitions

- **A single-echo EPI (TE ≈ 30 ms) is sub-optimal because of the huge variability of T2* across brain regions**



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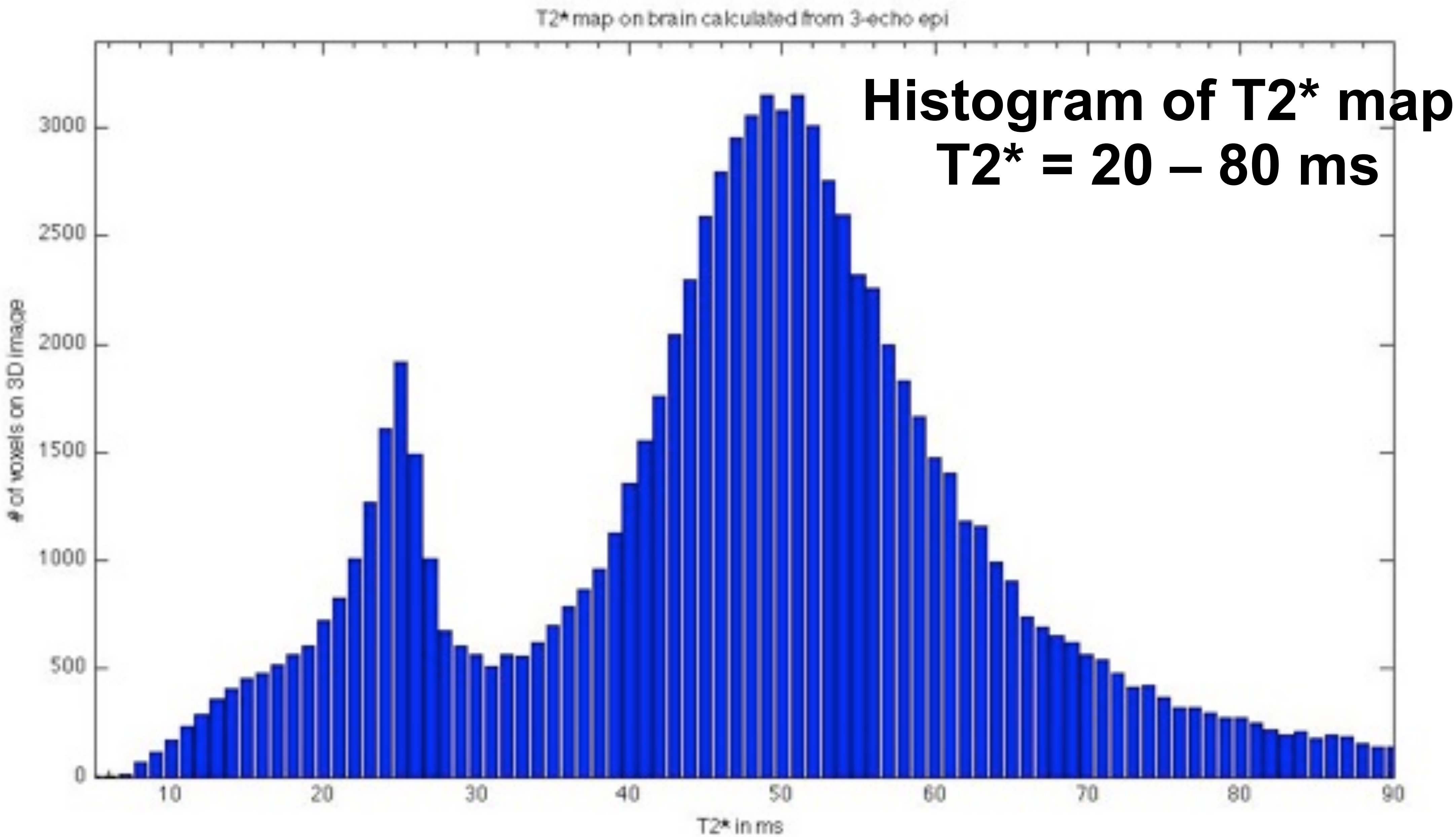
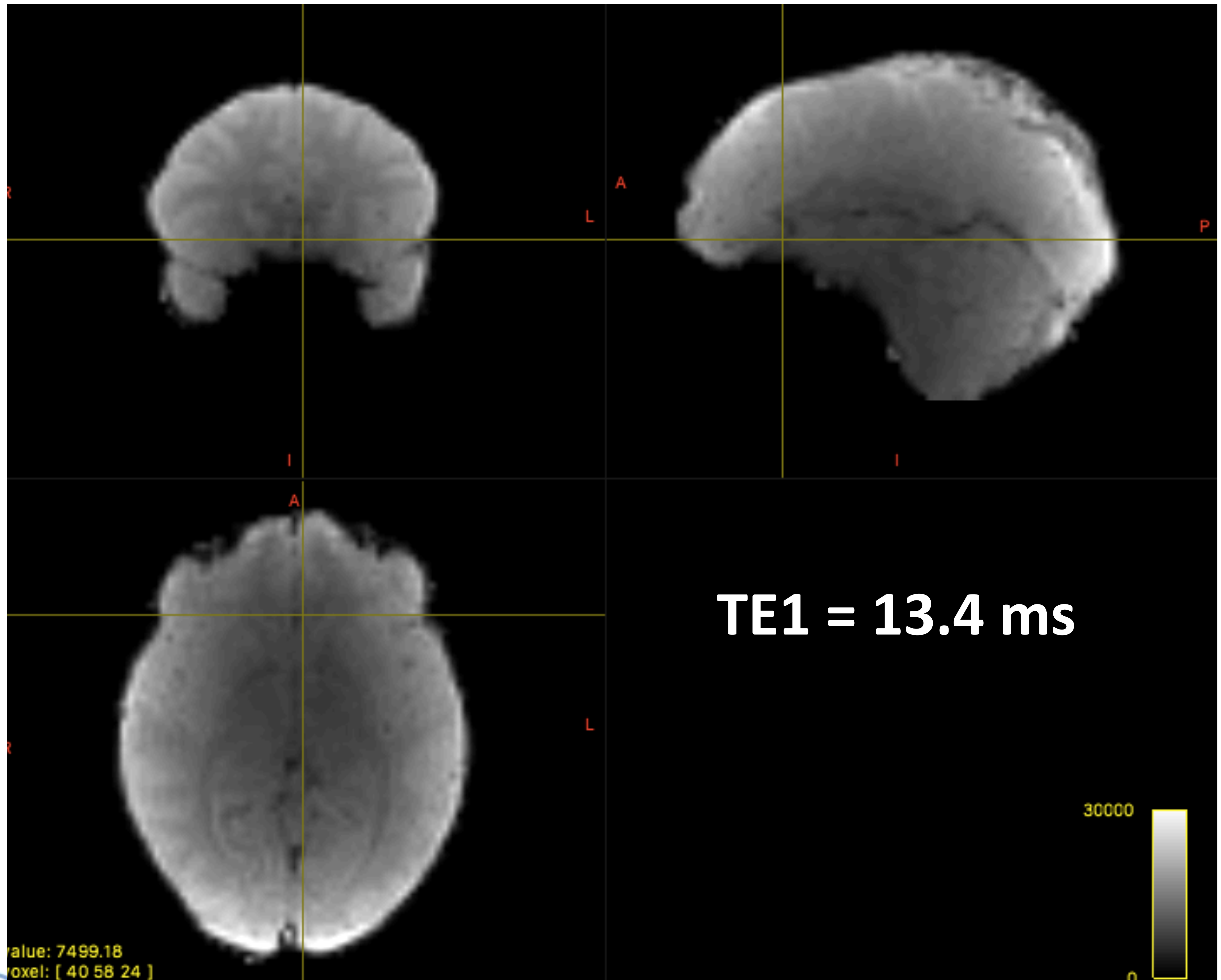


Next step : Multi-Echo acquisitions

- **EPI Multi-bande Multi-Echo (MB 3 ME 3, iPAT 2, TR 1425 ms)**



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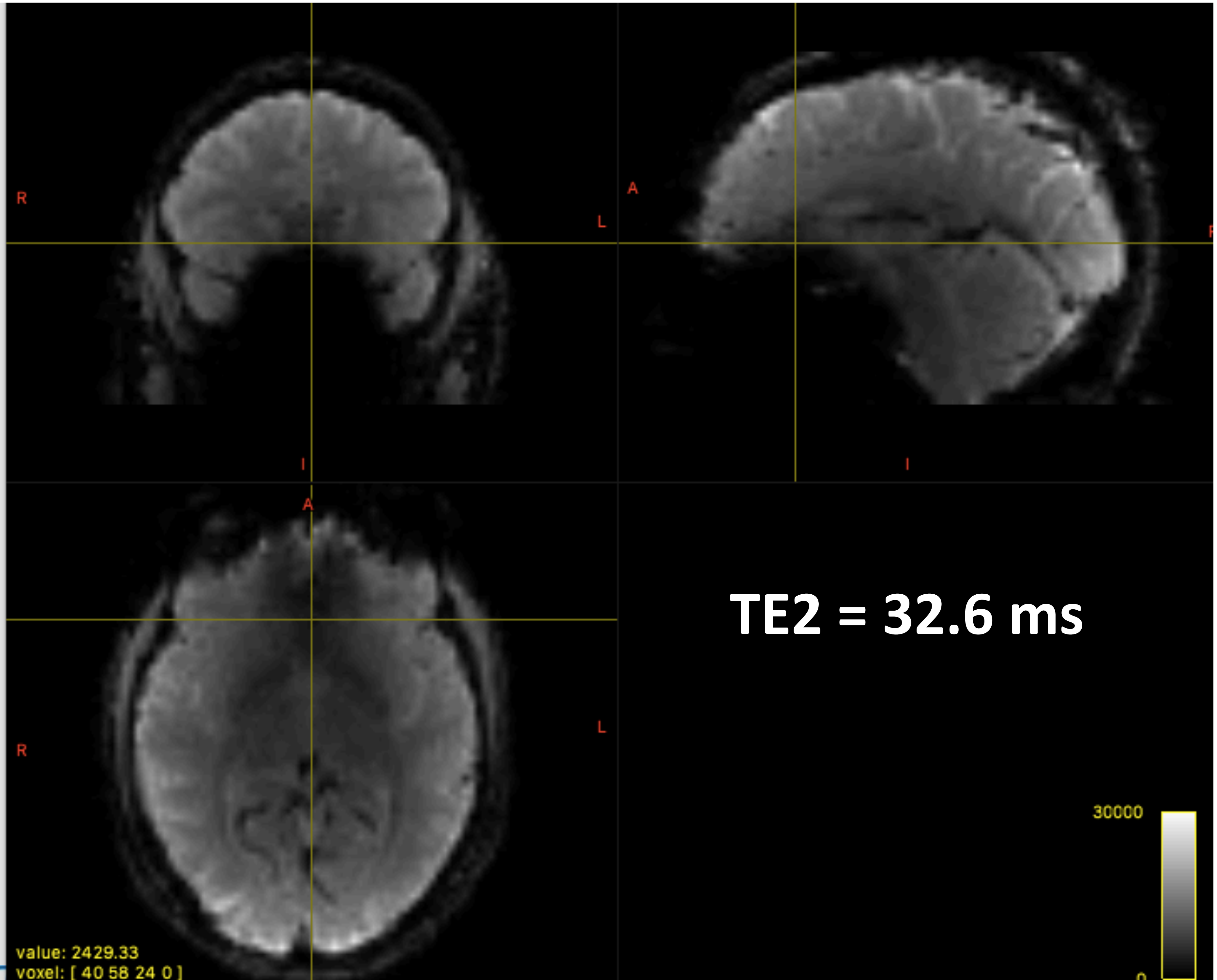

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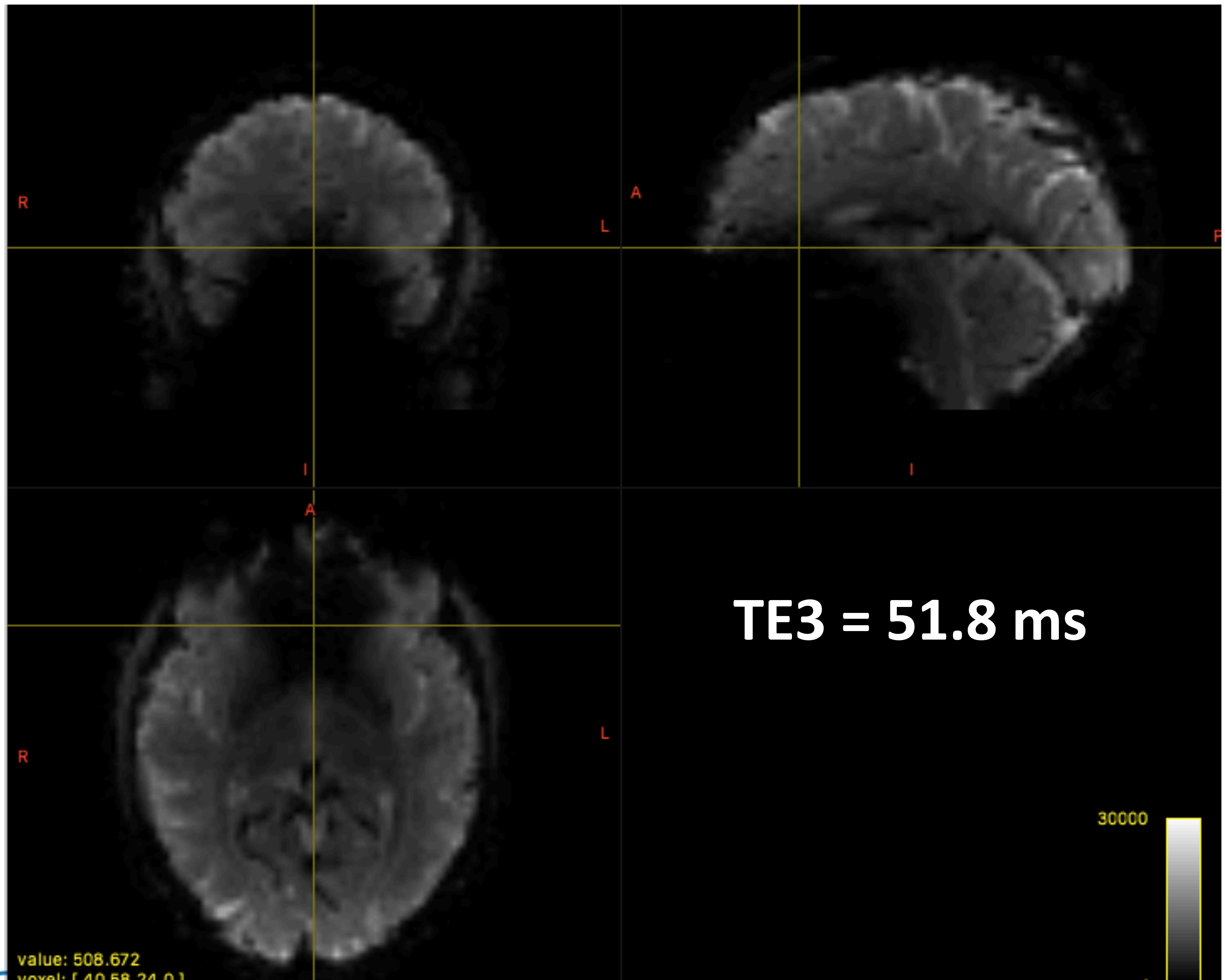
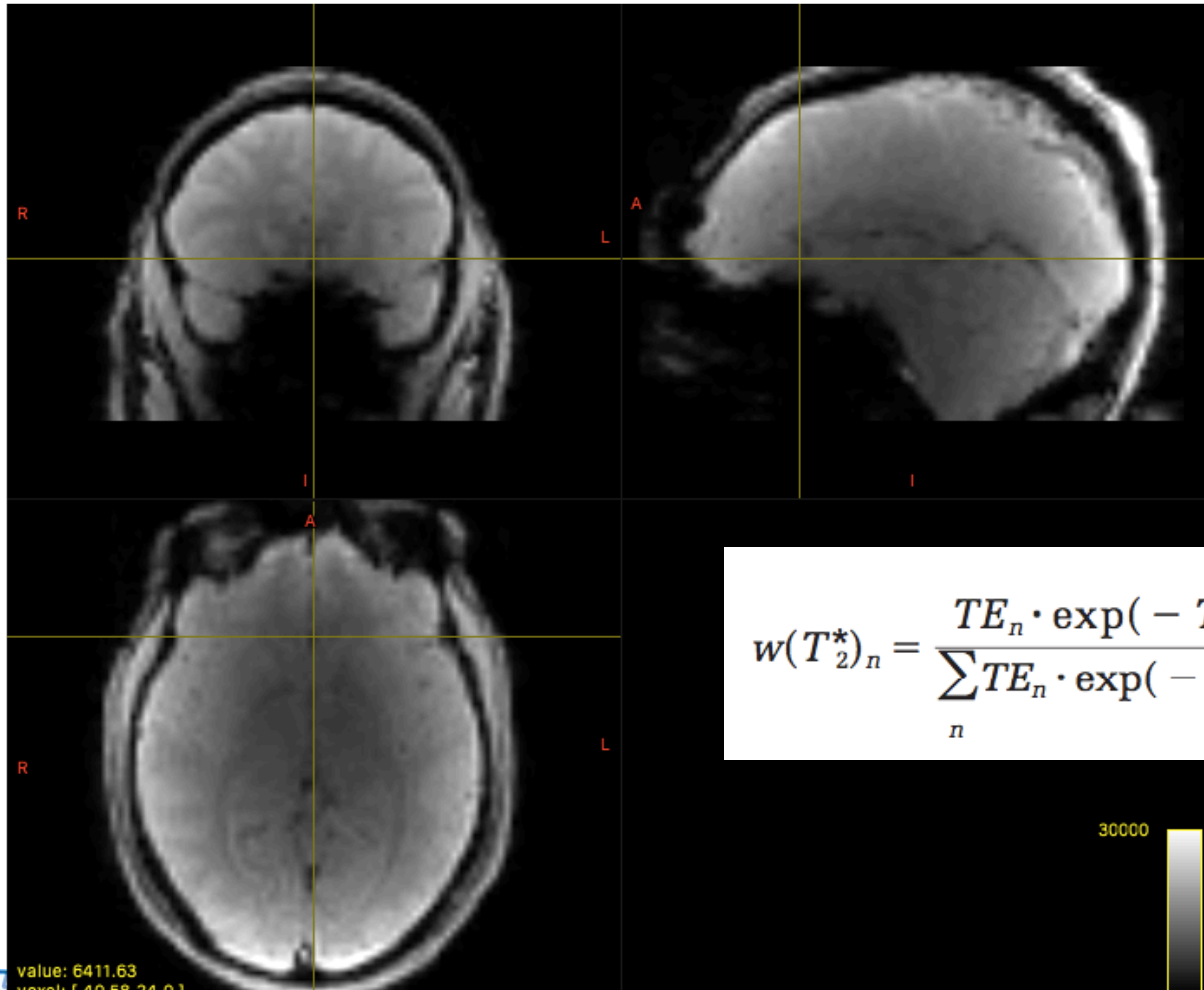
- **EPI Multi-bande Multi-Echo (MB 3 ME 3, iPAT 2, TR 1425 ms)**



Next step : Multi-Echo acquisitions

- --> 1/ Multi-Echo combination (Poser & al, 2006)

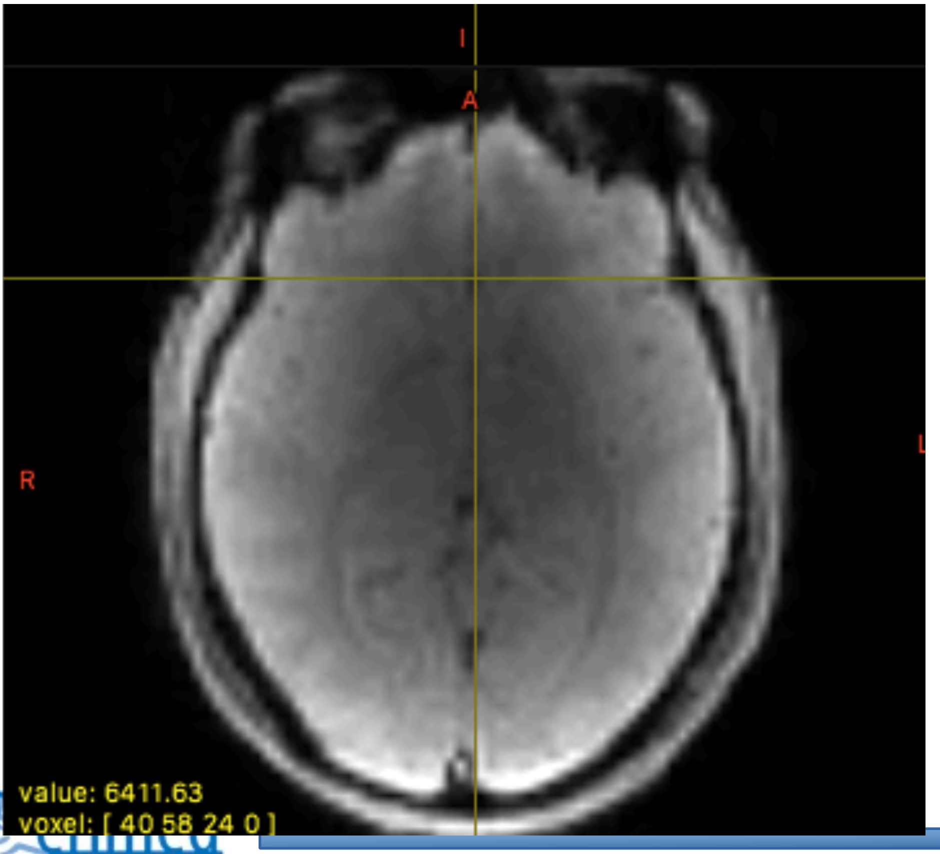


$$w(T_2^*)_n = \frac{TE_n \cdot \exp(-TE_n/T^*_{2(fit)})}{\sum_n TE_n \cdot \exp(-TE_n/T^*_{2(fit)})}$$

Next step : Multi-Echo acquisitions

- → 1/ Multi-Echo combination (Poser & al, 2006)

Multi-echo fMRI offers clear advantages for imaging brain regions such as the orbitofrontal cortex and inferior temporal lobes, which are prone to susceptibility distortions and signal dropouts



Next step : Multi-Echo acquisitions

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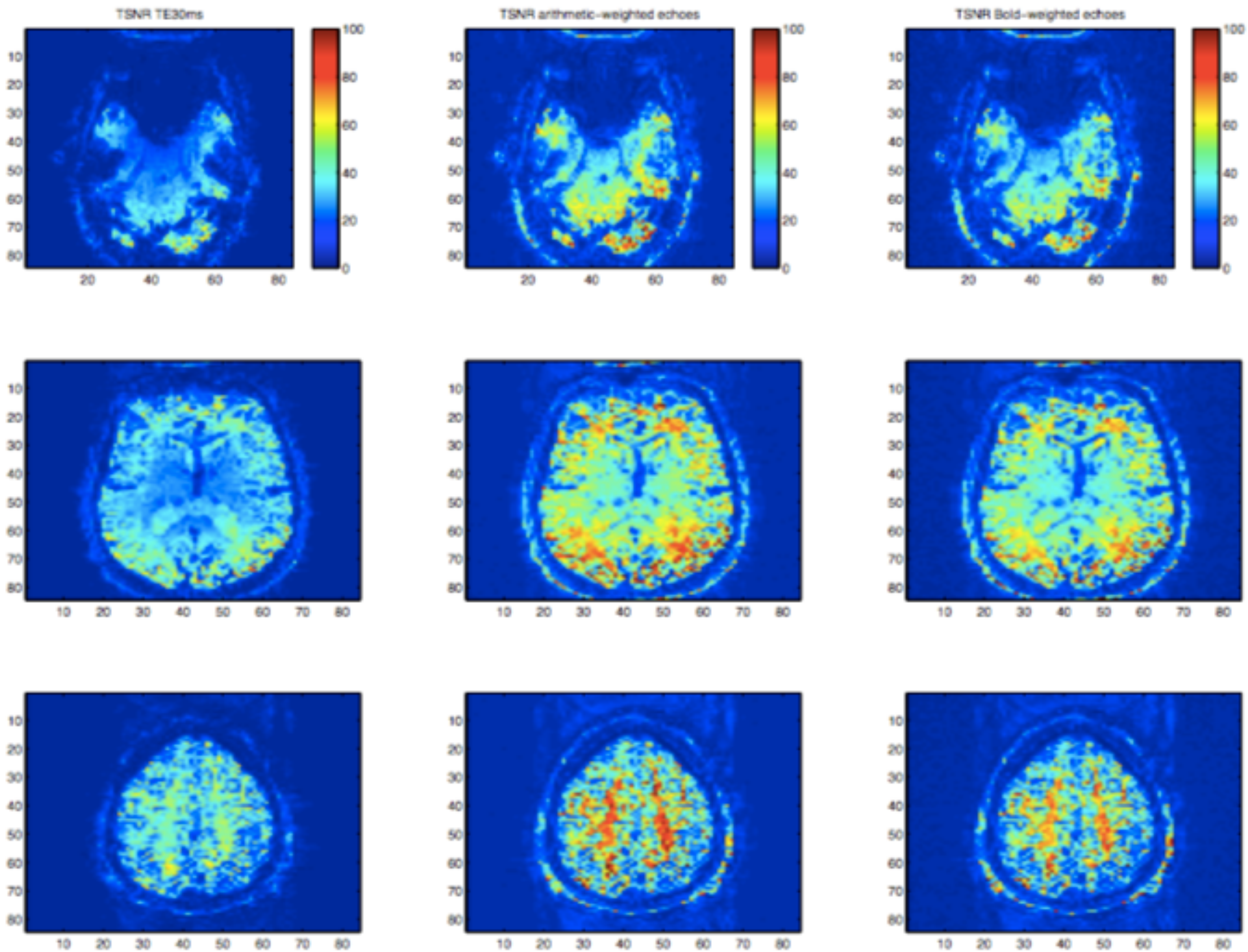


Next step : Multi-Echo acquisitions

- → **2/ Multi-Echo acquisitions for denoising**

- **Signals can be recorded at a short TE which is assumed to have minimal T2*- weighting and mainly sensitive to fluctuations in the net magnetization S0.**

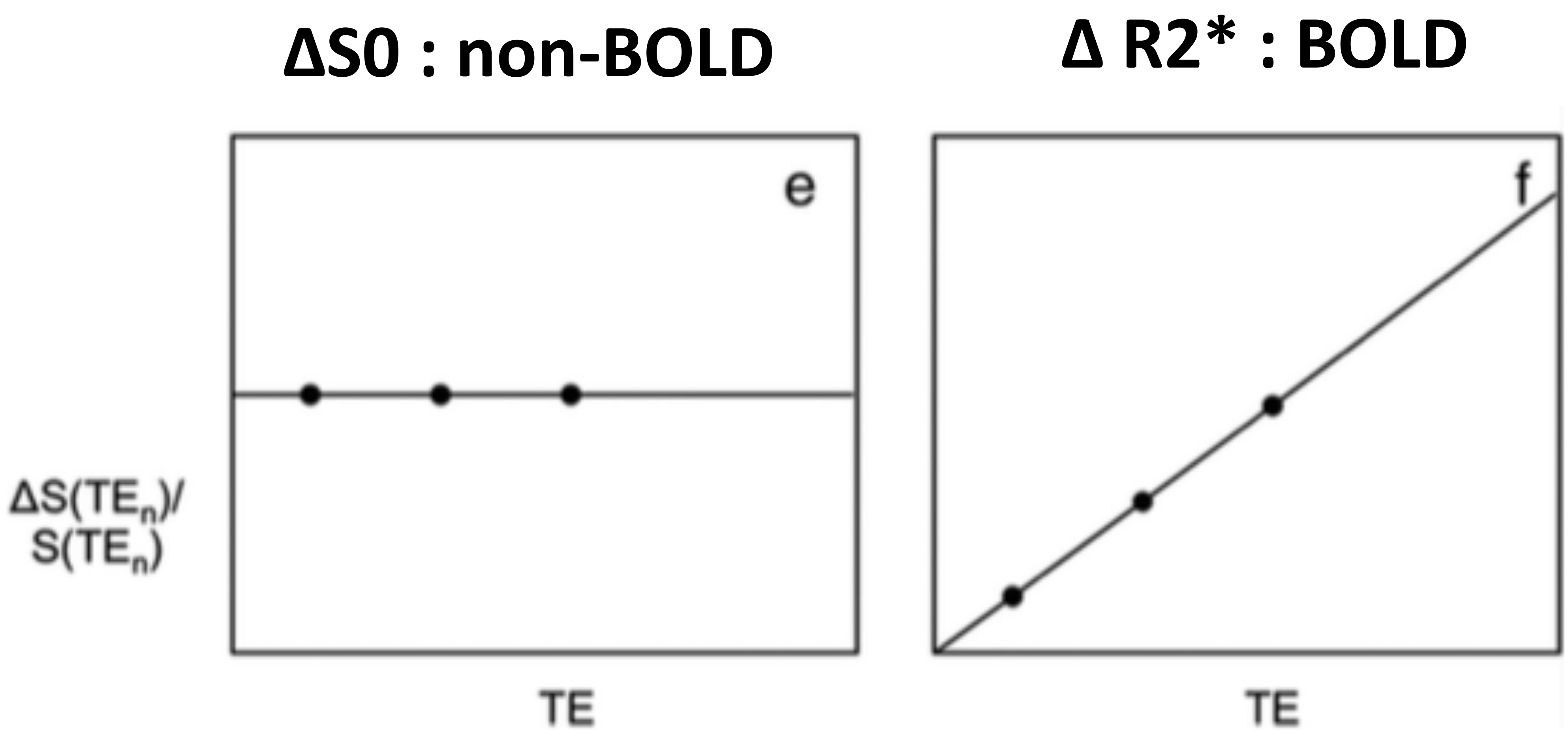
→ **The short TE signal can then be regressed out from time series acquired at a longer TE that is optimized for BOLD sensitivity (Bright and Murphy, 2013; Buur et al., 2008).**

Next step : Multi-Echo acquisitions

- → 2/ Multi-Echo acquisitions for denoising

  Kundu et al. (2012) proposed a multi-echo denoising strategy based on independent component analysis (ME- ICA).

  This method exploits the fact that BOLD components must exhibit a linear dependence with TE, whereas non-BOLD components must exhibit no dependence with TE.



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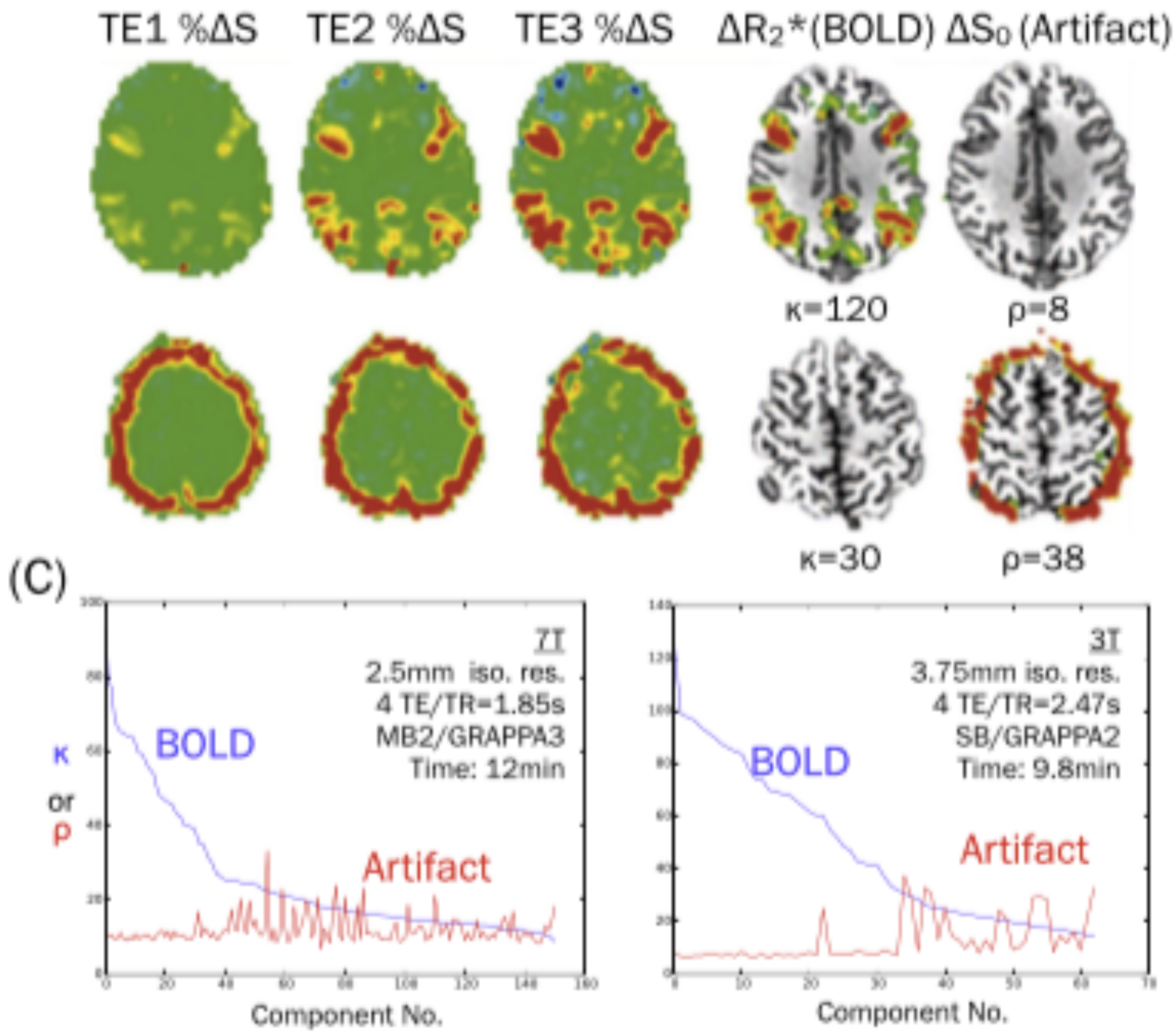

General Conclusion

- **Denoising BOLD fMRI data is crucial !**

- **It has to be done with a lot of care …**

References

- **Special issue of NeuroImage 2017**

NeuroImage 154 (2017) 128–149

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Methods for cleaning the BOLD fMRI signal

César Caballero-Gaudes[a,*], Richard C. Reynolds[b]

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- **PhysIO Toolbox**

Journal of Neuroscience Methods 276 (2017) 56–72

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Journal of Neuroscience Methods

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The PhysIO Toolbox for Modeling Physiological Noise in fMRI Data

Lars Kasper[a,b,*], Steffen Bollmann[c], Andreea O. Diaconescu[a], Chloe Hutton[d], Jakob Heinzle[a], Sandra Iglesias[a], Tobias U. Hauser[d,e], Miriam Sebold[f], Zina-Mary Manjaly[g], Klaas P. Pruessmann[b], Klaas E. Stephan[a,d,h]

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