Hamburg, June 8, 2014
Educational Course
"The Art and Pitfalls of fMRI Preprocessing"

Data-driven Structured Noise Removal (FIX)

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Overview

- **Noise sources** in fMRI data
- **Cleaning approaches** for fMRI data
- **ICA decomposition for structured noise removal**
  - Independent Component Analysis (ICA)
  - Characteristics of “good” and “bad” components: hand labelling
- An automated ICA-based cleaning approach: **FMRIB’s ICA-based Xnoiseifier (FIX)**
  - FIX cleaning approach
  - Validations/applications

Noise sources in fMRI data

- Head motion
- Cardiac pulse
- Respiration
- Susceptibility
- Hardware

How noise affects fMRI data analysis?

- Task-based fMRI (GLM-based analysis): ***a-priori* hypothesis** of the signal of interest. If noise is **correlated with the task-related activity** it can produce false activations/deactivations/etc.

- Resting state fMRI: **NO *a-priori* hypothesis** about the signal of interest: **any correlation with noise** will produce false positives

Cleaning approaches for fMRI data

- Band-pass temporal filtering

! the removal of high frequencies may remove signal that contributes to the resting state networks (Niazy et al., 2011)

- Regression of motion parameters

! often not capable of completely remove the effect of motion

Alternatives:

- spike removal ("scrubbing") (Power et al., 2012)
- Higher number of motion parameters (Satterthwaite et al., 2013)

- Regression of global (mean) signal

! the removal of global signal introduces spurious anti-correlations that are difficult to interpret (Murphy et al., 2009)

Alternatives:

- regression of mean WM signal and mean CSF signal (Weissenbacher et al., 2009)

Cleaning approaches for fMRI data

- Physiological recordings (RETROICOR - Glover et al., 2000; Shmueli et al., 2007; regression of RVT - Birn et al., 2006)

  ! need external physiological recordings

- Multi-echo EPI sequences (Bright and Murphy 2013; Kundu et al., 2012)

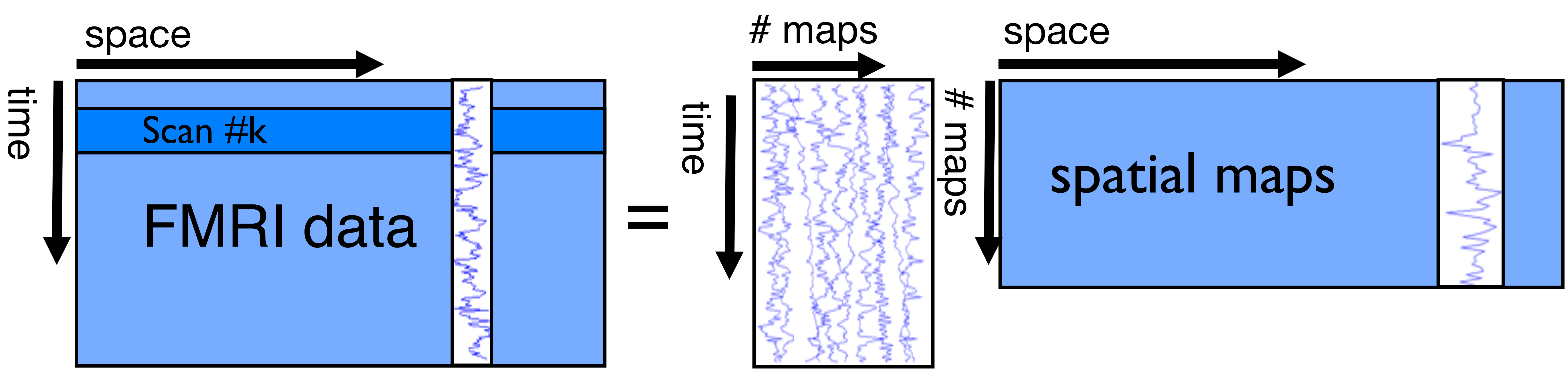
  ! need of specific acquisition sequence

- Independent Component Analysis (ICA)
  - Data-driven
  - No need for external recordings or specific sequence
  - Able to identify and remove different sources of noise
  - ! the components need to be classified

ICA decomposition
for structured noise removal

Independent Component Analysis (ICA)

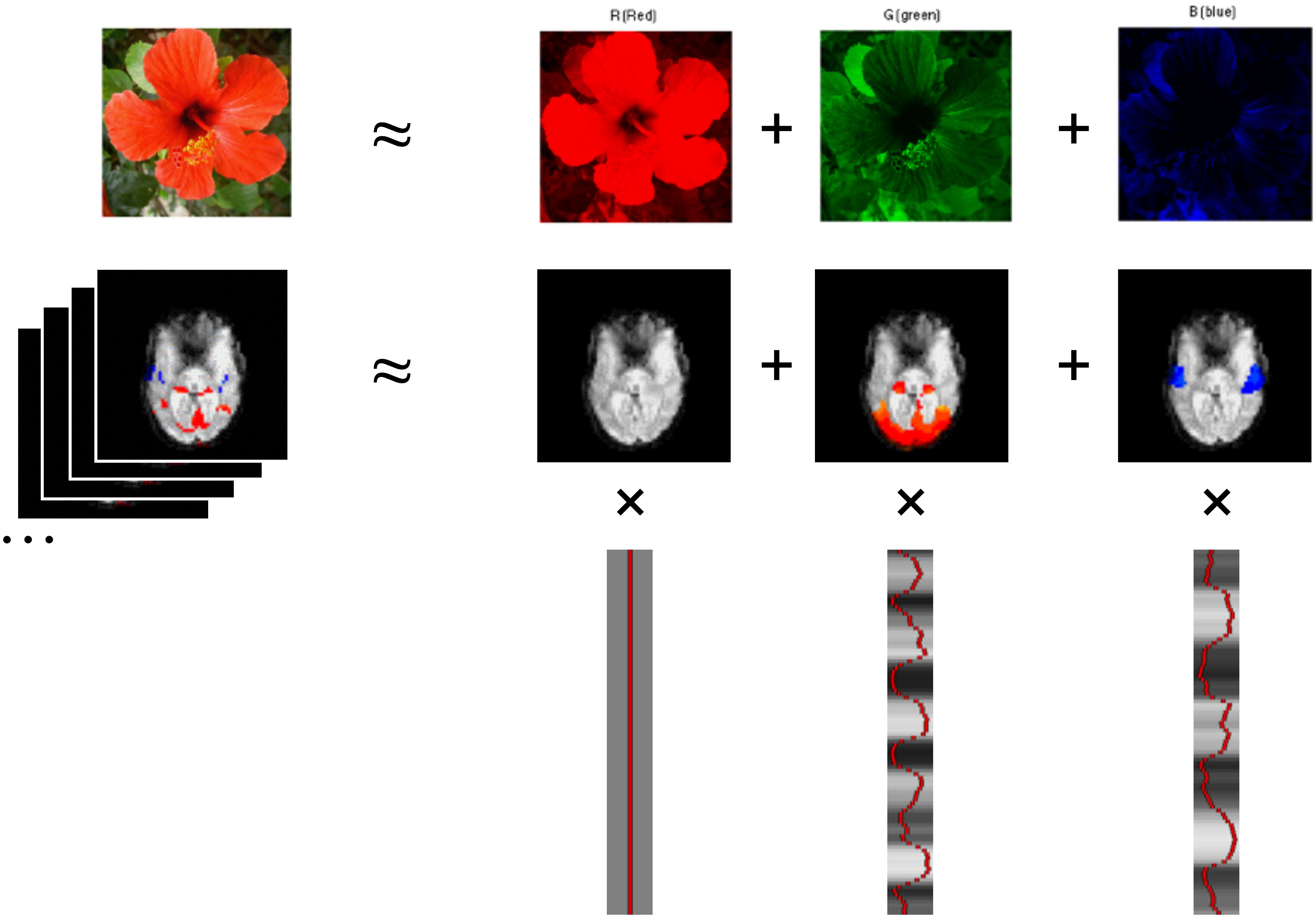
- Data-driven multivariate analysis: Decomposes data into a set of distinct spatial maps each with its own distinct time-course



- SPATIAL ICA for fMRI: data is represented as a 2D matrix and decomposed into a set of spatially independent maps and a set of time-courses

What are components?

(what does ICA output?)



How to use ICA to identify noise and clean the data?

1. Standard preprocessing: rigid-body head motion correction, drift removal (high-pass temporal filtering), (optional) spatial smoothing
2. Single-subject ICA to decompose the preprocessed data into a set of independent components.
3. Identification of noisy components: independent components (ICs) classification
4. Removal of the contribution of those components from the preprocessed data

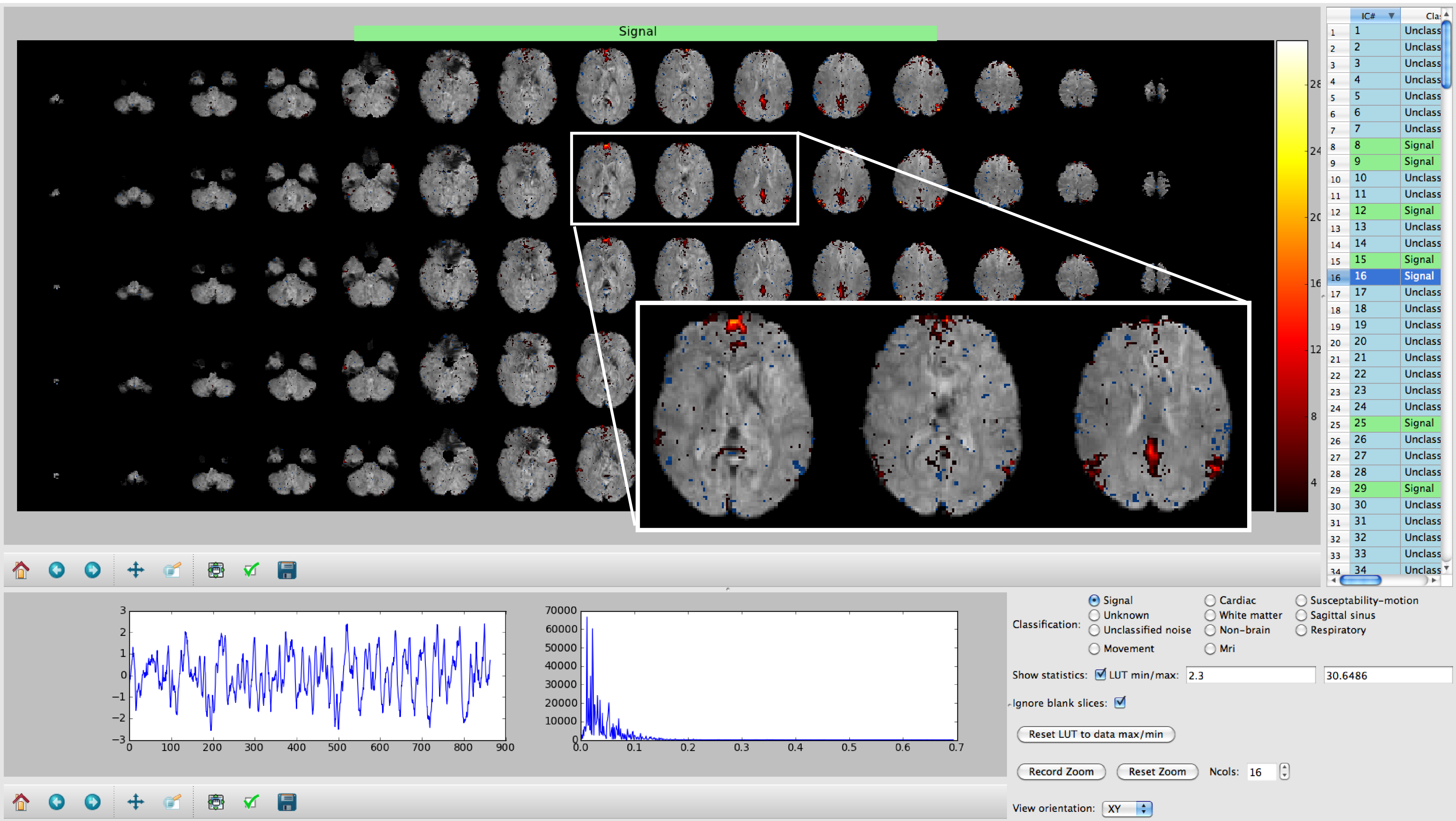
Currently available ICA-based cleaning methods

- Identification of **task-related** components (Thomas et al., 2002)
- Analysis of the Fourier decomposition of **time series** (Kochiyama et al., 2005)
- Match with **spatial patterns** of physiological **noise** (Perlbarg et al., 2007)
- Analysis of **spatiotemporal** features (Tohka et al., 2008; De Martino et al., 2007)

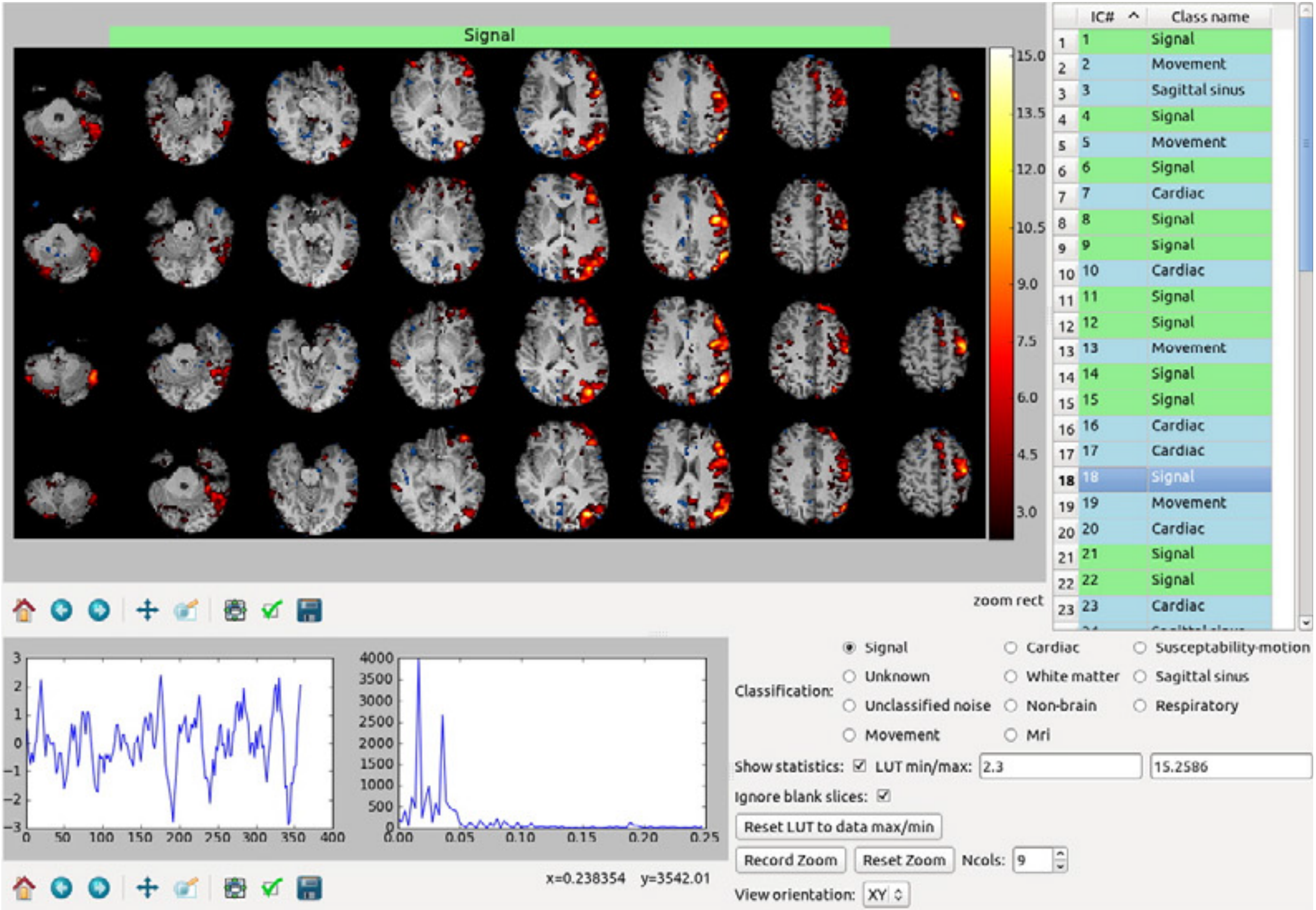
Characteristics of “good” (i.e. predominantly signal) and “bad” (i.e. predominantly noise) components:

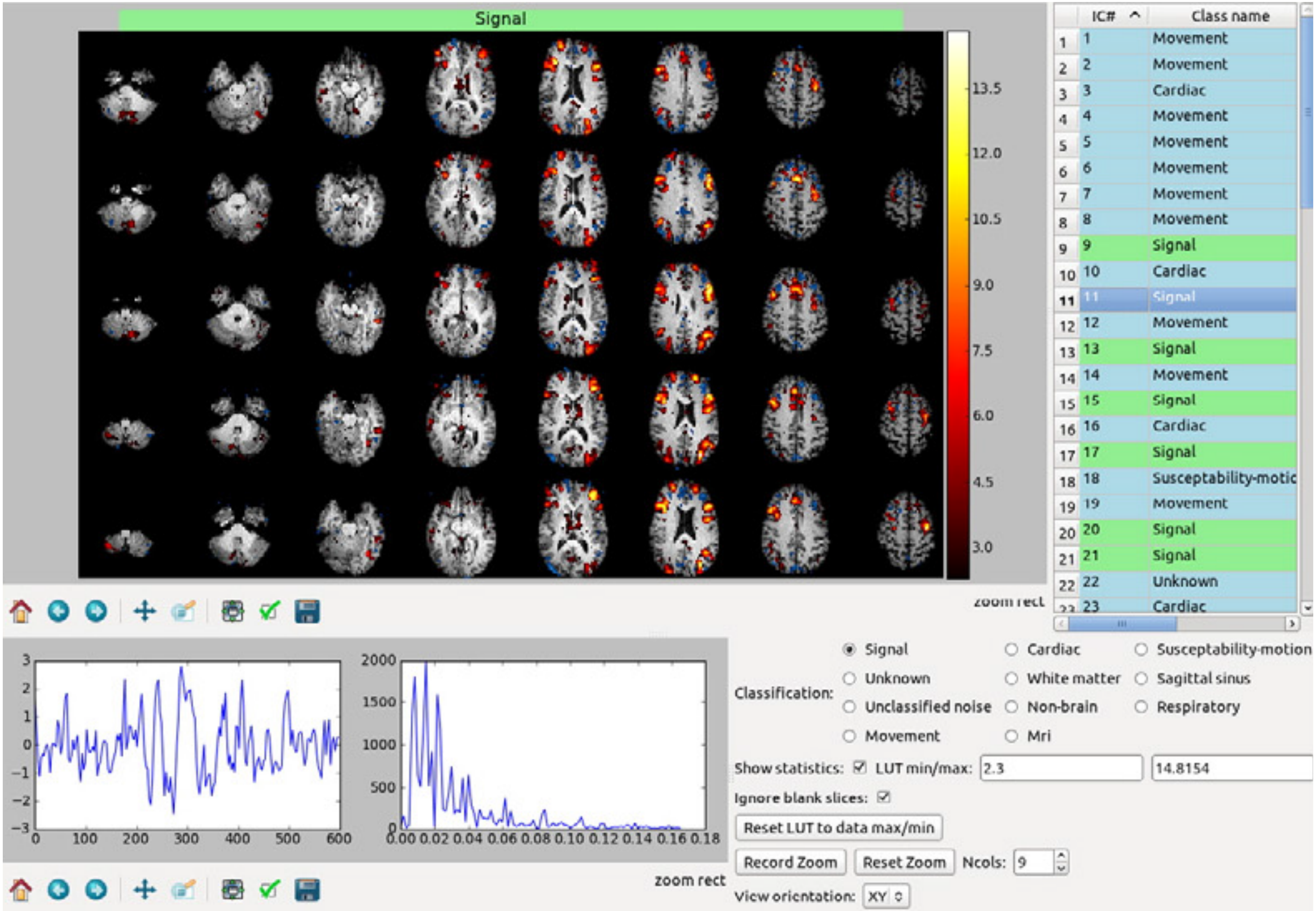
hand labelling of the ICs

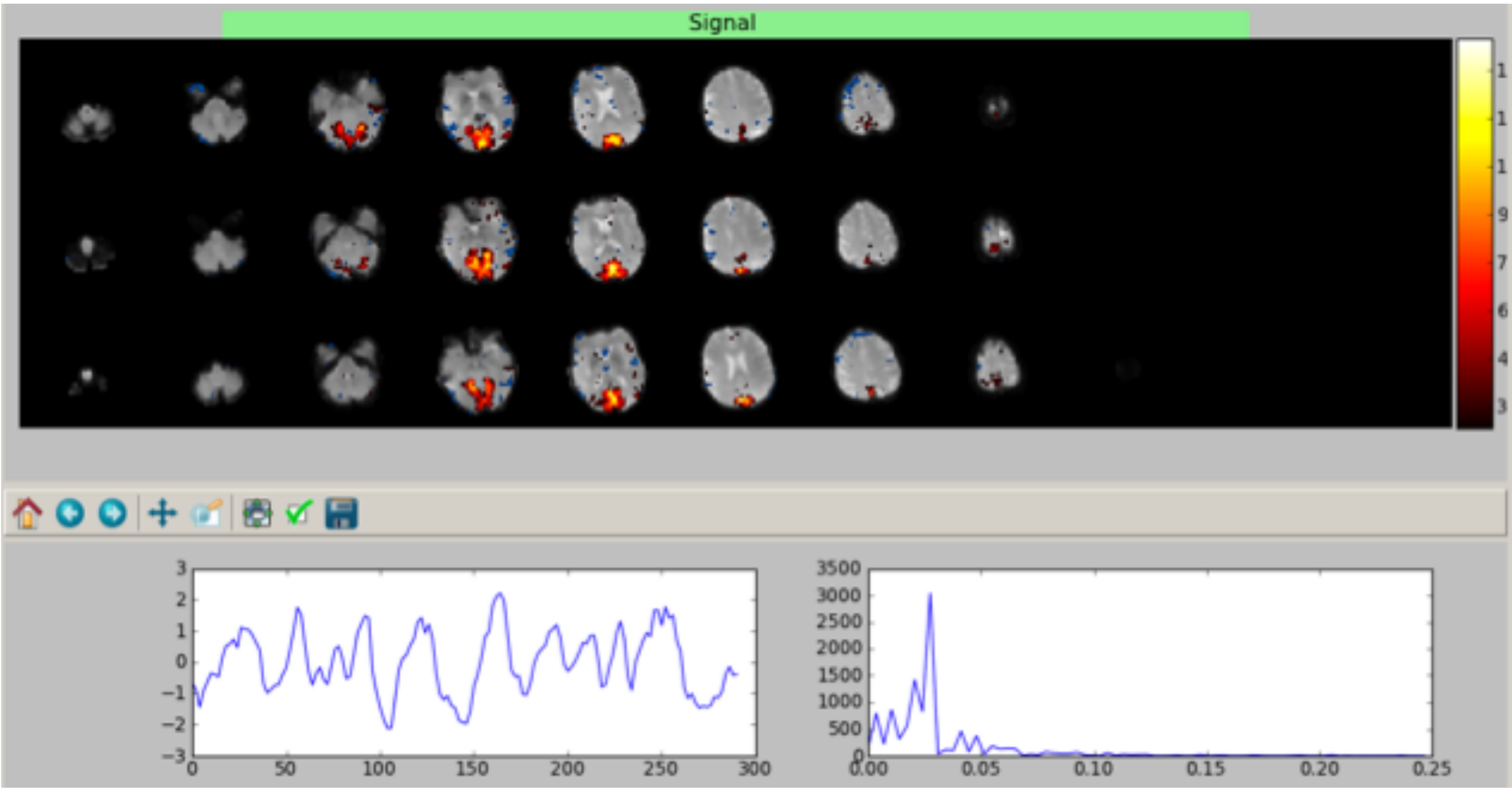
Examples of good components: DMN



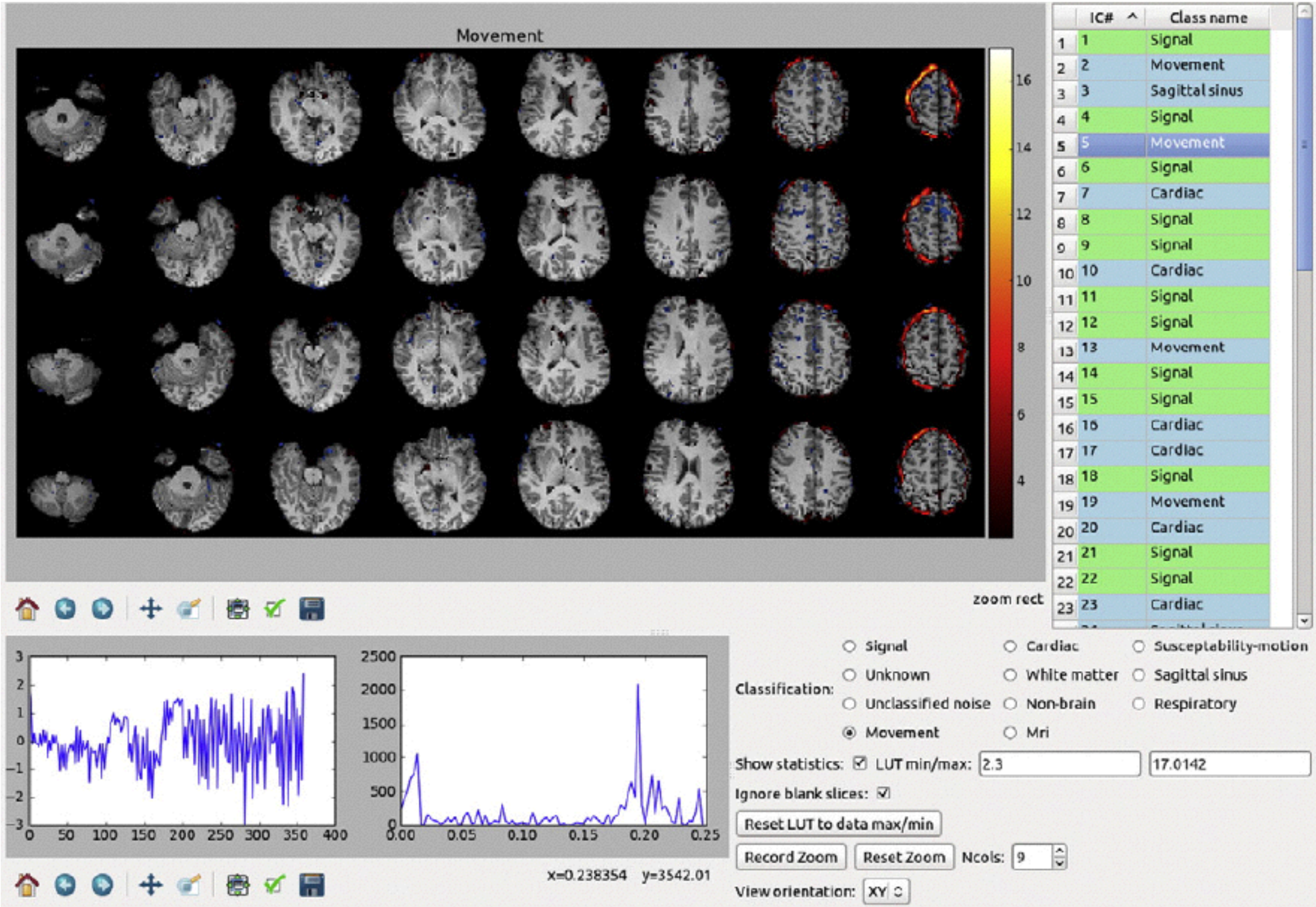
Visualisation tool: Melview (David Flitney)


Signal
15.0
13.5
12.0
10.5
9.0
7.5
6.0
4.5
3.0
IC#
Class name
1 1 Signal
2 2 Movement
3 3 Sagittal sinus
4 4 Signal
5 5 Movement
6 6 Signal
7 7 Cardiac
8 8 Signal
9 9 Signal
10 10 Cardiac
11 11 Signal
12 12 Signal
13 13 Movement
14 14 Signal
15 15 Signal
16 16 Cardiac
17 17 Cardiac
18 18 Signal
19 19 Movement
20 20 Cardiac
21 21 Signal
22 22 Signal
23 23 Cardiac
zoom rect
3
2
1
0
−1
−2
−3
0 50 100 150 200 250 300 350 400
4000
3500
3000
2500
2000
1500
1000
500
0
0.00 0.05 0.10 0.15 0.20 0.25
x=0.238354 y=3542.01
Classification:
Signal
Unknown
Unclassified noise
Movement
Cardiac
White matter
Non-brain
Mri
Susceptability-motion
Sagittal sinus
Respiratory
Show statistics:
LUT min/max:
2.3
15.2586
Ignore blank slices:
Reset LUT to data max/min
Record Zoom
Reset Zoom
Ncols:
9
View orientation:
XY

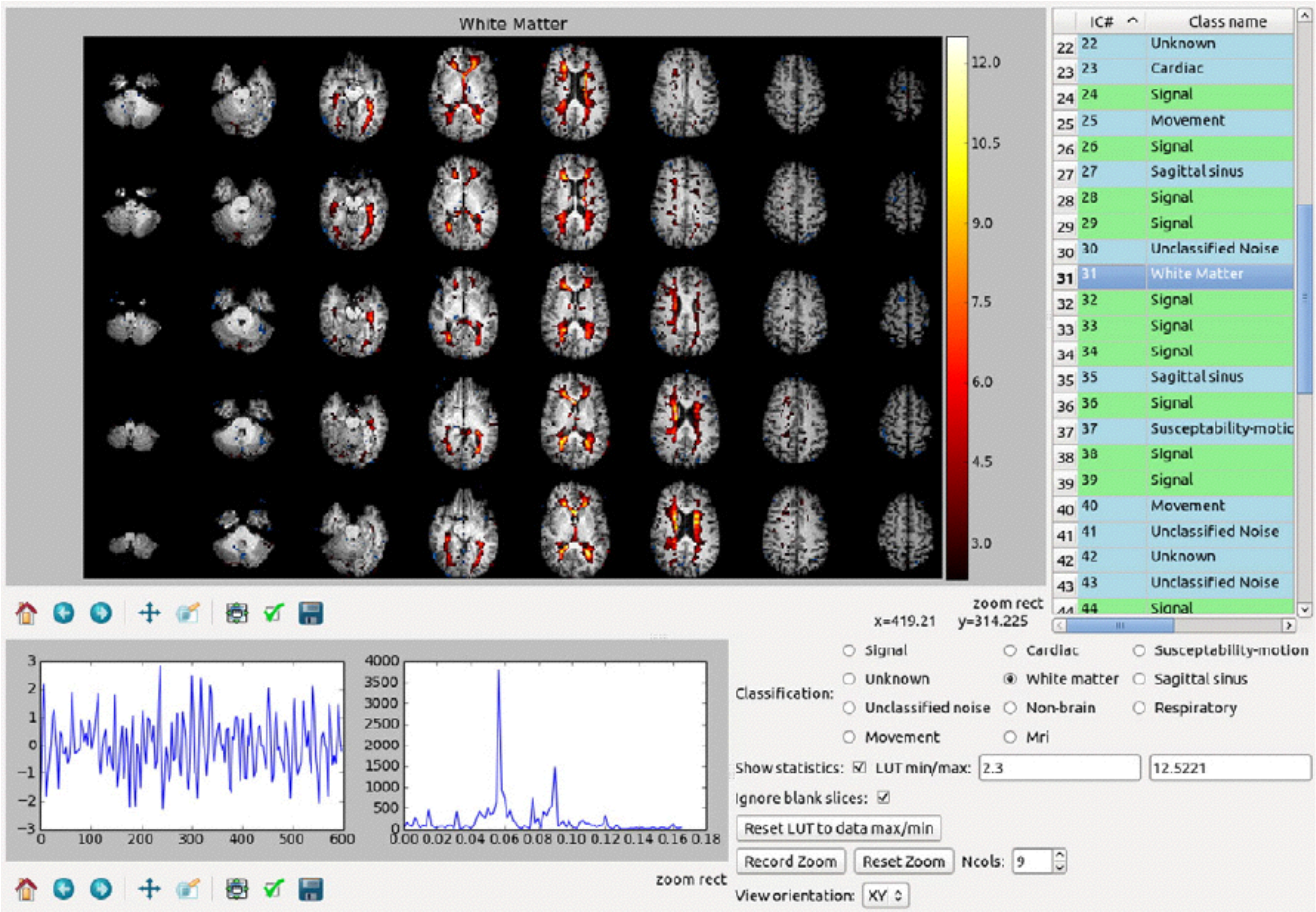

Signal
13.5
12.0
10.5
9.0
7.5
6.0
4.5
3.0
IC#
Class name
1 1 Movement
2 2 Movement
3 3 Cardiac
4 4 Movement
5 5 Movement
6 6 Movement
7 7 Movement
8 8 Movement
9 9 Signal
10 10 Cardiac
11 11 Signal
12 12 Movement
13 13 Signal
14 14 Movement
15 15 Signal
16 16 Cardiac
17 17 Signal
18 18 Susceptability-motic
19 19 Movement
20 20 Signal
21 21 Signal
22 22 Unknown
23 Cardiac
zoom rect
Classification:
Signal
Cardiac
Susceptability-motion
Unknown
White matter
Sagittal sinus
Unclassified noise
Non-brain
Respiratory
Movement
Mri
Show statistics:
LUT min/max:
2.3
14.8154
Ignore blank slices:
Reset LUT to data max/min
Record Zoom
Reset Zoom
Ncols:
9
View orientation:
XY
zoom rect
3
2
1
0
−1
−2
−3
0
100
200
300
400
500
600
2000
1500
1000
500
0
0.00 0.02 0.04 0.06 0.08 0.10 0.12 0.14 0.16 0.18


Signal
3
2
1
0
−1
−2
−3
0
50
100
150
200
250
300
3500
3000
2500
2000
1500
1000
500
0
0.00
0.05
0.10
0.15
0.20
0.25

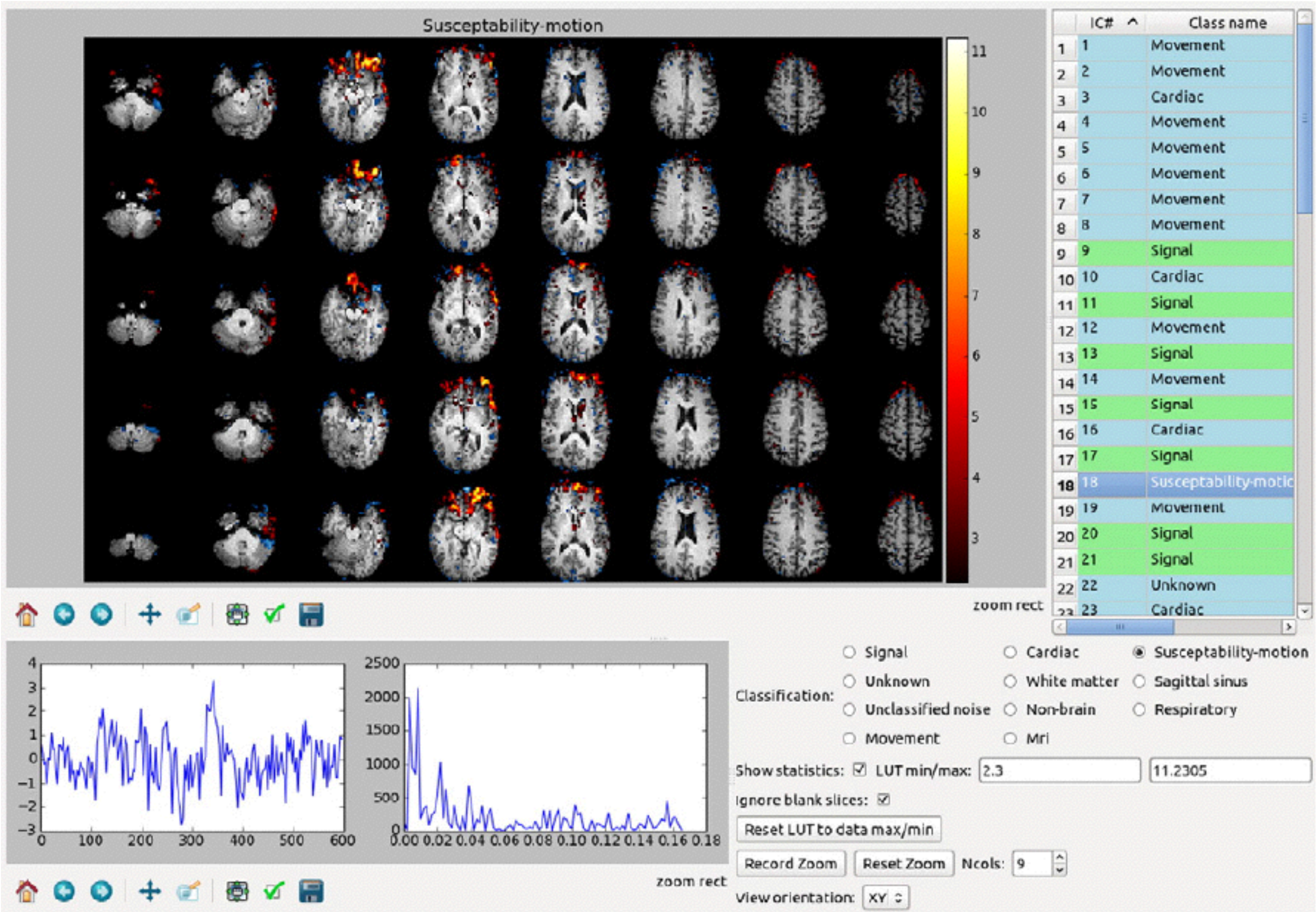
Examples of bad components: motion-related



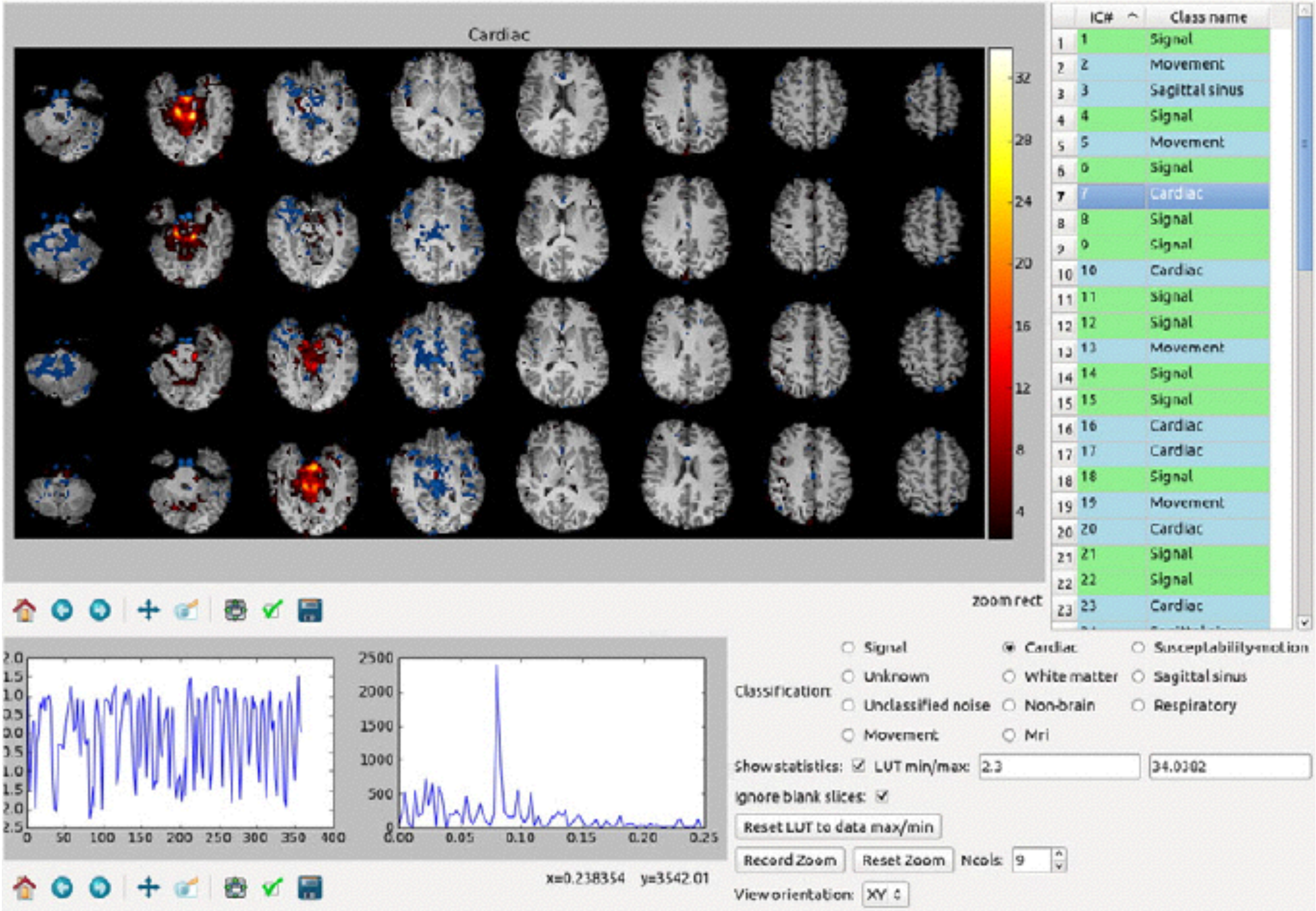
White Matter



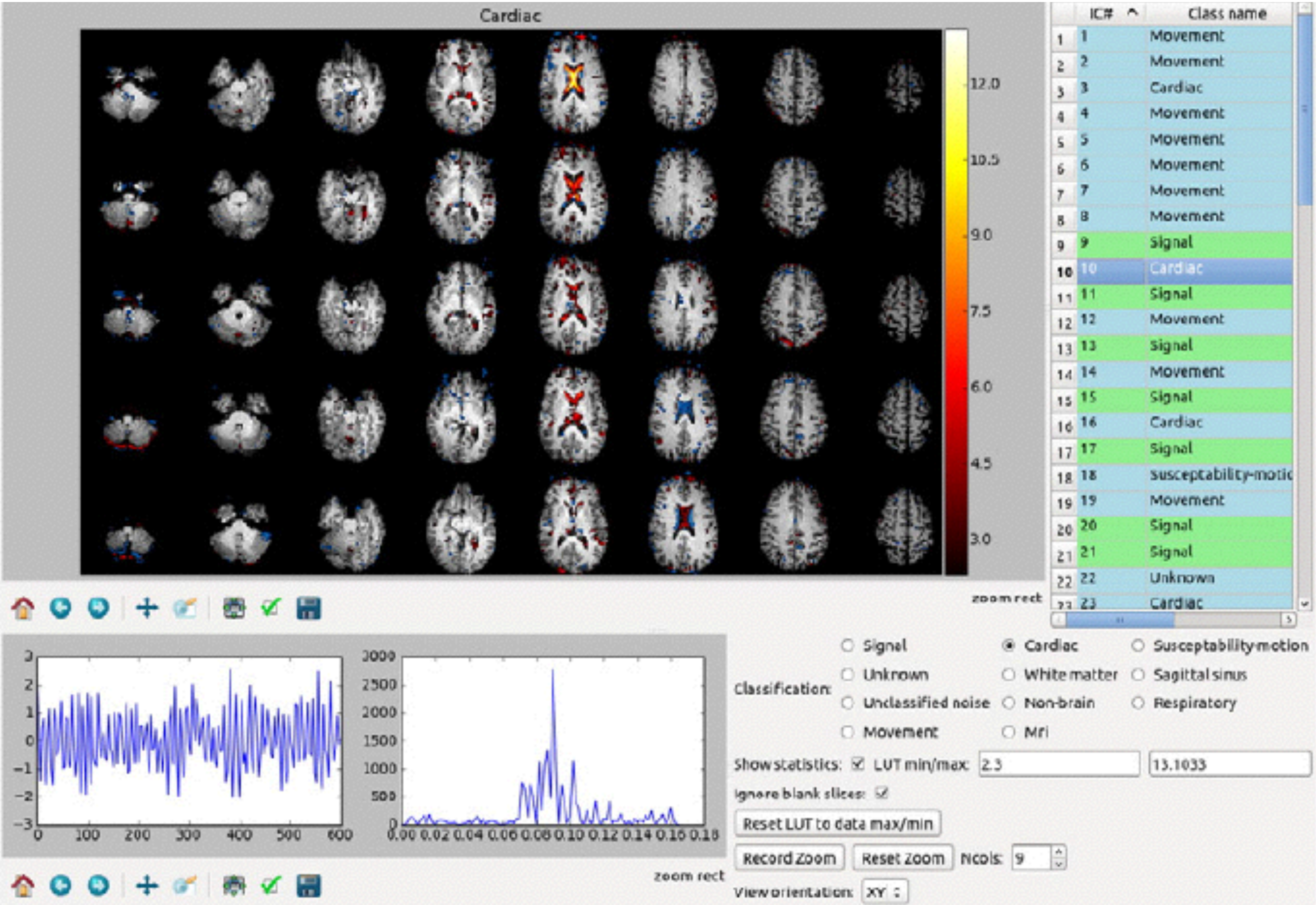
Susceptibility-motion



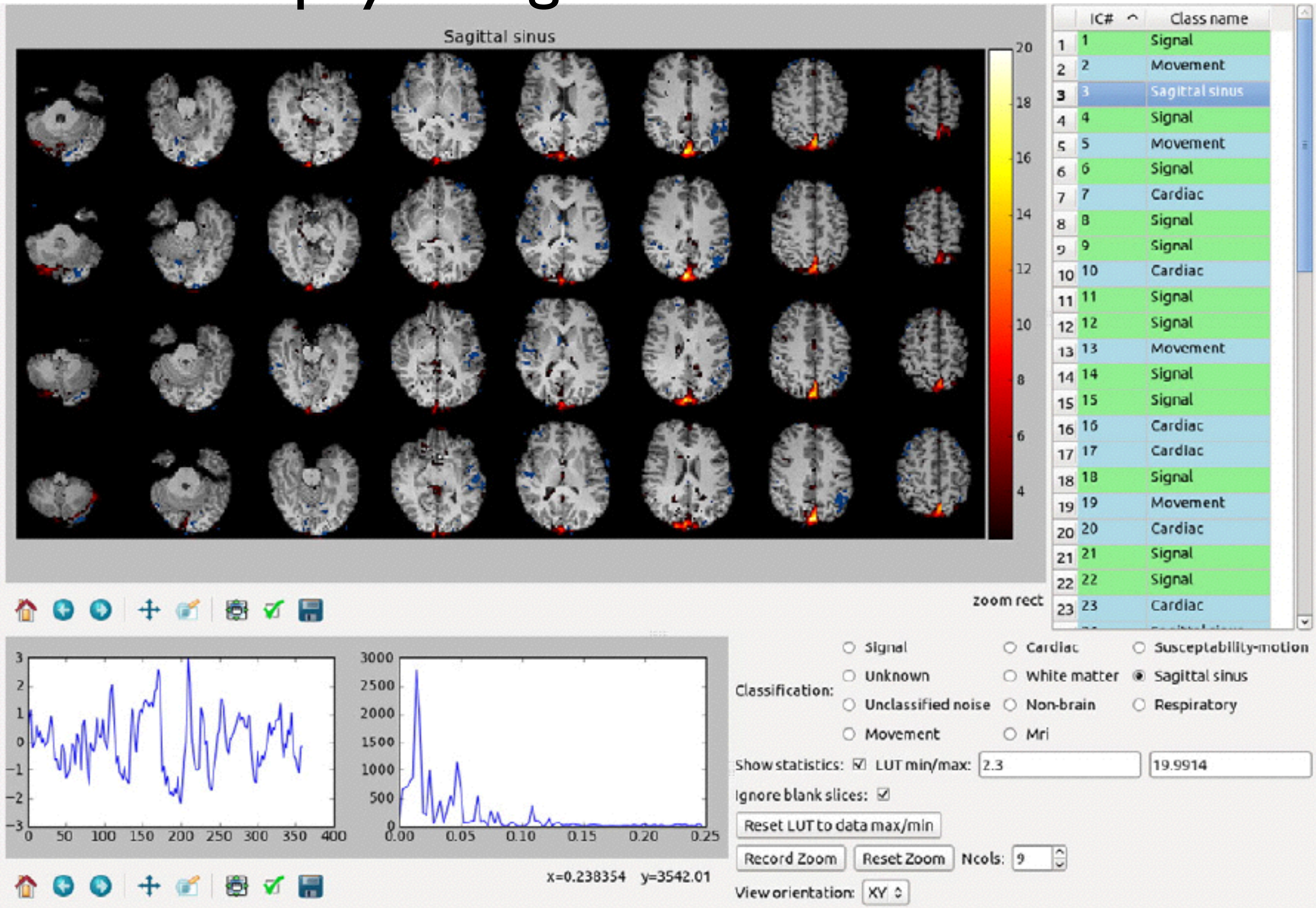
physiological artefacts 1/3



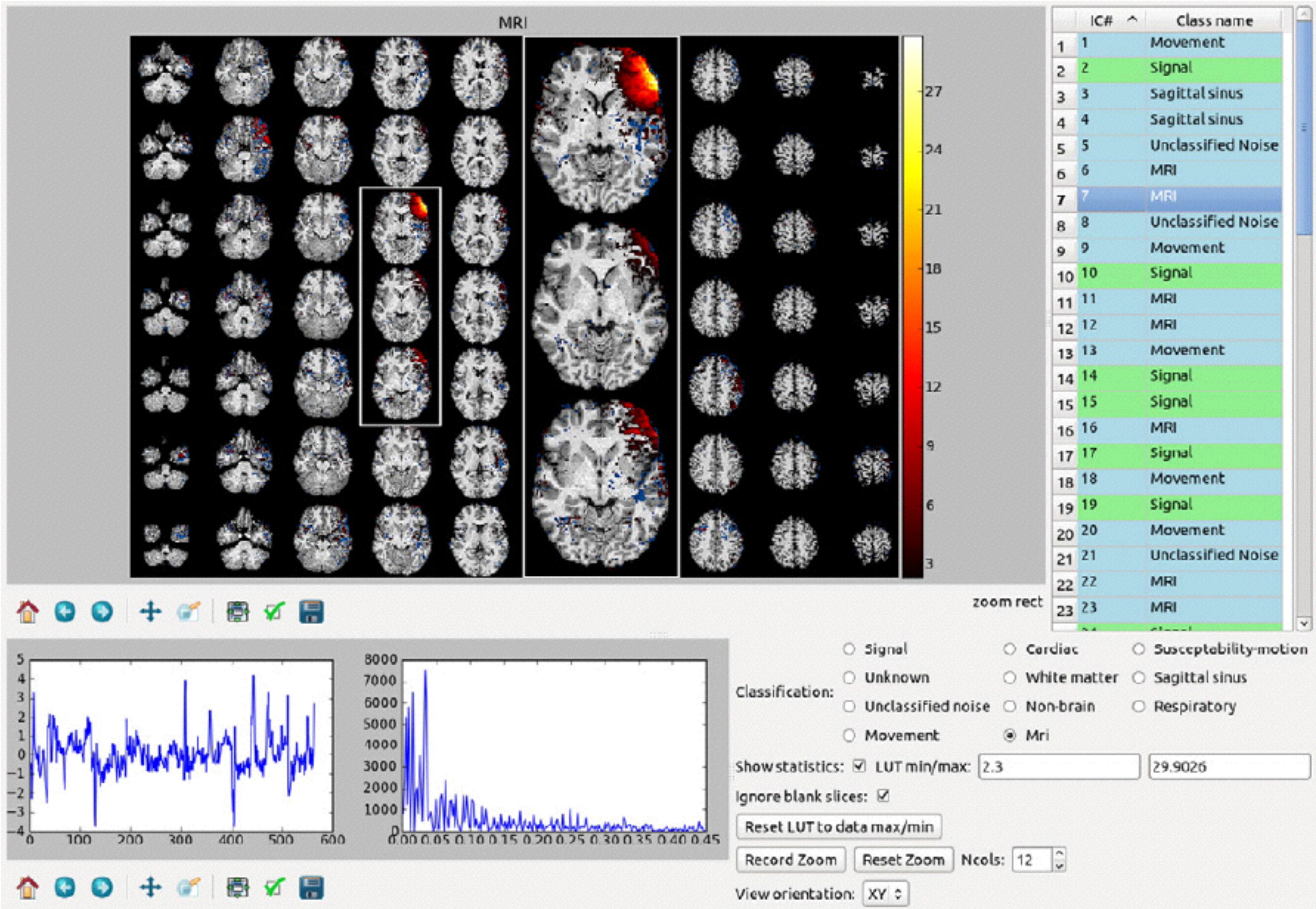
physiological artefacts 2/3



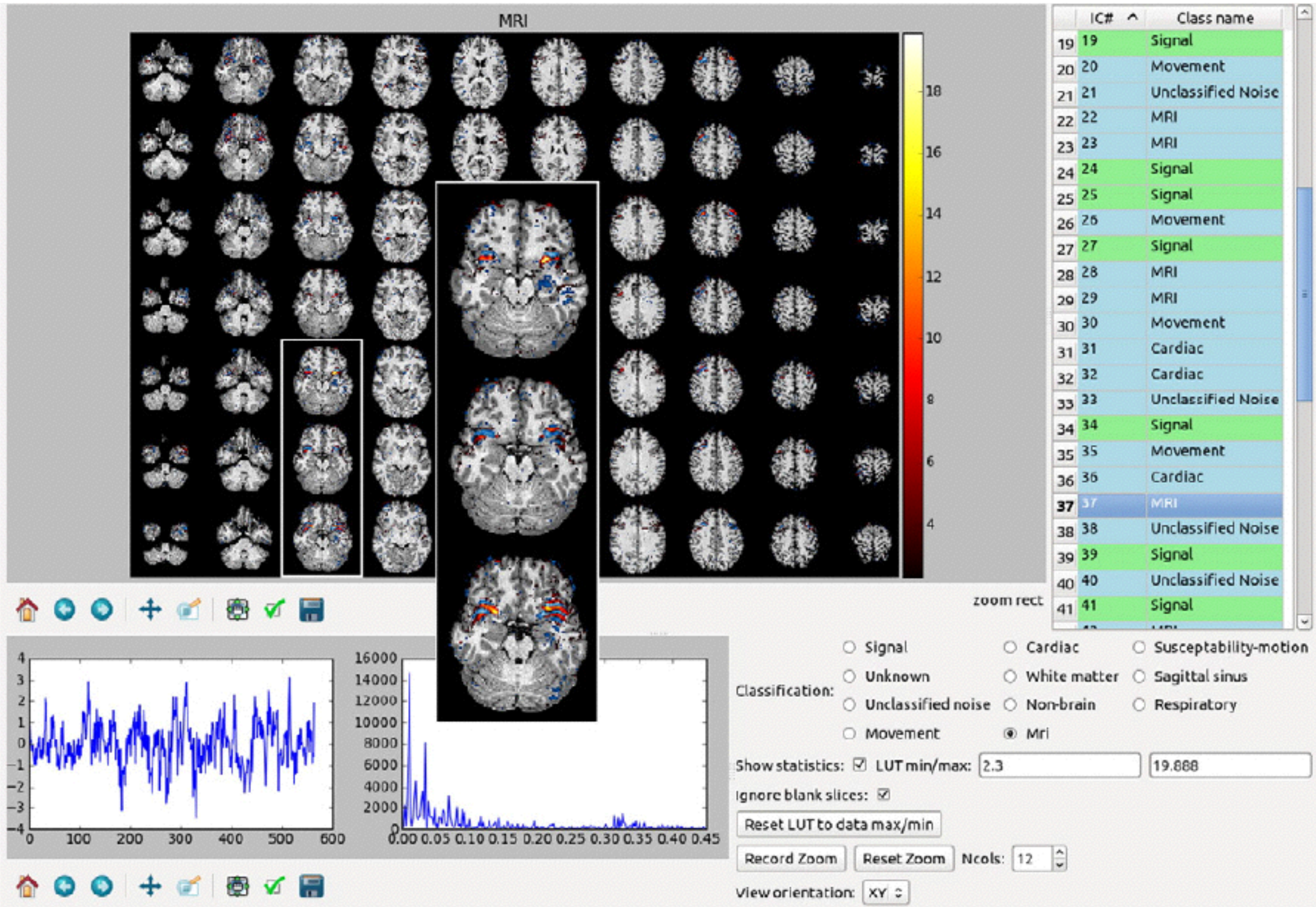
physiological artefacts 3/3



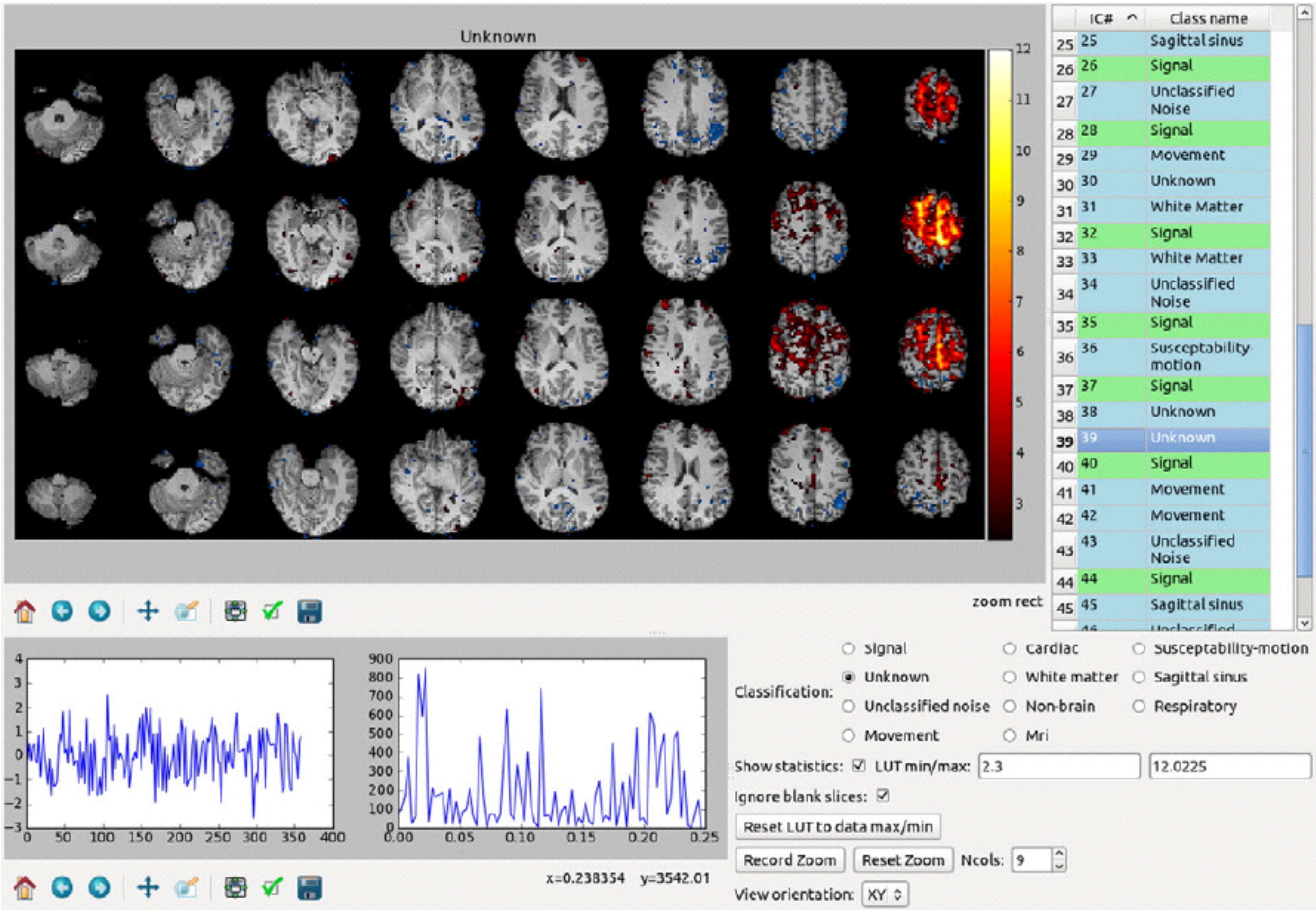
MRI acquisition/reconstruction artefacts 1/2



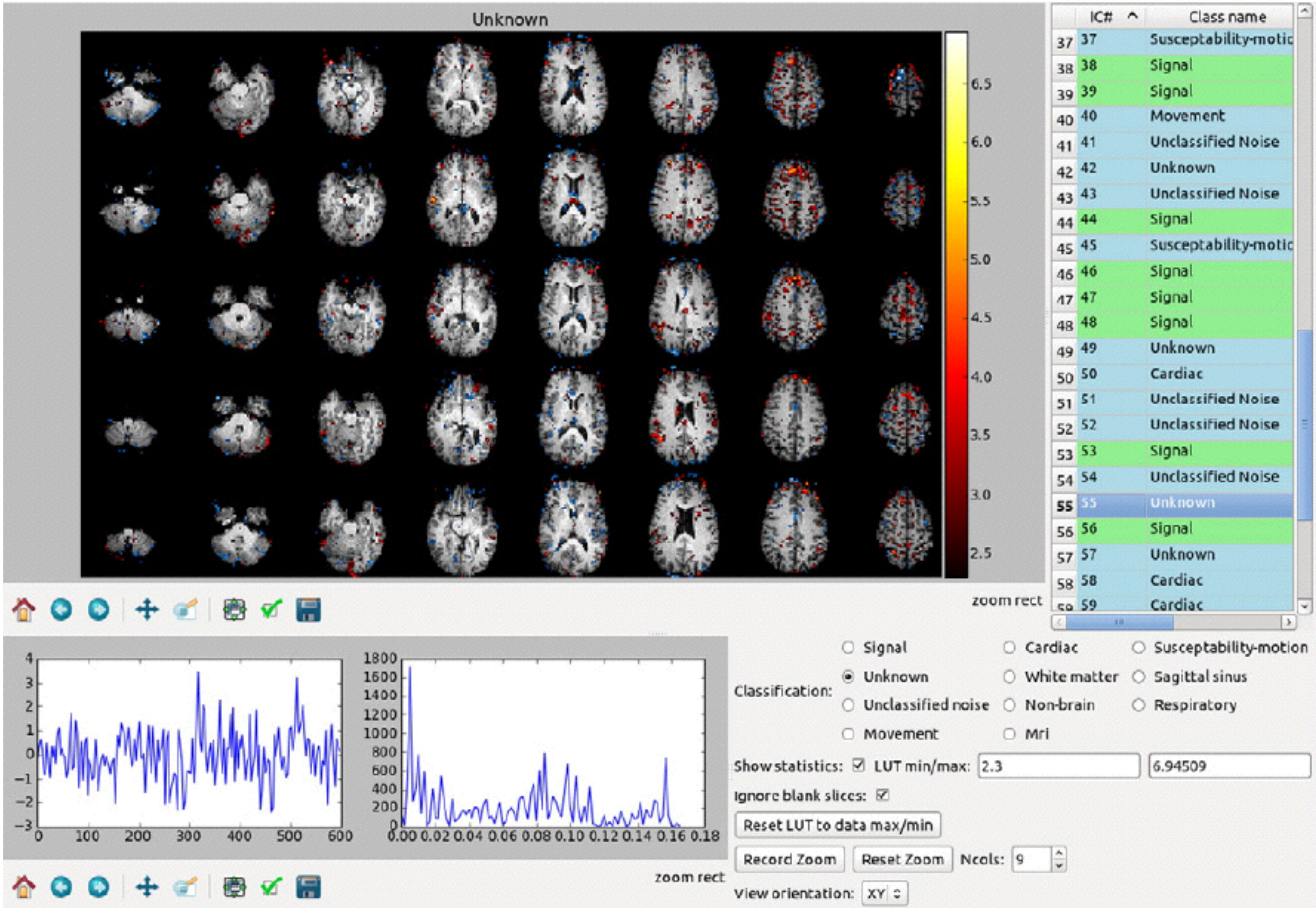
MRI acquisition/reconstruction artefacts 2/2



Examples of "Unknown" components 1/2



Examples of "Unknown" components 2/2



How to evaluate a component?

By looking at:

- Thresholded **spatial map** (usually abs(Z)=2.3)
- **Temporal power spectrum**
- **Time series**
- (If needed: unthresholded spatial maps)

… BUT hand labelling

- is time consuming
- relies on the operator's expertise

An automated ICA-based cleaning approach:
FMRIB's ICA-based Xnoiseifier (FIX)

Reza Salimi, Ludo Griffanti, Steve Smith et al.,
FMRIB, Oxford

Salimi-Khorshidi et al.
NeuroImage 2014

Griffanti et al.
NeuroImage 2014

FIX cleaning approach

1. Standard **preprocessing**: rigid-body head motion correction, drift removal (high-pass temporal filtering), (optional) spatial smoothing
2. **Single-subject ICA** decomposition with automatic dimensionality estimation (using MELODIC, part of FSL)
3. Components' **features extraction**
4. **Automatic classification** of components
   - Classifier **training** and evaluation of accuracy
5. **Noise removal** (regress bad ICA time courses & 24 motion parameters out of preprocessed data)

3. Features extraction

- Hand-labelling: operator's **qualitative evaluation** of the characteristics of spatial maps, temporal power spectra and time courses

- FIX: calculation of about 180 spatial and temporal **quantitative measures** (features) for each component

Examples of spatial features

Spatial features' subclass	Signal characteristic	Noise characteristic
Clusters' size and spatial distribution	Low number of large clusters	High number of small clusters
Voxels overlaying bright/dark raw data voxels	More overlap with GM intensity	Overlap with e.g. blood vessels
Percent of (i.e. overlap with) brain boundary	Low overlap	High overlap
Masked-based features	Overlap with GM mask	Overlap with WM, CSF, vessels masks
Other spatial features	…	…

Examples of temporal features

Temporal features' subclass	Signal characteristic	Noise characteristic
Jump (i.e. sudden changes) amplitudes in the time series	Fairly smooth time series	Large jump
Autoregressive properties (temporal smoothness)	High temporal autocorrelation	Low temporal autocorrelation
Distributional properties of the time series	Fairly normal	Bimodal or long-tailed
Distribution of power in frequency domain (Fourier transform)	Low frequency	High frequency
Temporal correlation with reference time series	More GM correlated	More WM, CSF, motion correlated

4. ICs' classification

- Hand-labelling: **human classification** in good vs bad components **with multiple *if-then* rules**

- FIX: **hierarchical classifier** (hierarchical fusion of k-NN, support vector machine, decision trees)

- Need of a **training dataset** to inform the classifier
    - Training datasets available with the tool
    - Study specific training datasets recommended

Classifier training and evaluation of accuracy

- **Hand labelling** of at least 10 (the more the better) subjects
- Classifier **training**
- Leave-One-Out (LOO) testing: to allow evaluating **accuracy** (TPR = % of Good components correctly classified; TNR = % of Bad components correctly classified)
- **Threshold** choice: to control balance between high-TPR vs high-TNR; e.g., for conservative cleanup, set threshold low (high TPR)

Example of FIX Classification Accuracy Output

threshold			2	5	10	20	30	40	50
Mixed datasets, 61 subjects	TPR	98.7	98.4	**98.4**	96.4	94	92.5	90.9	89.9
	TNR	51.4	65.4	**68.1**	75.1	83.6	88.5	91.5	93
Whitehall 2, No MB, 25 subjects 3x3x3mm, 3s, 10mins, hp=100s **Median across subjects, thresh=5: (100,99.3)**		97.8	97.8	**97.8**	96.3	94.6	93	92	90.8
		91.9	91.9	**92.2**	94.7	96.1	97.3	97.3	97.6
Whitehall 2, MB6, 25 subjects 2x2x2mm, 1.3s, 10mins, hp=100s		98.6	98.5	98.2	**98.1**	96.2	96.2	96.2	96.2
		95	95.1	97.7	**98.2**	98.6	98.9	98.9	99
HCP Phase 2, MB8, 25 subjects 2x2x2mm, 0.7s, 4x15mins, hp=2000s **Median across subjects, thresh=5: (100,99.3)**		99.7	**99.6**	**99.3**	99.1	99	98.5	97.7	6.7
		96.7	**97.2**	**99**	99.3	99.4	99.5	99.6	99.7

Example of FIX classification output

```
filtered_func_data.ica
1, Unknown, False
2, Unknown, False
3, Unclassified Noise, True
4, Unclassified Noise, True
5, Unclassified Noise, True
6, Unclassified Noise, True
7, Unclassified Noise, True
8, Unclassified Noise, True
9, Unclassified Noise, True
10, Unclassified Noise, True
11, Unclassified Noise, True
12, Unclassified Noise, True
13, Signal, False
14, Unclassified Noise, True
15, Signal, False
16, Unclassified Noise, True
17, Unclassified Noise, True
18, Signal, False
19, Unclassified Noise, True
20, Unclassified Noise, True
21, Unclassified Noise, True
22, Signal, False
23, Unclassified Noise, True
24, Signal, False
25, Signal, False
26, Unclassified Noise, True
27, Signal, False
28, Unknown, False
29, Unclassified Noise, True
30, Unclassified Noise, True
31, Unclassified Noise, True
32, Signal, False
33, Unclassified Noise, True
34, Unclassified Noise, True
35, Unclassified Noise, True
36, Unclassified Noise, True
37, Signal, False
38, Signal, False
39, Unclassified Noise, True
40, Unclassified Noise, True
41, Unknown, False
42, Signal, False
43, Unclassified Noise, True
44, Signal, False
45, Unknown, False
[3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 17, 19, 20, 21, 23, 26,
29, 30, 31, 33, 34, 35, 36, 39, 40, 43]
```

- A report of FIX classification is created for each subject
- Only bad components will be removed from the data
- Unknown components will be kept: conservative approach

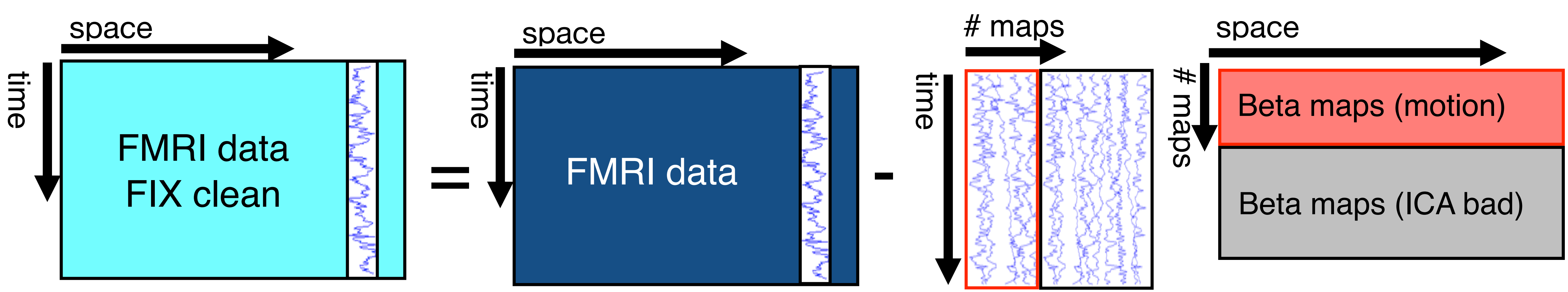
5. Noise removal

Satterthwaite et al. NeuroImage 2013

- regression of the contribution of **24 motion parameters**:
  - 3 rotation + 3 translation
  - temporal derivatives of the previous 6
  - squares of the previous 12
- regression of the contribution of the **noise components** identified by the classifier

How to regress out noise components?

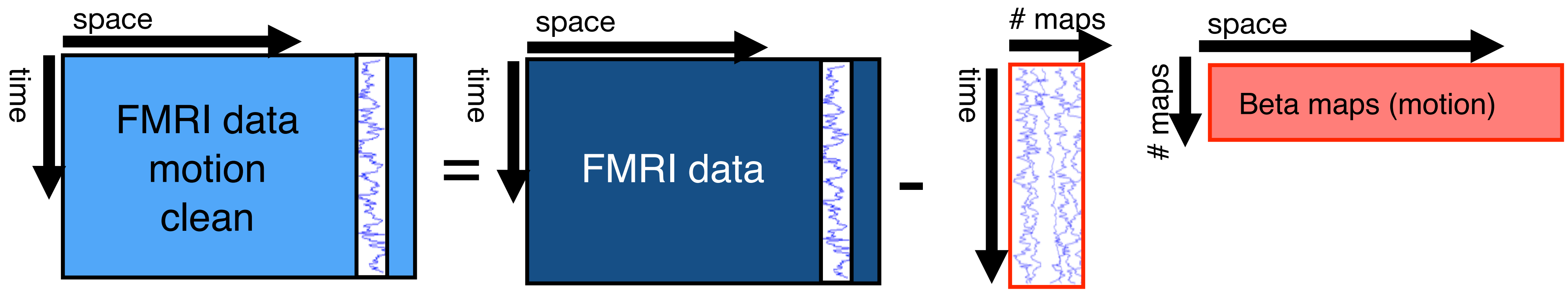
- **<u>AGGRESSIVE approach:</u>** regression of the full space of all the **noise components (ICA bad)** and the motion confounds out of the 4D pre-processed data:



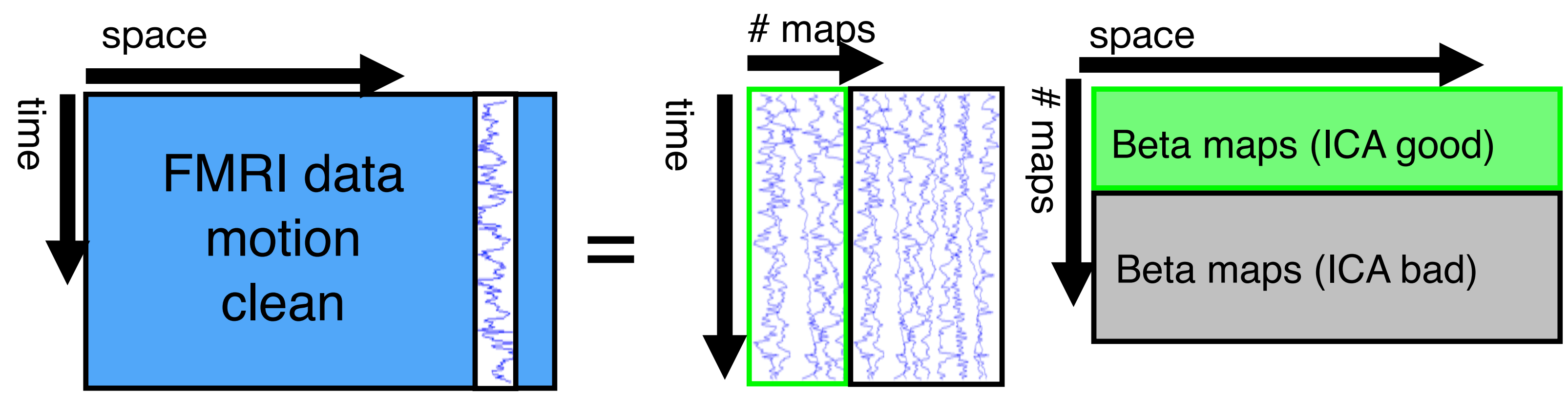
Not taking into account of possible shared variance between the good and the bad components

- **SOFT approach:**

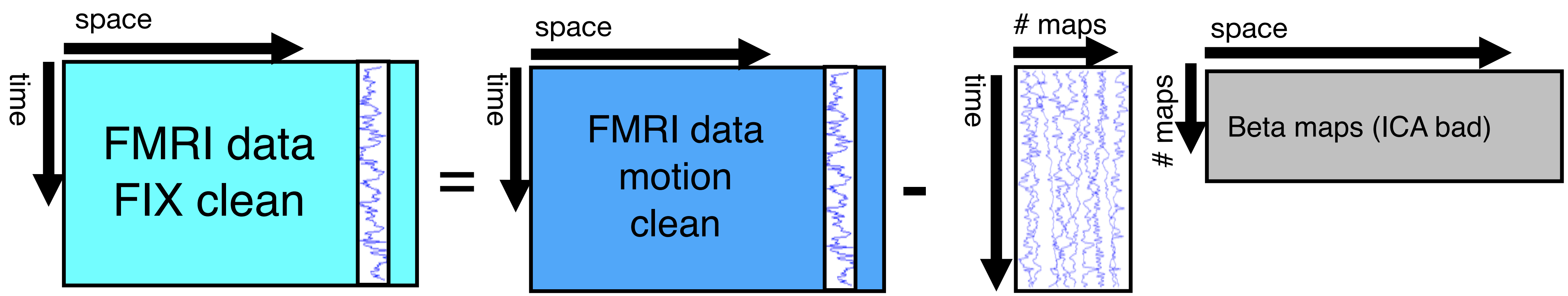
1) regression of the full space of the motion confounds from both the data and from all the ICA component timeseries:



2) estimation of the contribution of both good and bad components in order to identify the noise specific variance:



3) removal of the unique contribution of the bad components from the data:



…mathematically

- **AGGRESSIVE approach**: regression of the full space of all the noise components and the motion confounds (C) out of the 4D pre-processed data (Y):

$$Y_{clean}=Y-C\cdot(pinv(C)\cdot Y) \quad (C=[C_{motion}\ \mathrm{ICA(bad)}])$$

- **SOFT approach:**

1) regression of the full space of the motion confounds (C_{motion}) from both the data (Y) and from all the ICA component timeseries (ICA) :

$$Y_m=Y-C_{motion}\cdot(pinv(C_{motion})\cdot Y)$$

$$ICA_m=ICA-C_{motion}\cdot(pinv(C_{motion})\cdot ICA)$$

2) estimation of the contribution of both good and bad components in order to identify the noise specific variance:

$$\beta_{ICA}=pinv(ICA_m)\cdot Y_m$$

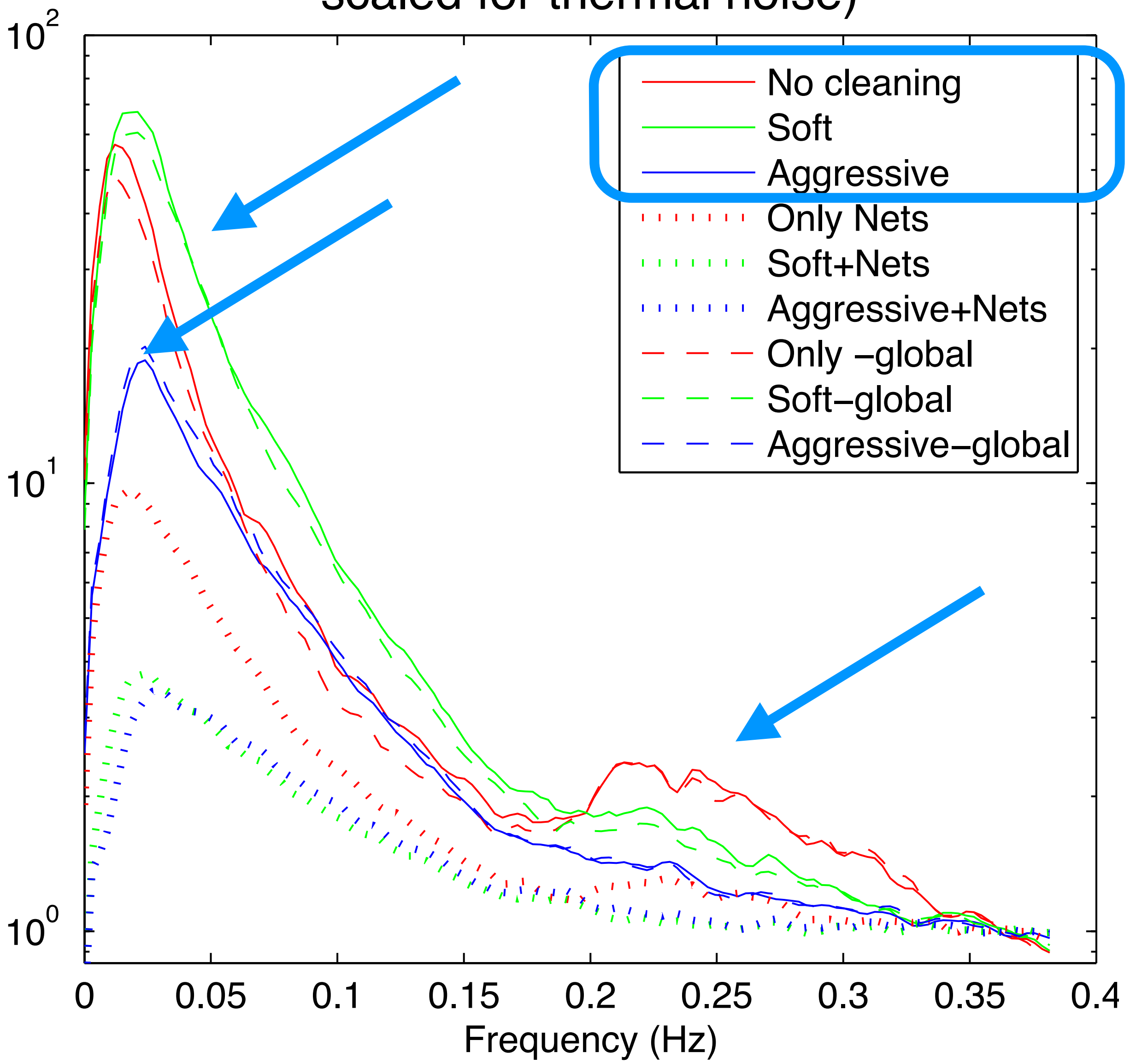
3) removal of the unique contribution of the bad components from the data:

$$\boldsymbol{Y_{clean}=Y_m-(ICA_m(bad)\cdot\beta_{ICA}\,(bad))}$$

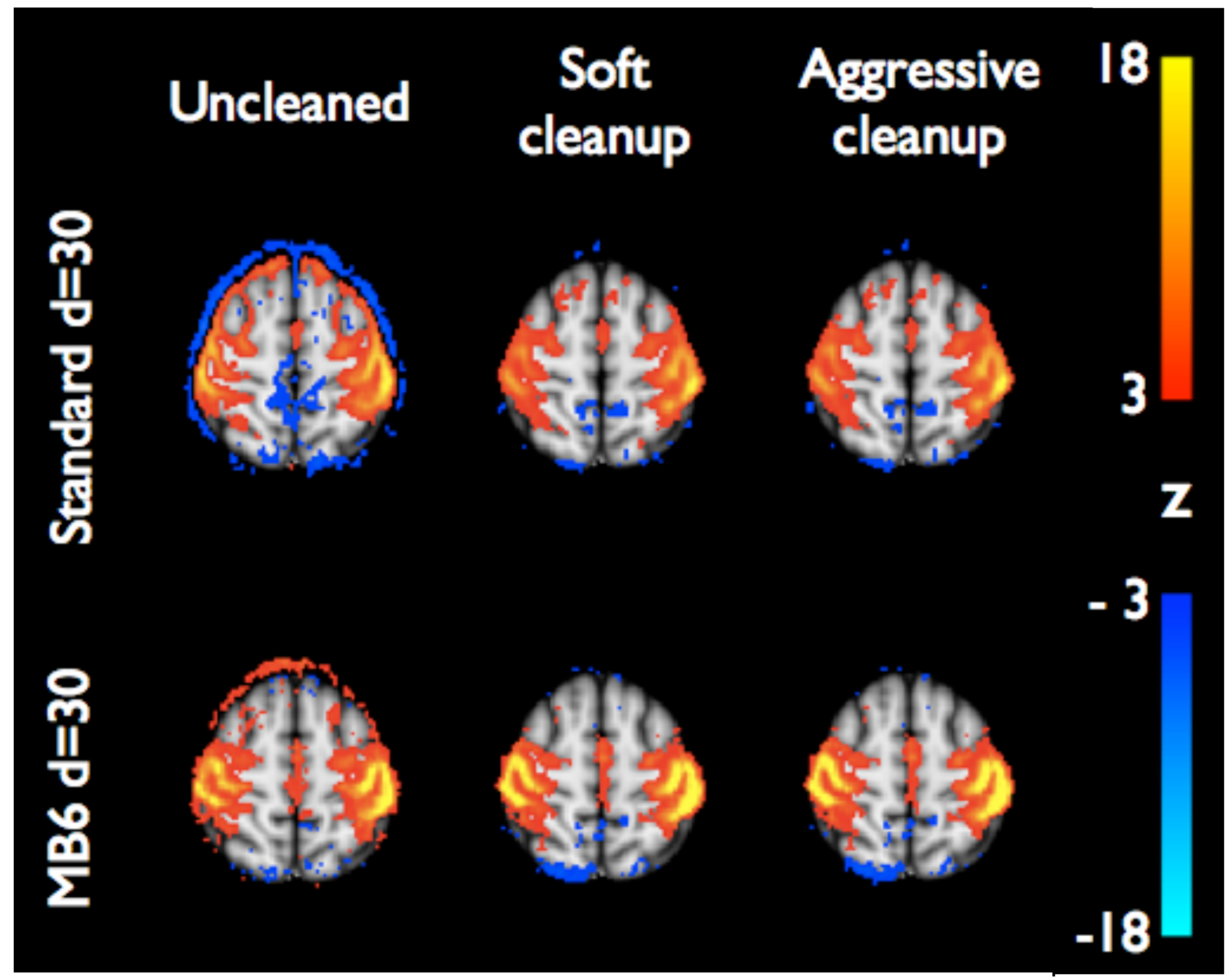
FIX tool validations/applications

Effectiveness of the cleaning procedure

Power Spectra
(mean across subjects and components, scaled for thermal noise)



Spatial Maps
(mean across subjects)

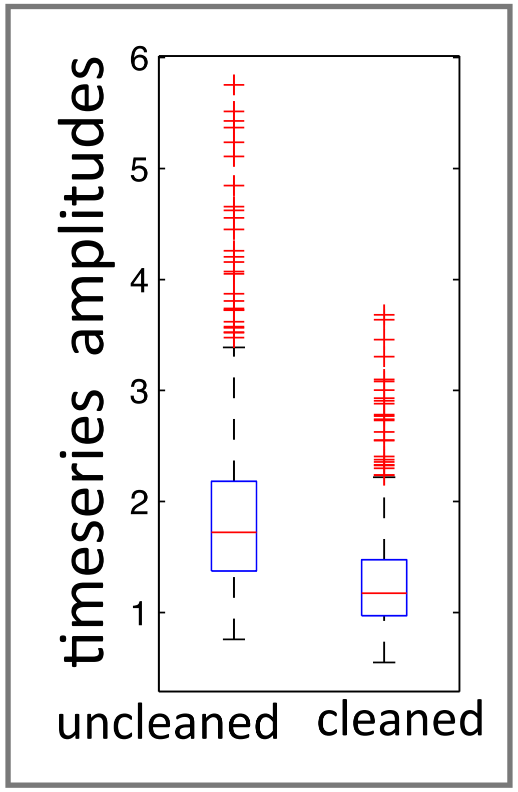


Griffanti et al., 2014

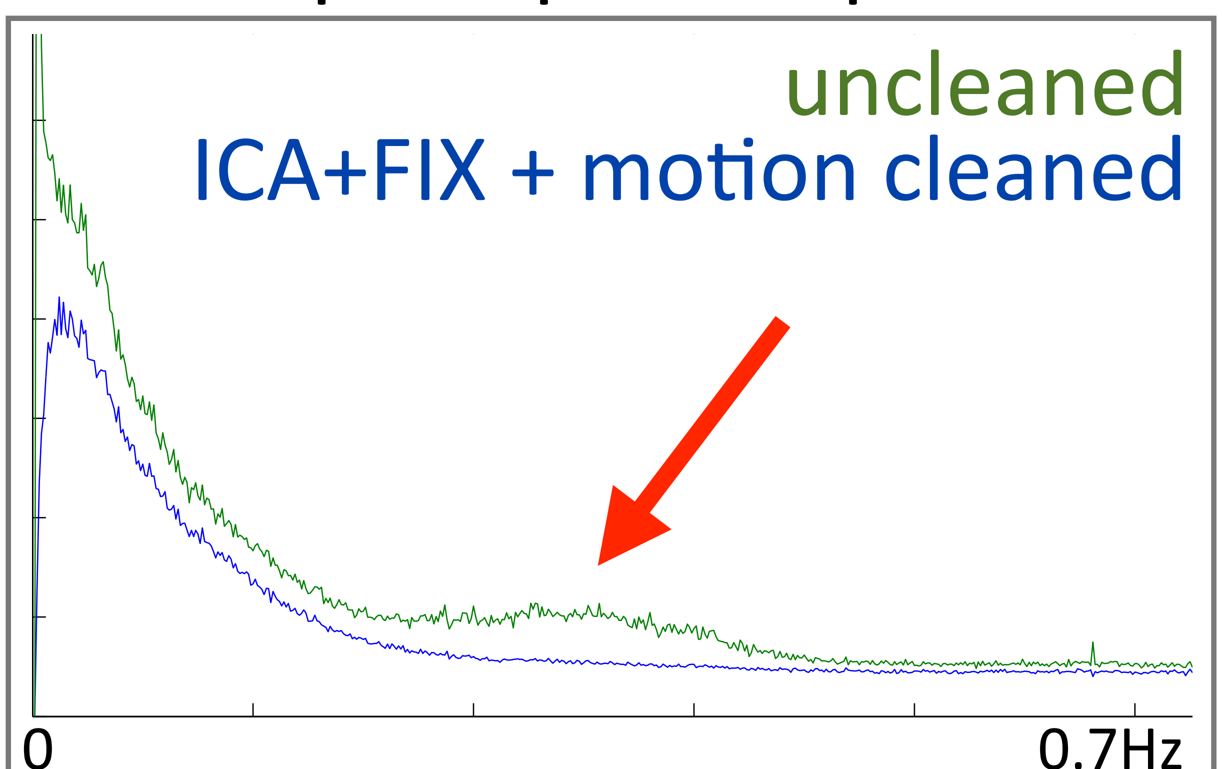
Similar results for the two approaches - "soft" is more conservative

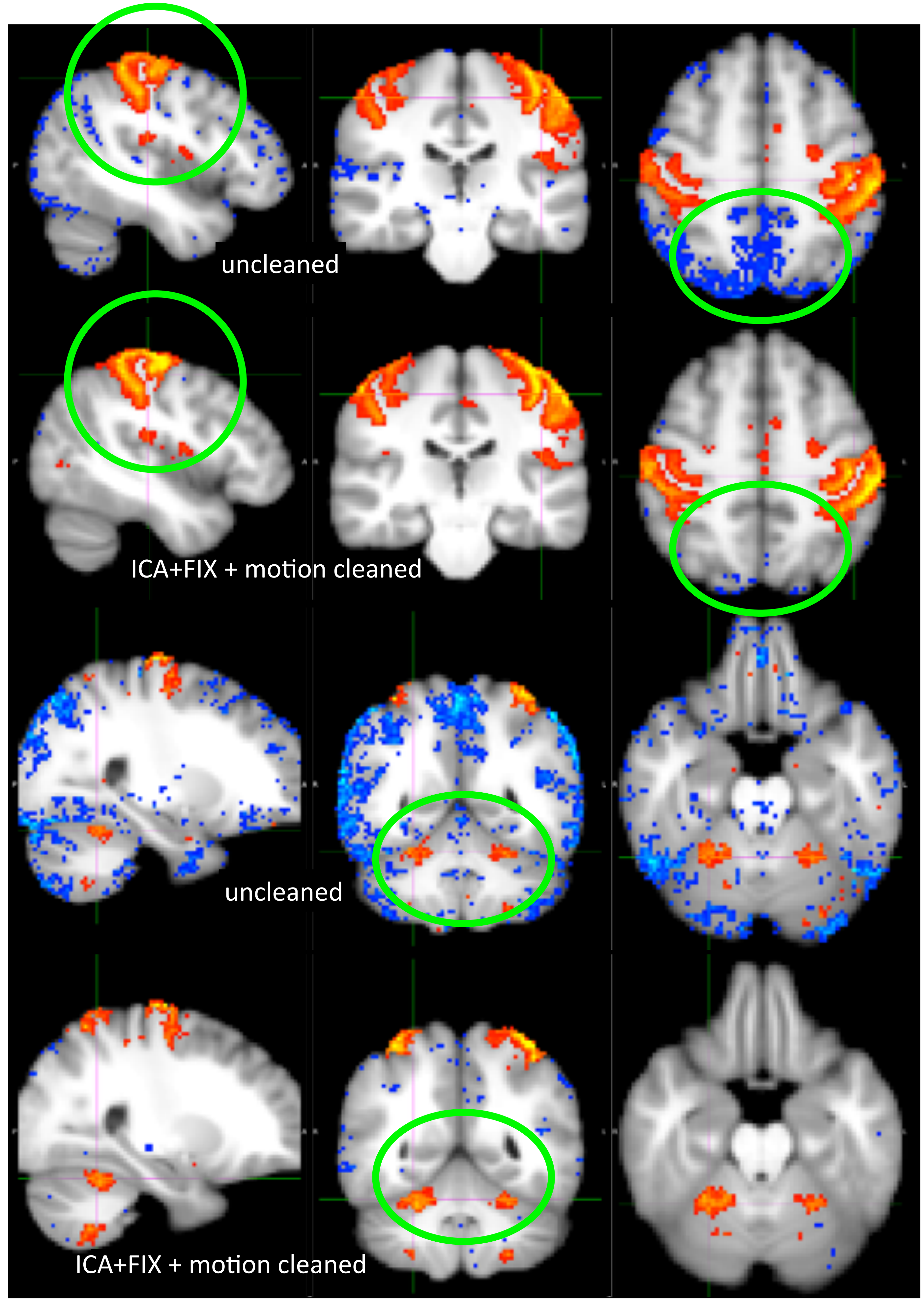
HUMAN Connectome PROJECT

Smith et al., 2013

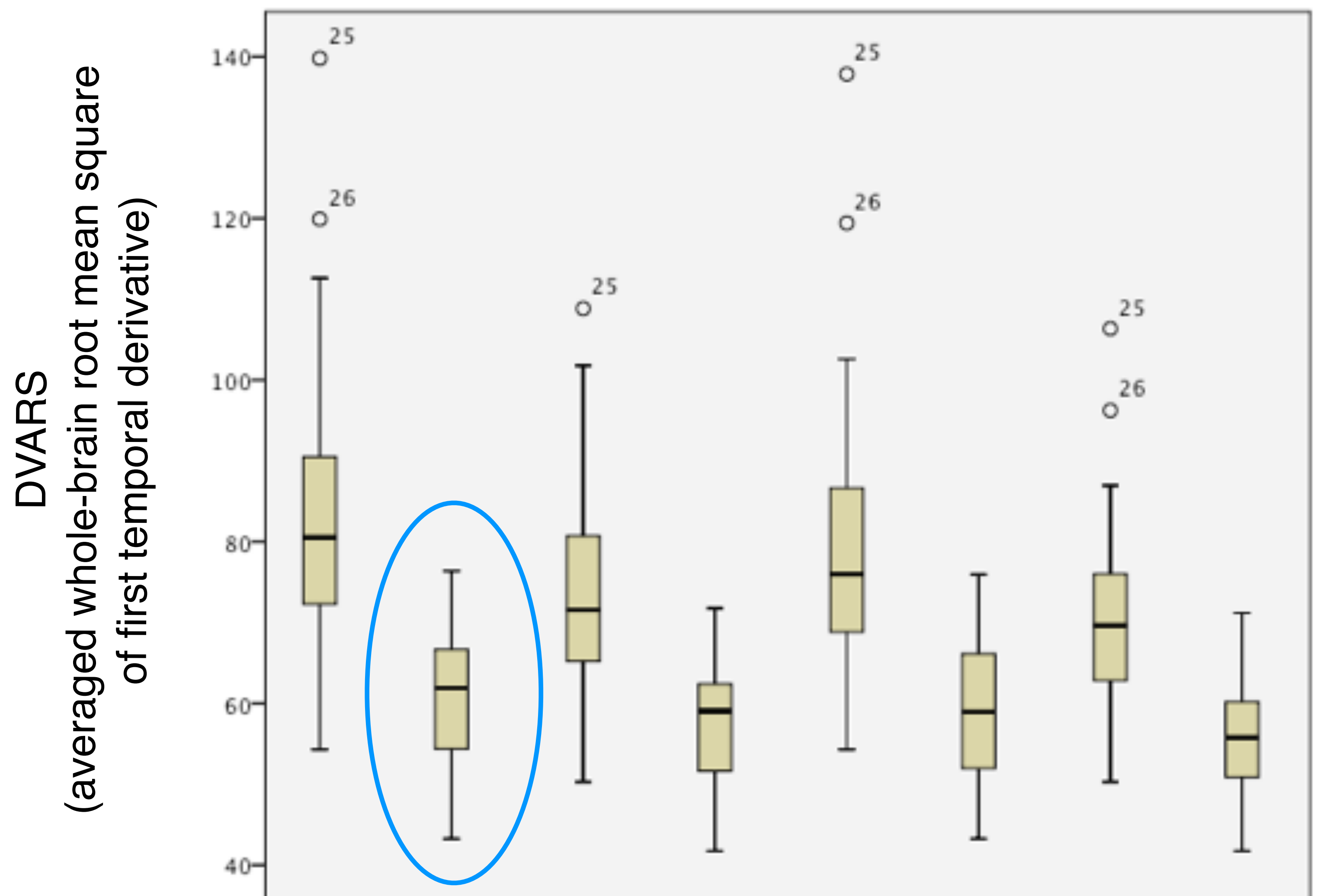


temporal power spectra





Comparisons with other methods: motion artefact reduction

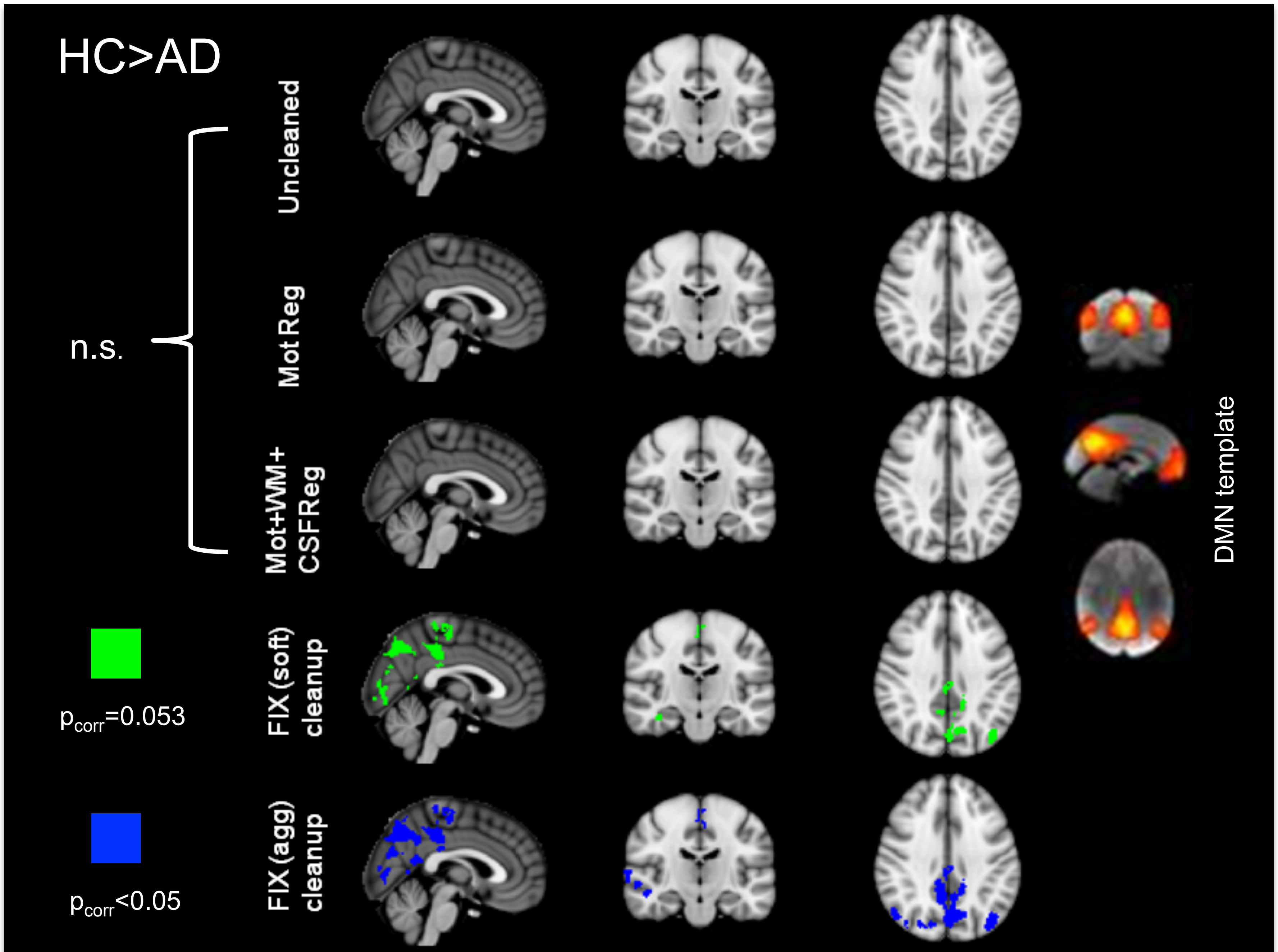


Standard pre-processing	✔	✔	✔	✔	✔	✔	✔	✔
FIX		✔		✔		✔		✔
Noise regression			✔	✔			✔	✔
Scrubbing					✔	✔	✔	✔

FIX provides the strongest reduction in volume-to-volume variance of signal intensity

Bijsterbosch et al., OHBM 2013

Comparisons with other methods: discrimination power



FIX allowed to detect the typical DMN alteration (decreased functional connectivity in the posterior cingulate cortex) in patients with mild to moderate Alzheimer's disease (n=20) with respect to a group of elderly healthy subjects (n=21)

Griffanti et al., ISMRM 2014

Conclusions

- fMRI data are affected by several sources of noise and an effective cleaning approach is needed especially for resting-state fMRI
- With FIX we are able to remove artefacts automatically and with confidence that we are not removing significant amount of non-artefact signal
- FIX tool is publicly available and different training dataset are provided, however the accuracy of the cleaning procedure benefits from study-specific training datasets
- Effective cleaning is already achieved by removing the unique variance of artefacts. A more aggressive denoising can be performed by removing the full variance of the artefacts, obtaining similar results, but at expense of potential signal loss.

Thank you

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http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FIX

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Klaus P. Ebmeier
Nicola Filippini
Clare E. Mackay
Karla L. Miller

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Christian F. Beckmann

Politecnico di Milano

Giuseppe Baselli

Center for Magnetic Resonance Research, University of Minnesota Medical School

Edward J. Auerbach
Steen Moeller
Junqian Xu
Essa Yacoub
Kamil Ugurbil