The strategies and challenges of noise reduction or removal

The least bad ways to remove noise

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NIH Summer Neuroimaging Course

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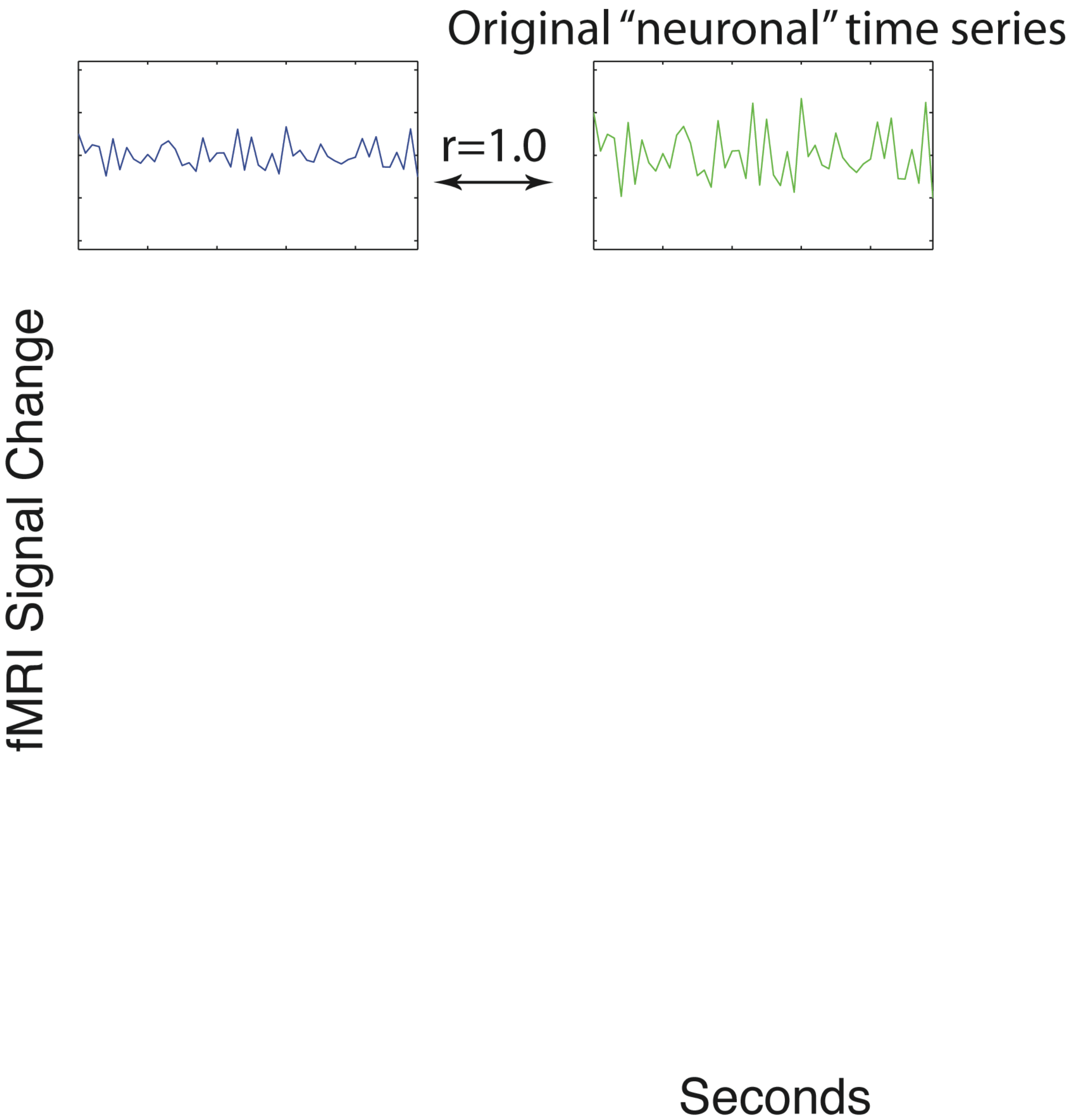
Noise

Stuff that gets in the way of of measuring what we want to measure

Noise is defined by each study’s goals

One study’s noise can be another study’s signal

Elements of the fMRI signal



Model-based fMRI
Noise that isn’t time-locked to a task is annoying.

Connectivity-based fMRI
Common noise across regions can contaminate results

Steps for dealing with noise

- Decide how to define signal and noise for a study
- Reduce noise during acquisition (last lecture)
- Attempt to remove noise from data
- Avoid analyses that are sensitive to biased noise

Philosophies of noise reduction methods

1. What we think data should look like
   Limited by our assumptions

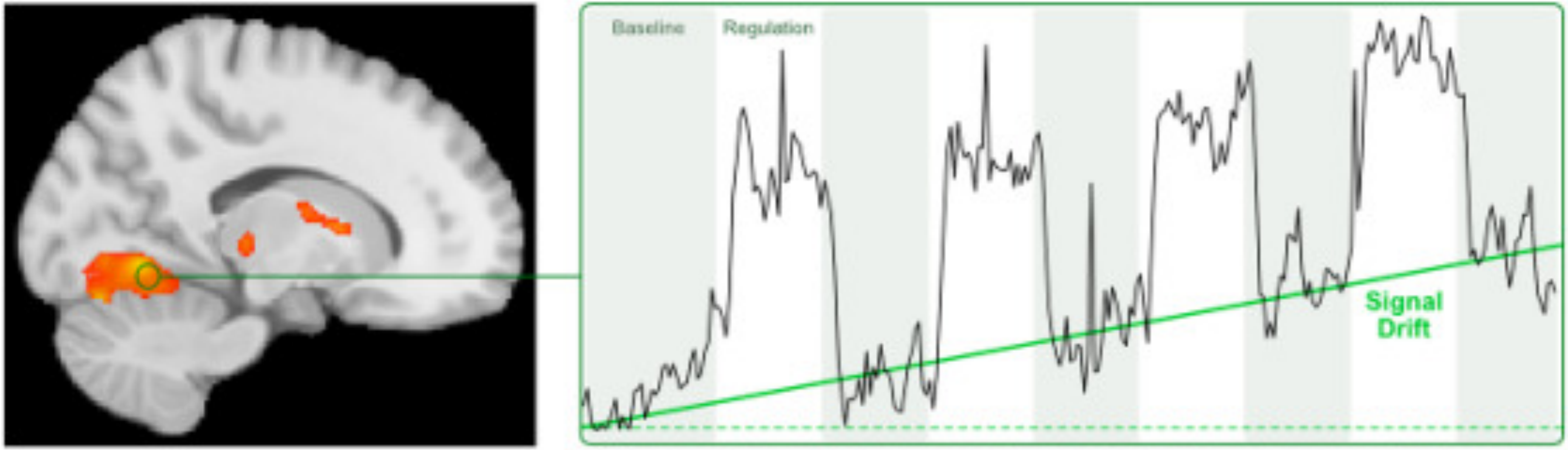
2. Based on external measures of noise
   Limited by how accurately those measures relate to fMRI noise

3. Based on physical properties of the data
   Limited by what those physical properties do or don’t separate

In actual processing/denoising pipelines, these philosophies mix

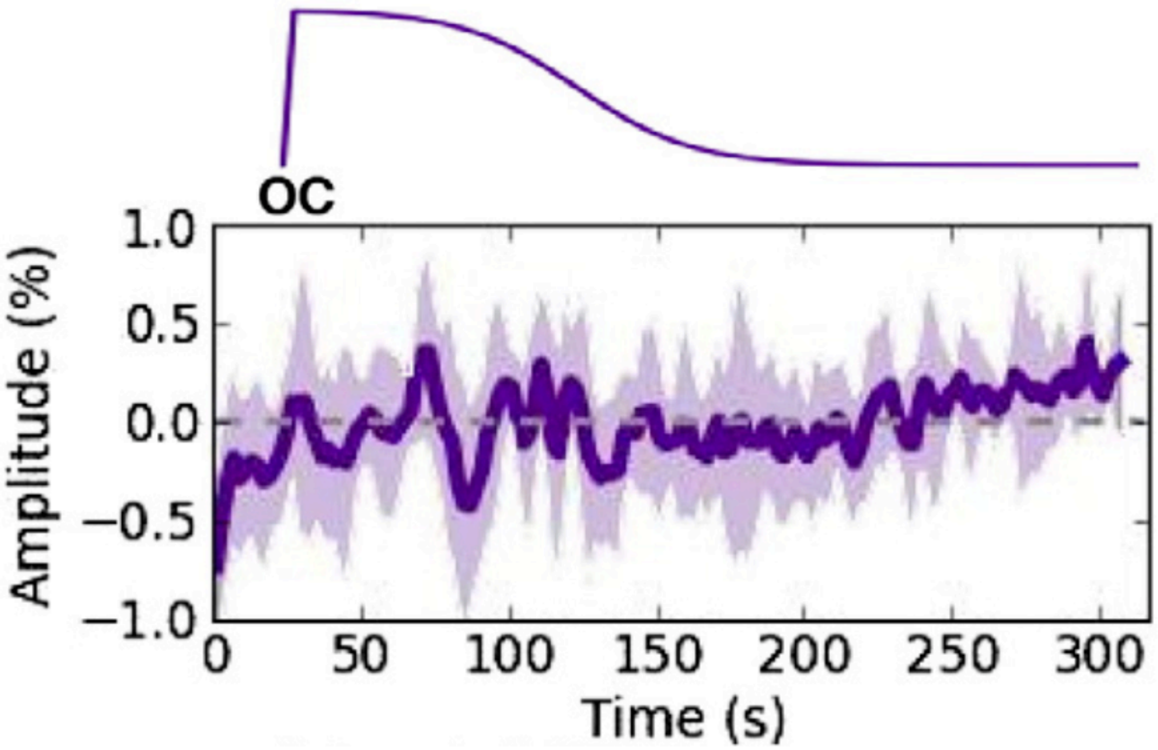
Removing what we think is noise

Slow signal drift



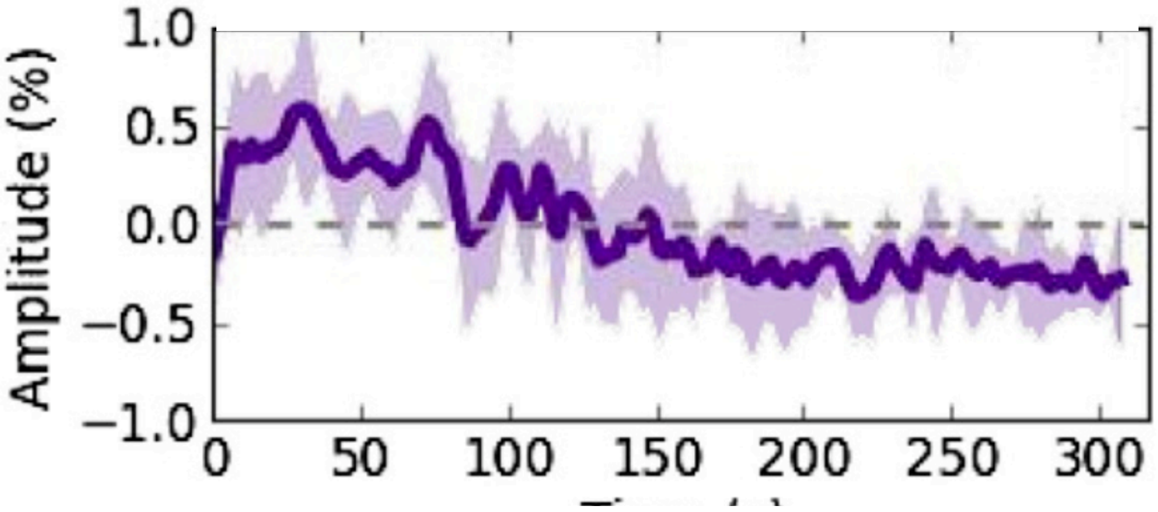
Kopel, Sladky et al, NeuroImage 2019

Is slow signal drift always noise?

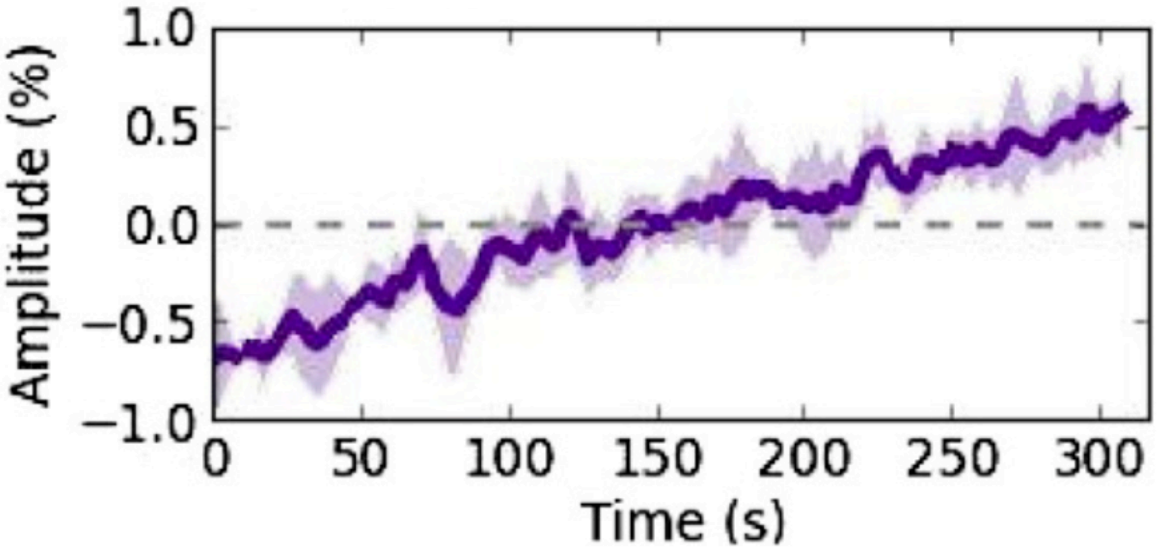


The non-denoised response to a flashing checkerboard with a slowly decreasing contrast

Multi-echo: Denoised



Multi-echo: The removed noise

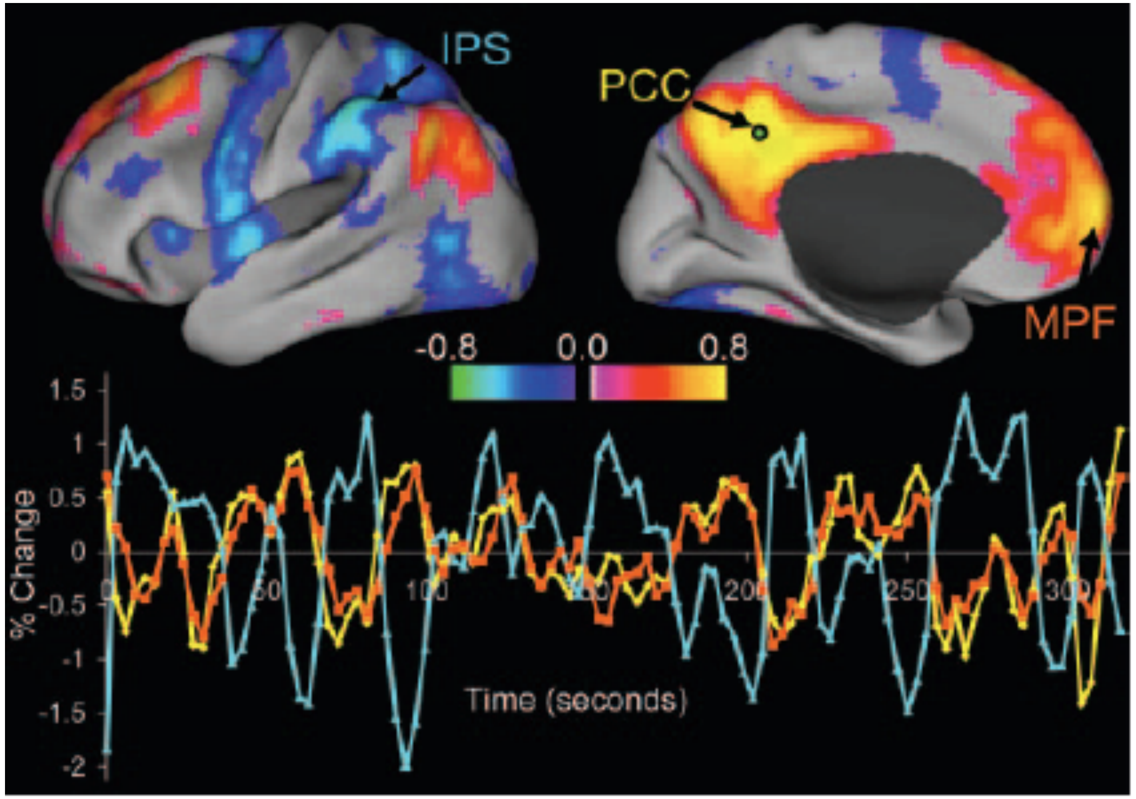


Evans, Kundu et al NeuroImage 2015

Removing what we think is noise

Global Signal Regression Case Study

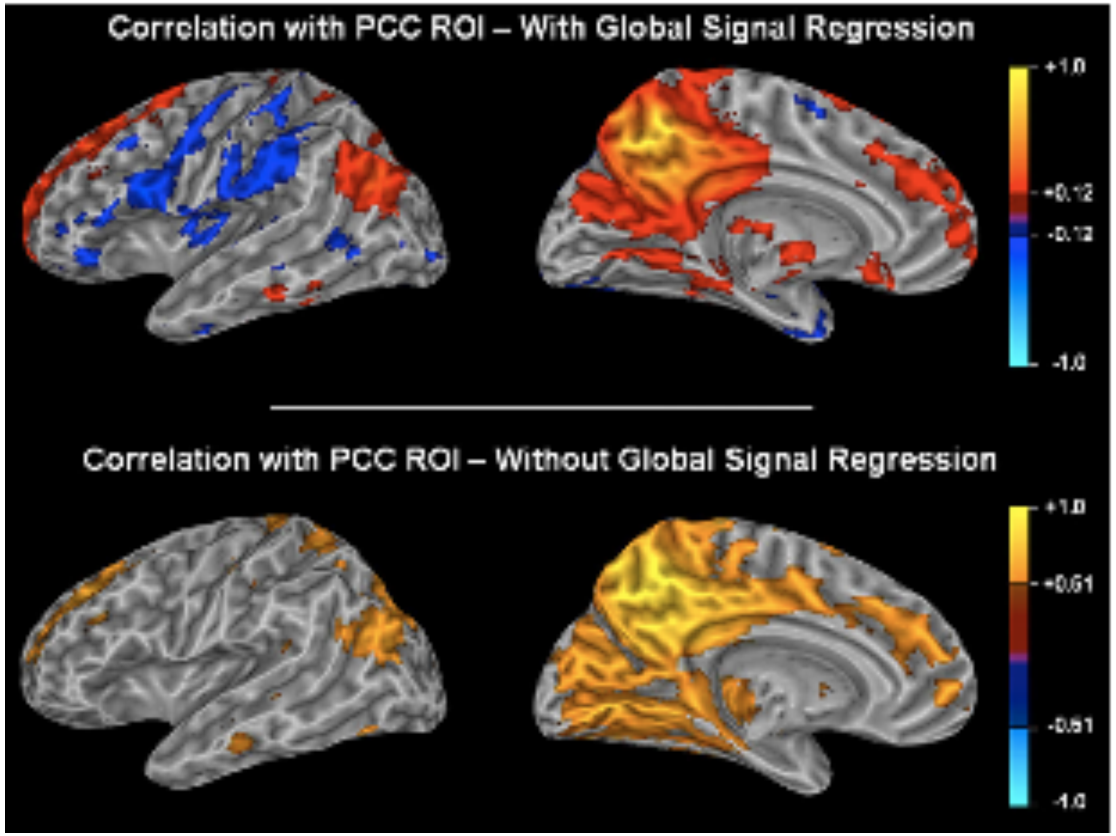
The human brain is intrinsically organized into dynamic, anticorrelated functional networks



Fox et al, *PNAS 102, 2005*

Removing what we thought was is noise

Correlations to the Posterior Cingulate



Murphy et al Neuroimage 2009

Removing the global signal was supposed to remove non-neural fluctuations, but it also induces anti-correlations

Removing uncharacterized signals can cause uncharacterized population differences

The global signal includes neural information

Altered global brain signal in schizophrenia

Genevieve J. Yang[a,b,c,1], John D. Murray[d,1], Grega Repovs[e], Michael W. Cole[f], Aleksandar Savic[a,c,g], Matthew F. Glasser[h], Christopher Pittenger[a,b,c,i], John H. Krystal[a,c,j], Xiao-Jing Wang[d,k], Godfrey D. Pearlson[a,l,m], David C. Glahn[a,m], and Alan Anticevic[a,b,c,i,j,2]

Neural basis of global resting-state fMRI activity

Marieke L. Schölvinck[a,b], Alexander Maier[a], Frank Q. Ye[c], Jeff H. Duyn[d], and David A. Leopold[a,c,1]

The perils of global signal regression for group comparisons: a case study of Autism Spectrum Disorders

Stephen J. Gotts[1], Ziad S. Saad[2], Hang Joon Jo[2], Gregory L. Wallace[1], Robert W. Cox[2] and Alex Martin[1]*

Anti-correlated networks, global signal regression, and the effects of caffeine in resting-state functional MRI

Chi Wah Wong[a,b,*], Valur Olafsson[a,b], Omer Tal[a,b,c], Thomas T. Liu[a,b,c,*]

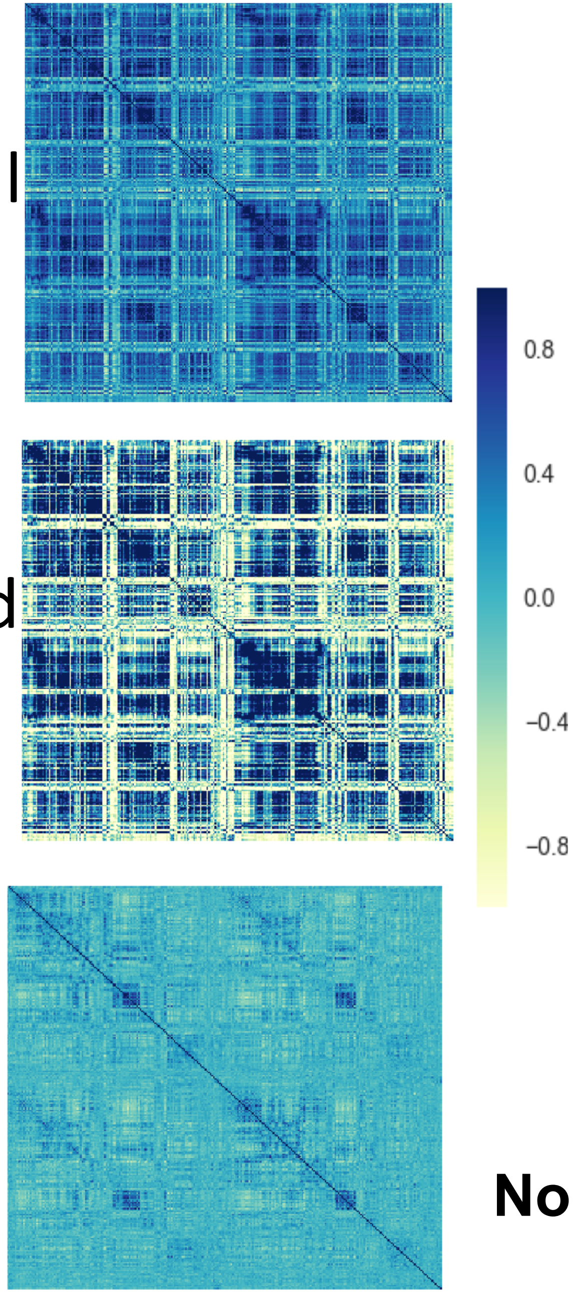
Global Signal Regression as a normalization tool

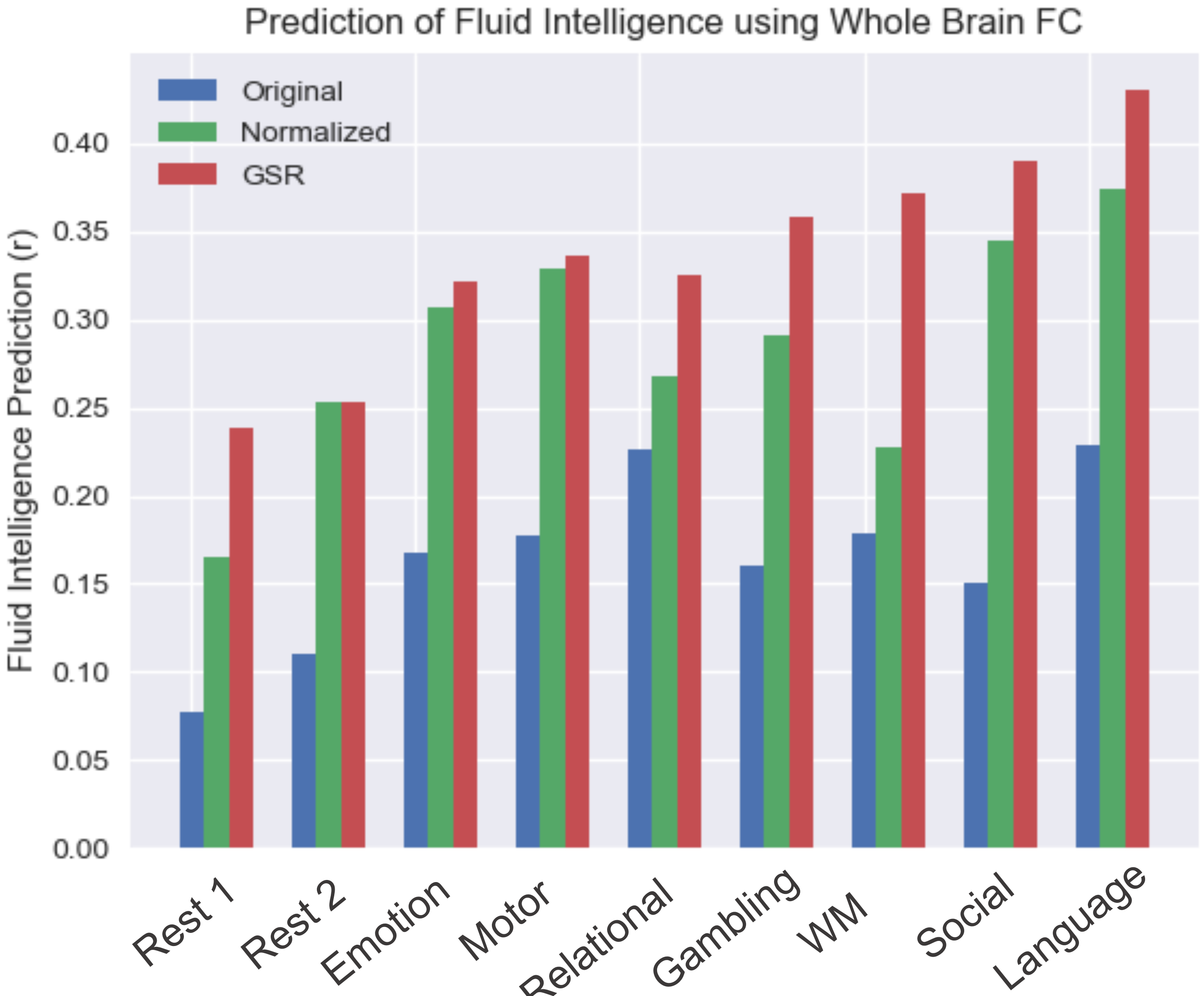
Topolski, Finn, et al
OHBM Meeting 2018

Original

Normalized

GSR





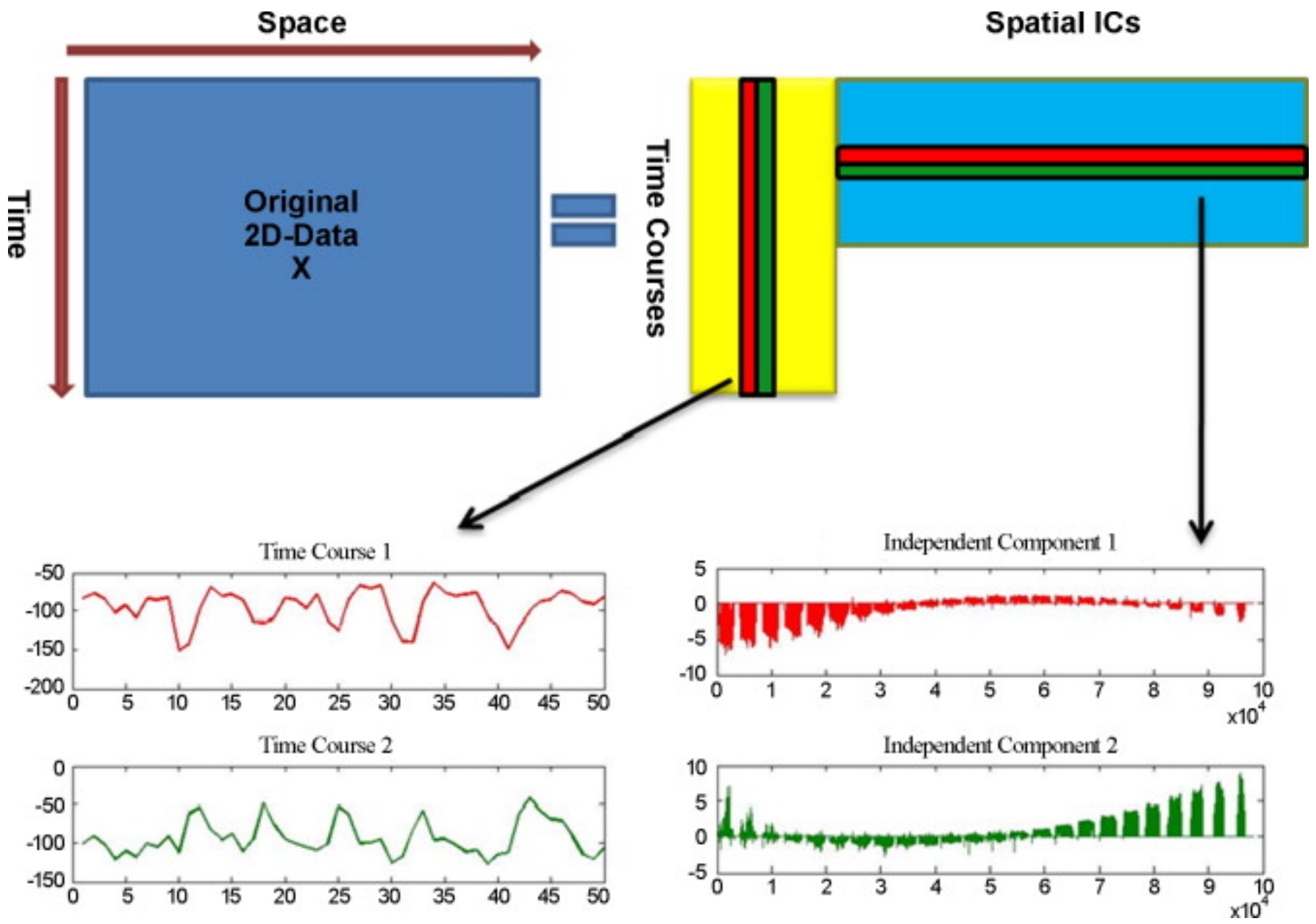
Similar observation: Li et al
www.biorxiv.org/content/
10.1101/548644v1

Noise removal interacts with analysis method choices

Global Signal Regression Case Study Summary

- Removing part of the data without examining what is or isn’t being removed can have unanticipated consequences
  - The original goal of GSR was to remove global noise sources to make it easier to examine specific correlation changes between brain regions
  - GSR makes it nearly impossible to neuroscientificially interpret precisely this type of change
- If GSR is used as a global normalization tool where one cares about relations between a system of brain areas rather than individual connections, may be more benign
  - More work is needed to see if it’s the best way normalize connectivity patterns across a population

Removing what we think is noise: ICA



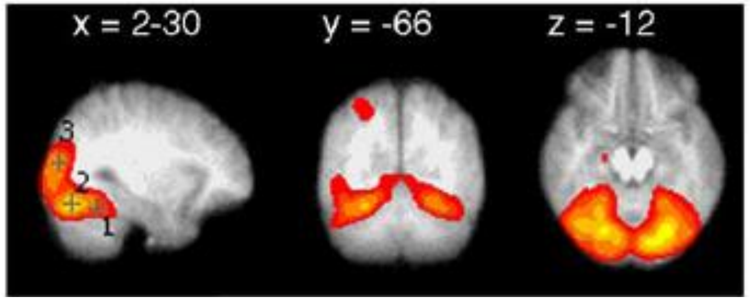
Data is decomposed into a set of spatially independent maps and a set of time courses

There are multiple methods for identifying relevant components
Also multiple ways to model groups of volunteers

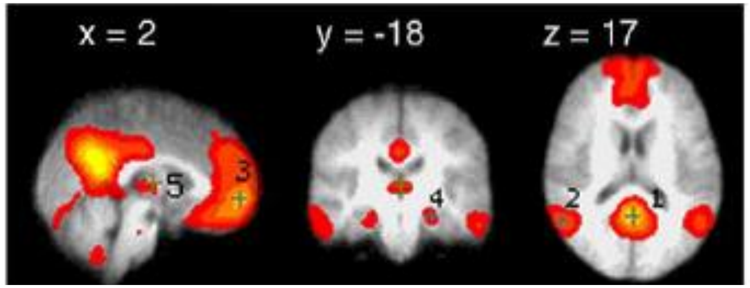
Li et al Computerized Medical Imaging and Graphics March 2009

5 brain networks using ICA

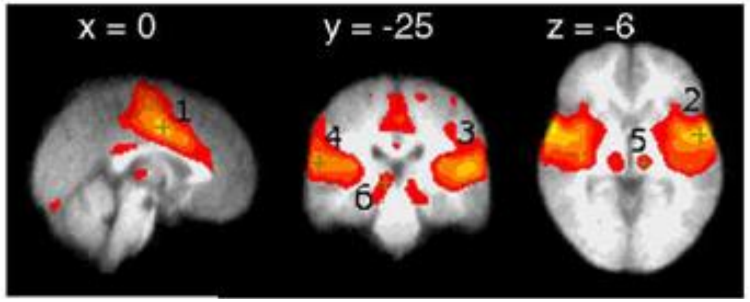
Visual



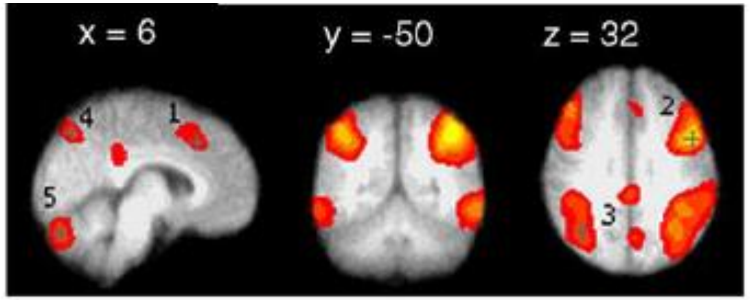
Visuospatial & Executive



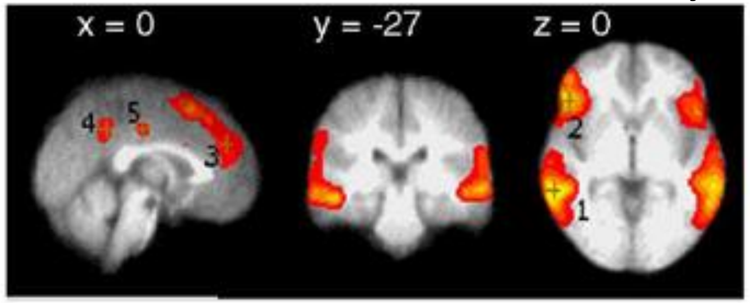
Sensory & Auditory



Dorsal “What” Pathway



Ventral “Where” Pathway



M. De Luca et al., *NeuroImage* 2006

Network names are based on knowledge from past research

ICA denoising framework

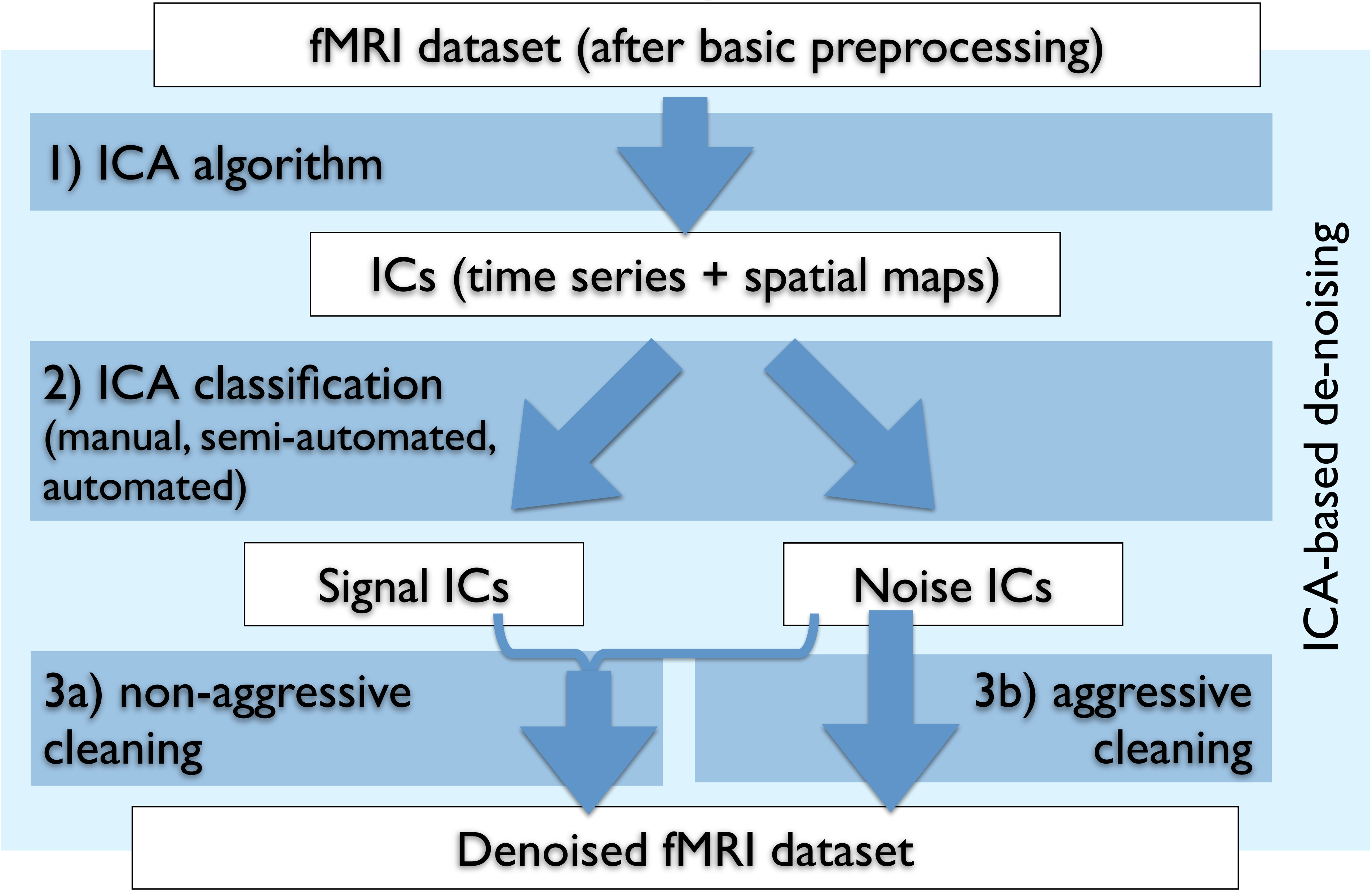
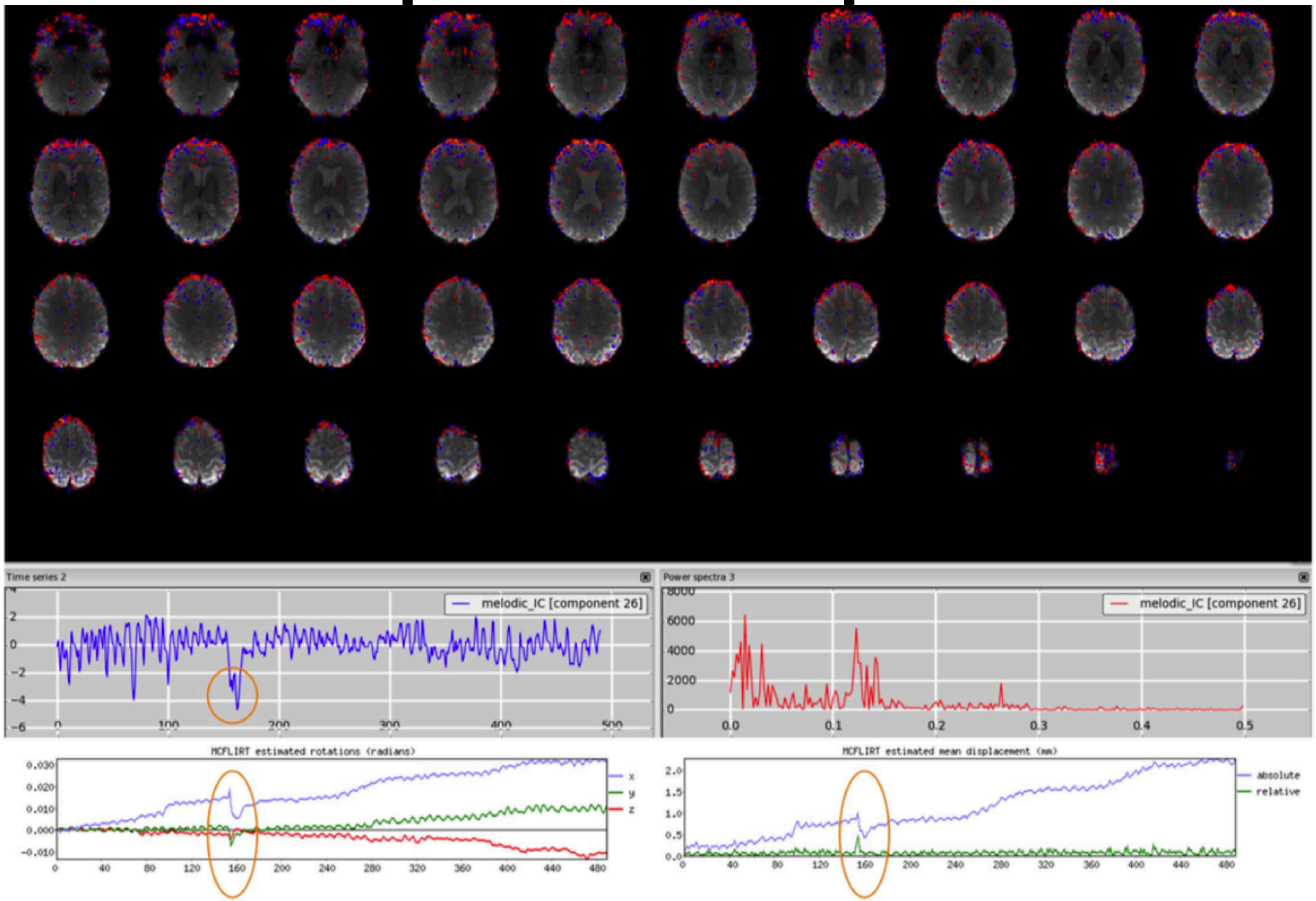


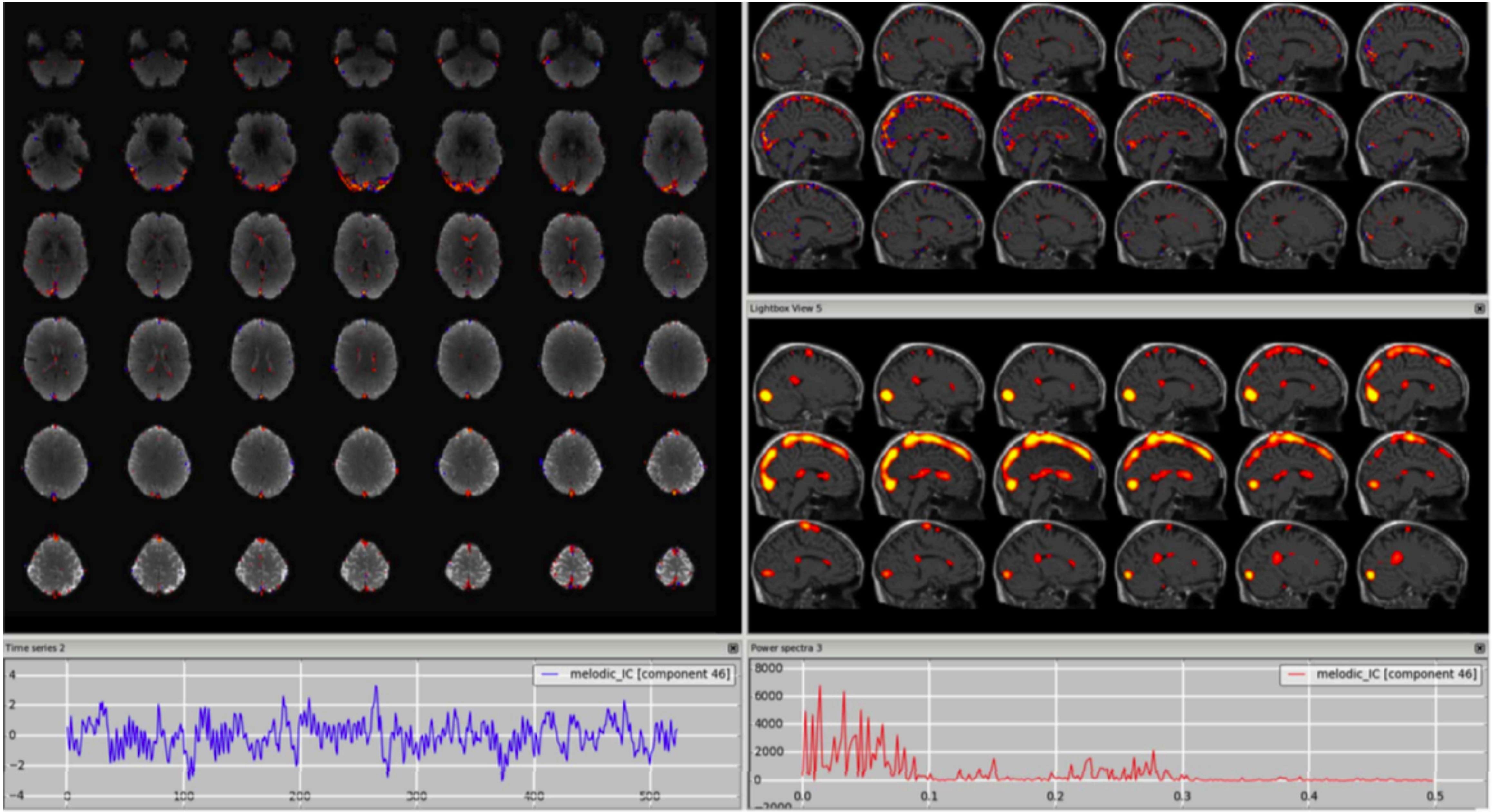
Image from: Ludovica Griffanti's OHBM 2017 Talk on "How-to use ICA for denoising"
"Advanced Methods for Cleaning up fMRI Time-Series" https://www.pathlms.com/ohbm/courses/5158/sections/7788

Sample ICA Components



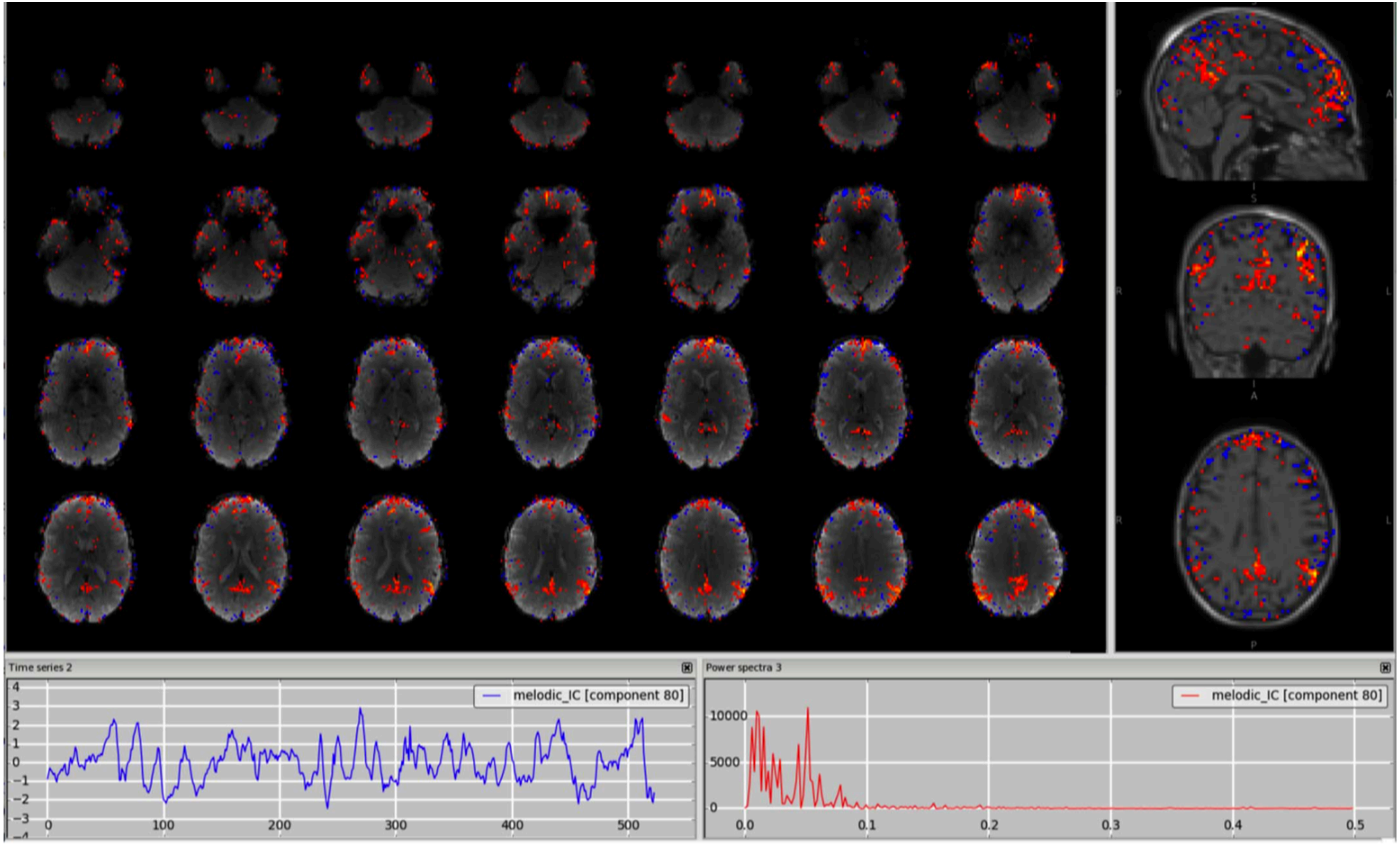
Griffanti et al NeuroImage 2017

Sample ICA Components



Griffanti et al NeuroImage 2017

Sample ICA Components



Griffanti et al NeuroImage 2017

Automated ICA Noise Removal

Approach	Purpose	#features	Classifier type	Training required?
SOCK [Bhaganagarapu et l., 2013]	multiple sources of noise	4	k-means clustering, 5 combinations of conditions	NO
FIX [Salimi-Khorshidi et al., 2014]	multiple sources of noise	>180	Hierarchical fusion (kNN, decision tree, SVM)	YES
Sochat et al., 2014	multiple sources of noise	246	Sparse Logistic Regression	YES
AROMA [Pruim et al., 2015]	Motion	4	Noise if exceeds at least one of 3 criteria	NO

Temporal ICA
[Glasser et al 2018]

Different type of ICA & used in conjunction with FIX

Image from: Ludovica Griffanti's OHBM 2017 Talk on "How-to use ICA for denoising"
"Advanced Methods for Cleaning up fMRI Time-Series" https://www.pathlms.com/ohbm/courses/5158/sections/7788

Removing what we think is noise

+ Possible with almost any fMRI data

+ Repeatedly shown to be useful & can be automated

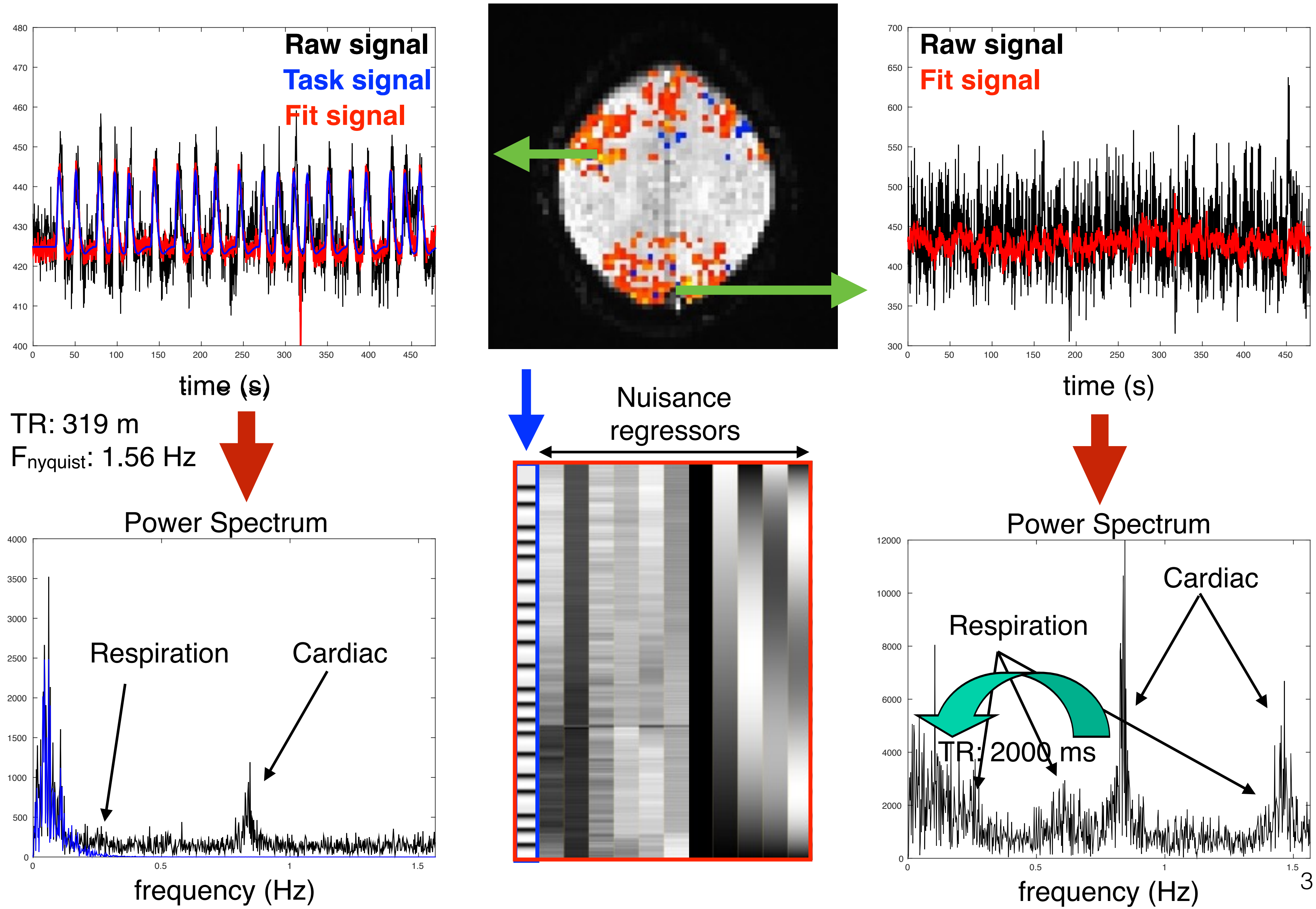
- If you don't know what you're removing:
  - You don't know if you're removing something different across individuals or populations in important ways
  - You risk losing neural interpretability of results

Noise reduction based on external measures of noise sources

Nuisance Regressors

- Respiration (rate, depth, and end tidal CO_2)
- Heart Pulsation
- Head motion (Regression & Censoring)

- These measures can either be from purely external devices or validated as being from the data
  - Sagittal Sinus time series, Cerebrospinal fluid, white matter, ANATICOR
  - Machine Learning Methods



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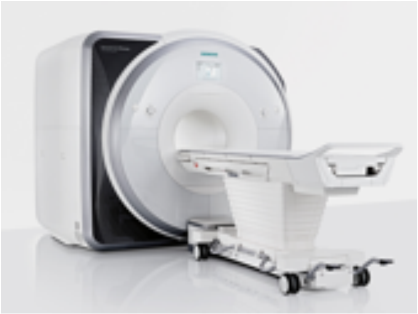

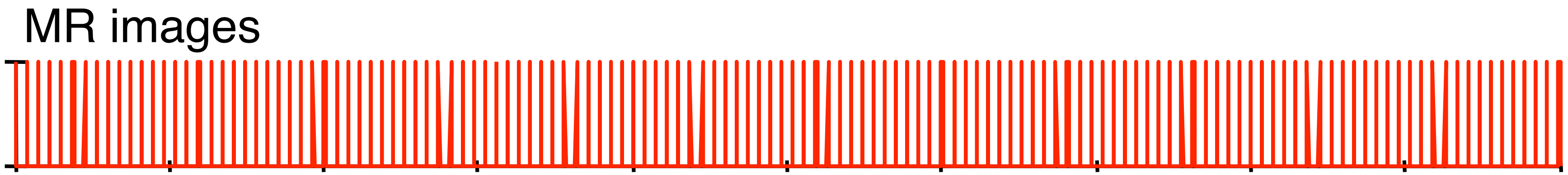

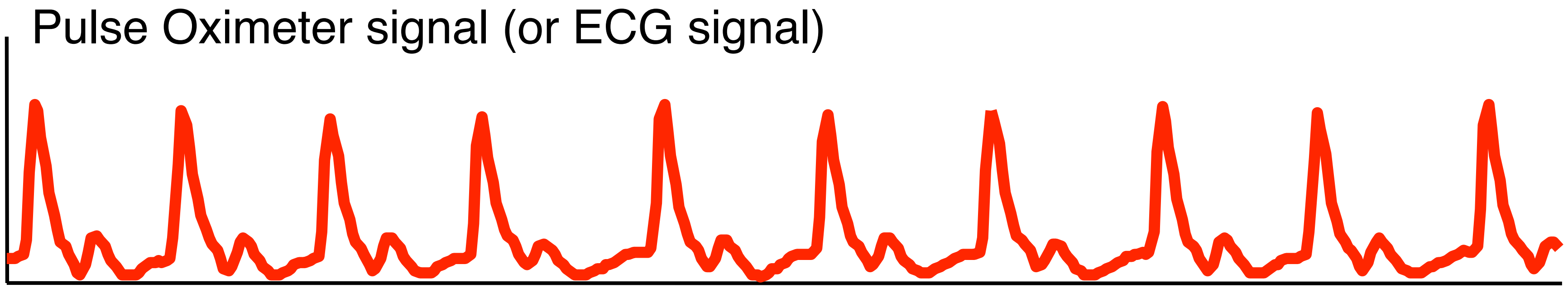

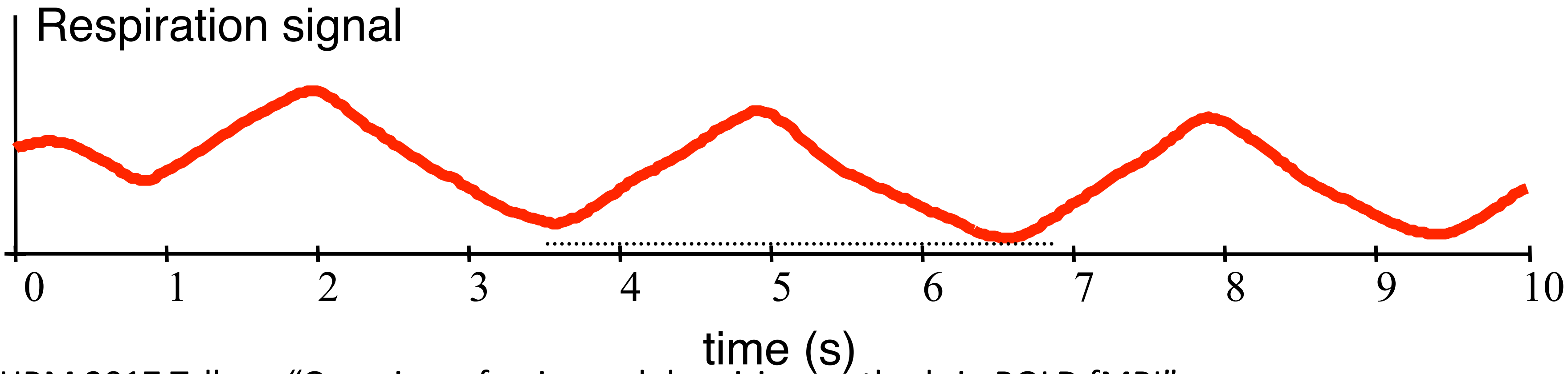

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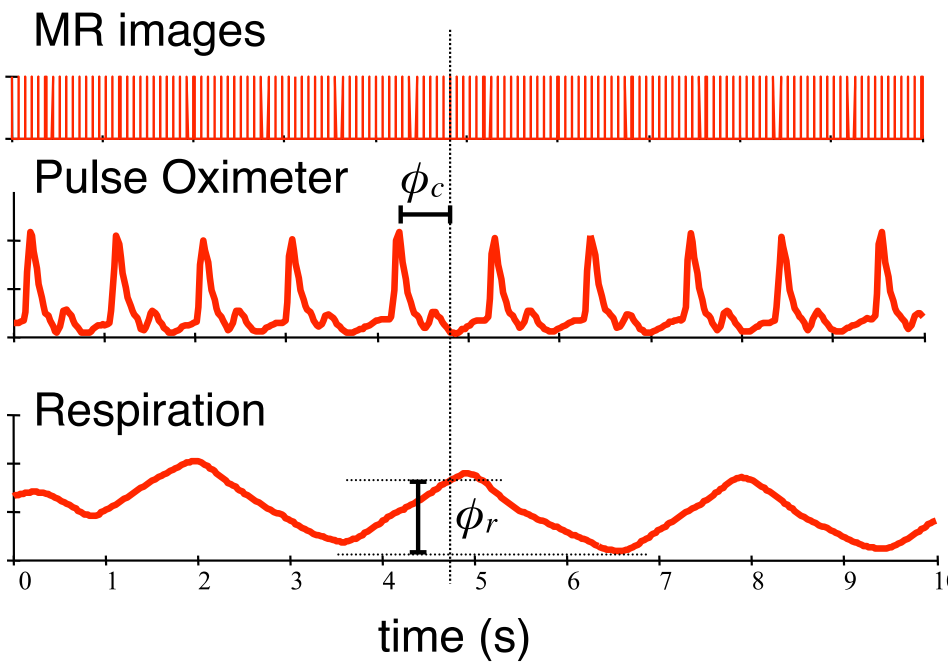
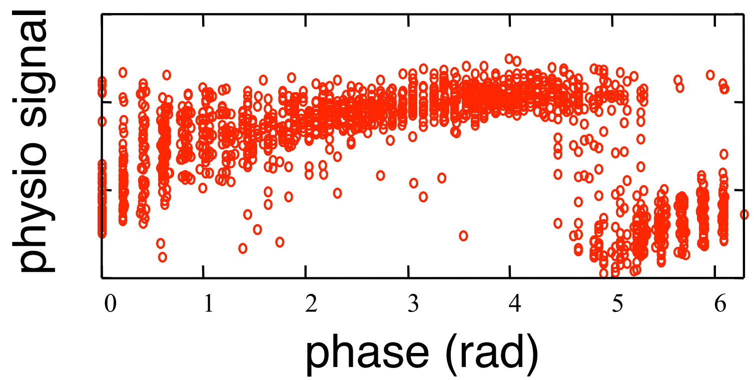
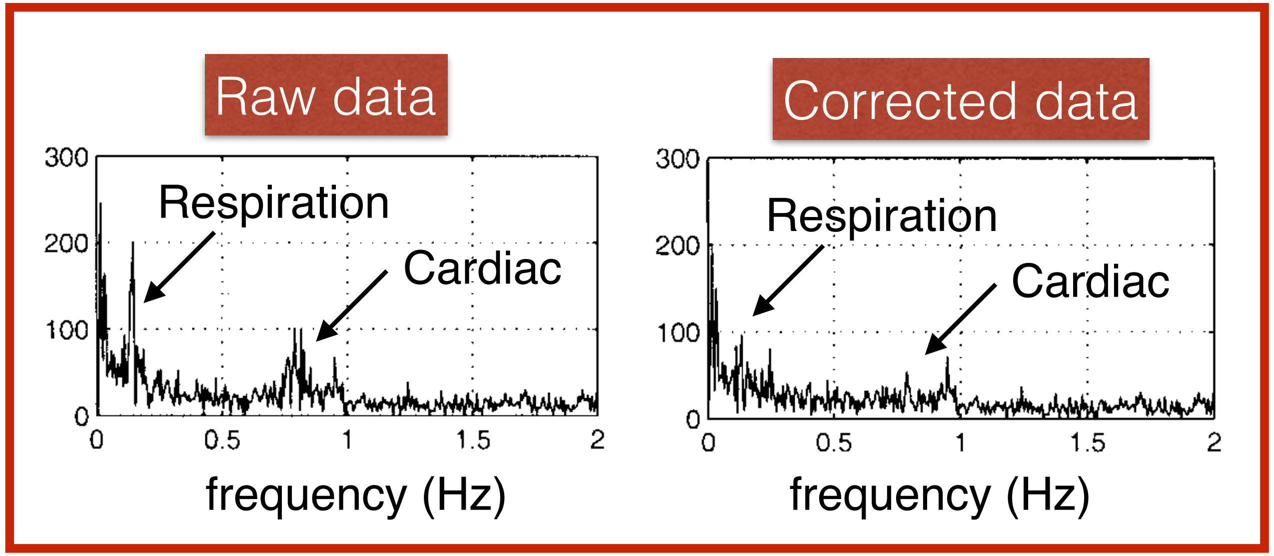
Figures courtesy of Rasmus Birn (University of Wisconsin-Madison)

RETROICOR (Glover et al MRM2000)





$$
\left\{
\begin{array}{c}
\cos(\phi_r) \\
\sin(\phi_r) \\
\cos(2\phi_r) \\
\sin(2\phi_r) \\
\cos(\phi_c) \\
\sin(\phi_c) \\
\cos(2\phi_c) \\
\sin(2\phi_c)
\end{array}
\right\}
$$



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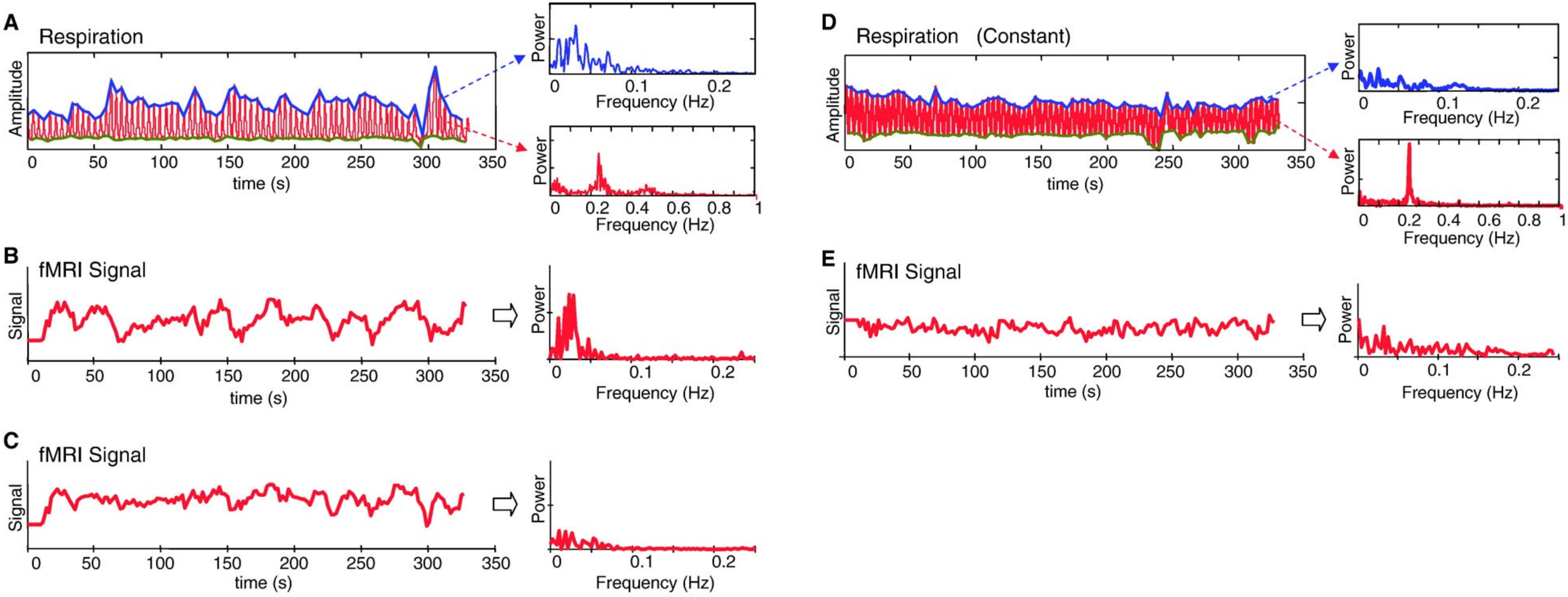
Respiration*Volume/Time (RVT)

Regular Breathing | Constant Breathing



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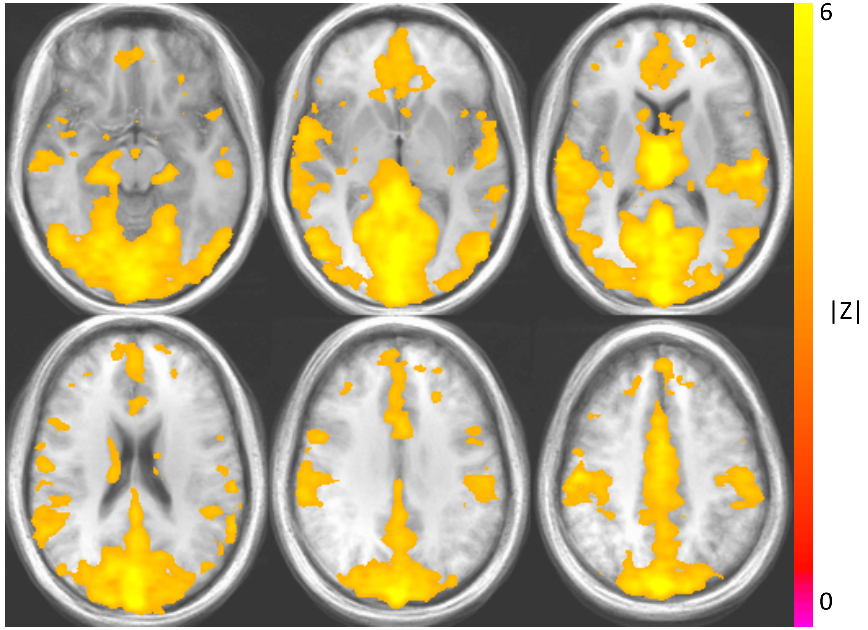
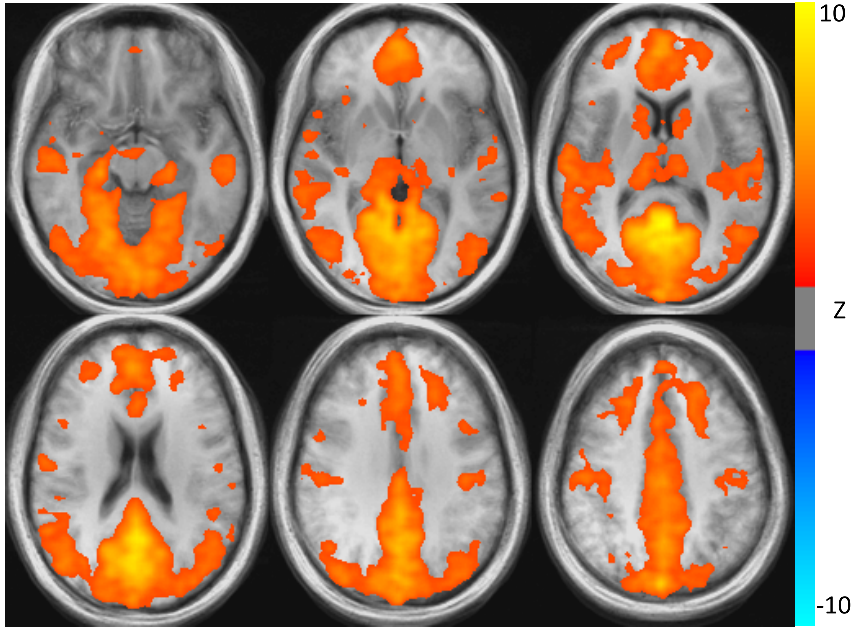
At best respiration and cardiac pulsation adds noise to regional connections. At worst it obscures neural connections.

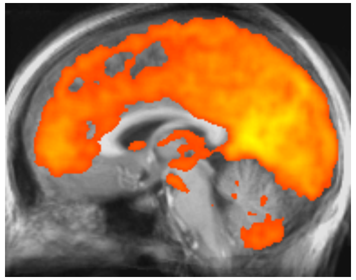
Respiration changes using RVT



Correlation (of PCC) at Rest



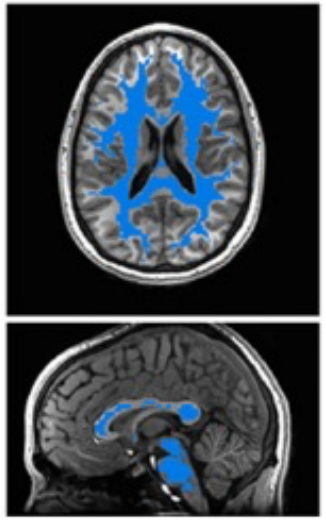
Group (n=10)



RVT = measuring and tracing (Respiration Volume)/time and removing it from the time series

Slide from Rasmus Birn

ANATICOR



White matter eroded (WMe)

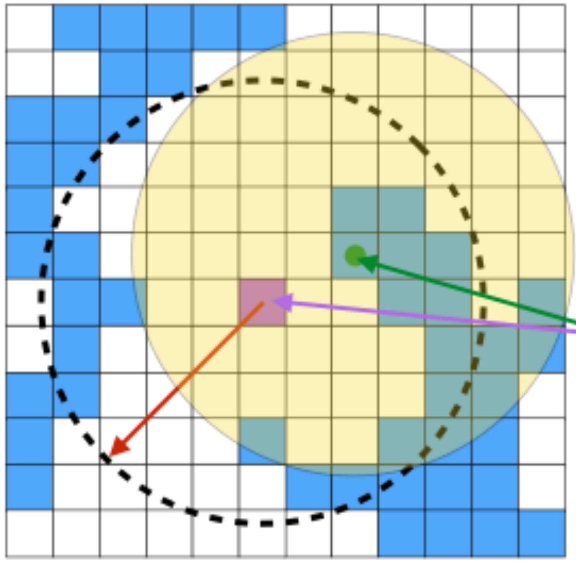
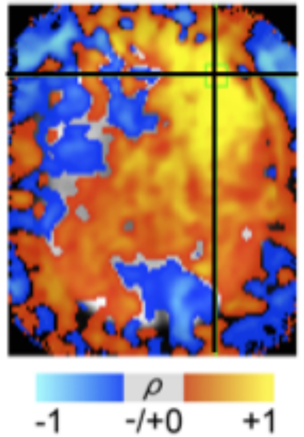


Figure adapted from Box Cox (AFNI)

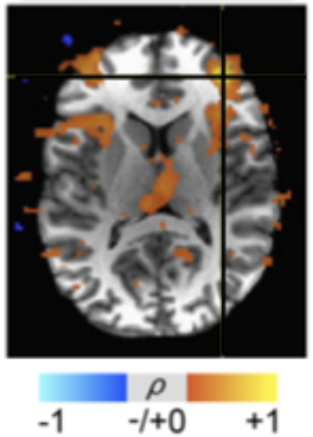
Average signal over WMe voxels inside 20 mm radius

Voxel-dependent nuisance regressors

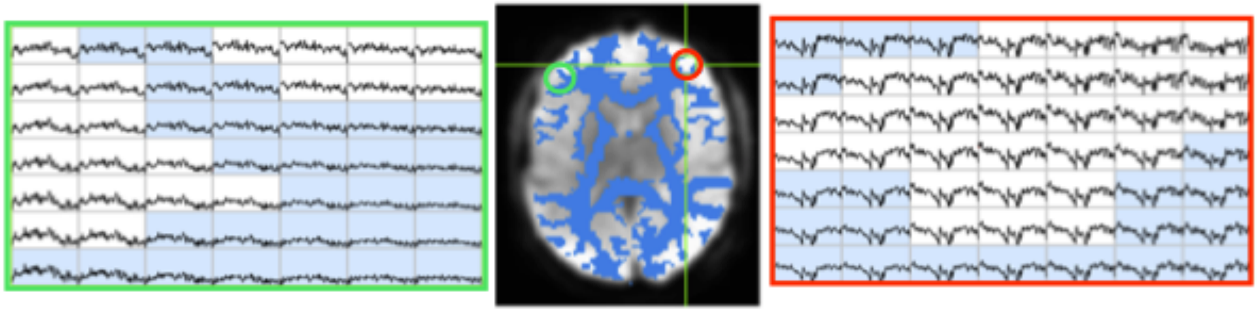
BEFORE ANATICOR



AFTER ANATICOR



LOCALIZED HARDWARE INSTABILITIES



Jo et al. NeuroImage 2010

Image from: César Caballero Gaudes OHBM 2017 Talk on “Overview of noise and denoising methods in BOLD fMRI”
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Nuisance Regression Approaches

+ Can be based on known external sources of noise

+ They clearly remove much of this noise

- Only as good as the models linking these external measures to fMRI fluctuations

- Where they fit in a preprocessing pipeline can be tricky

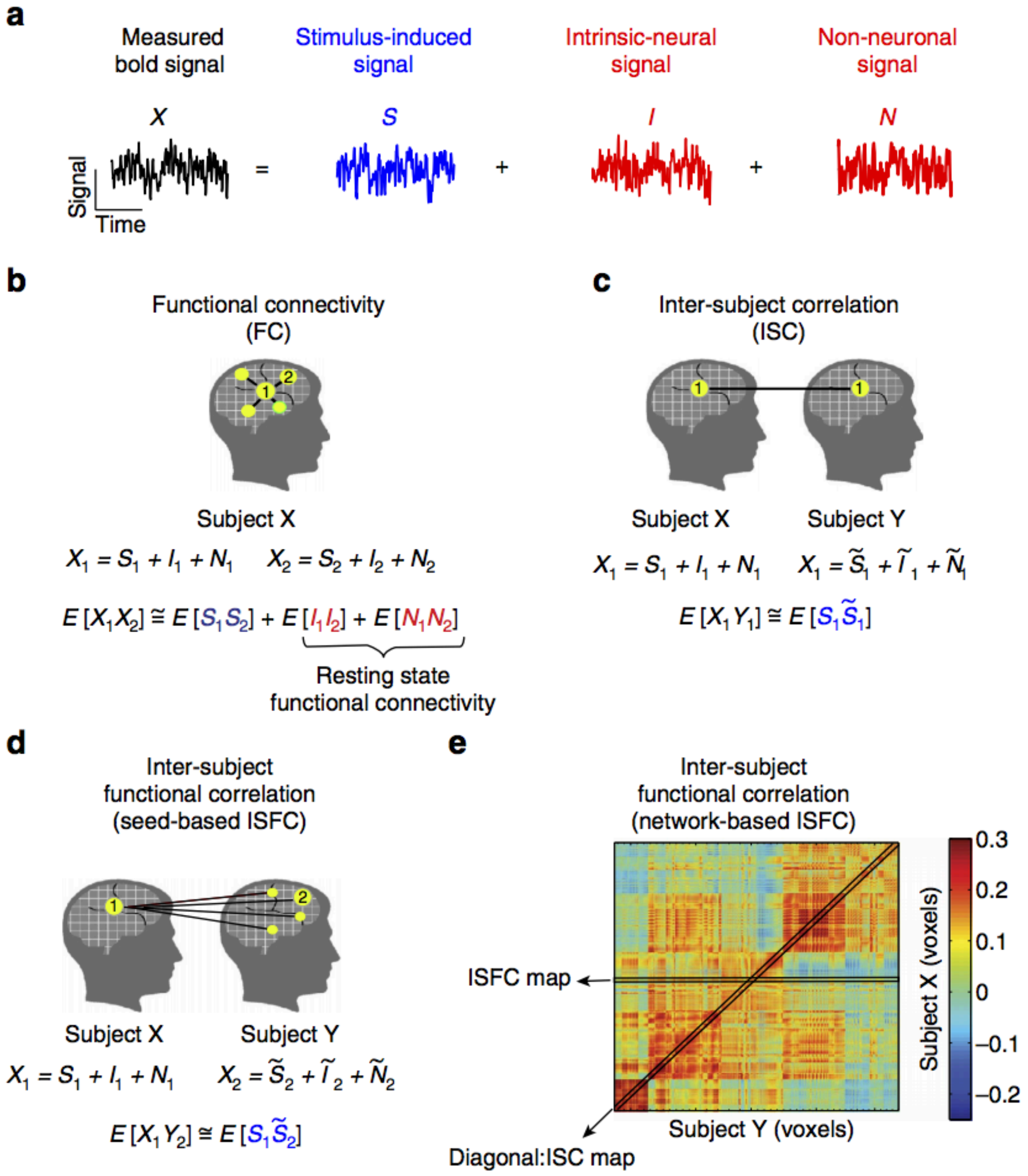
  Bright et al “Potential pitfalls when denoising resting state fMRI data using nuisance regression” NeuroImage 2017

Good general review of the many approaches:
Caballero Gaudes et al “Methods for cleaning the BOLD fMRI signal” NeuroImage 2017

Inter Subject Correlation

Assuming any signal fluctuations that are consistent across volunteers are unlikely to be noise

Simony, Honey, et al,
Nature Communications 2016

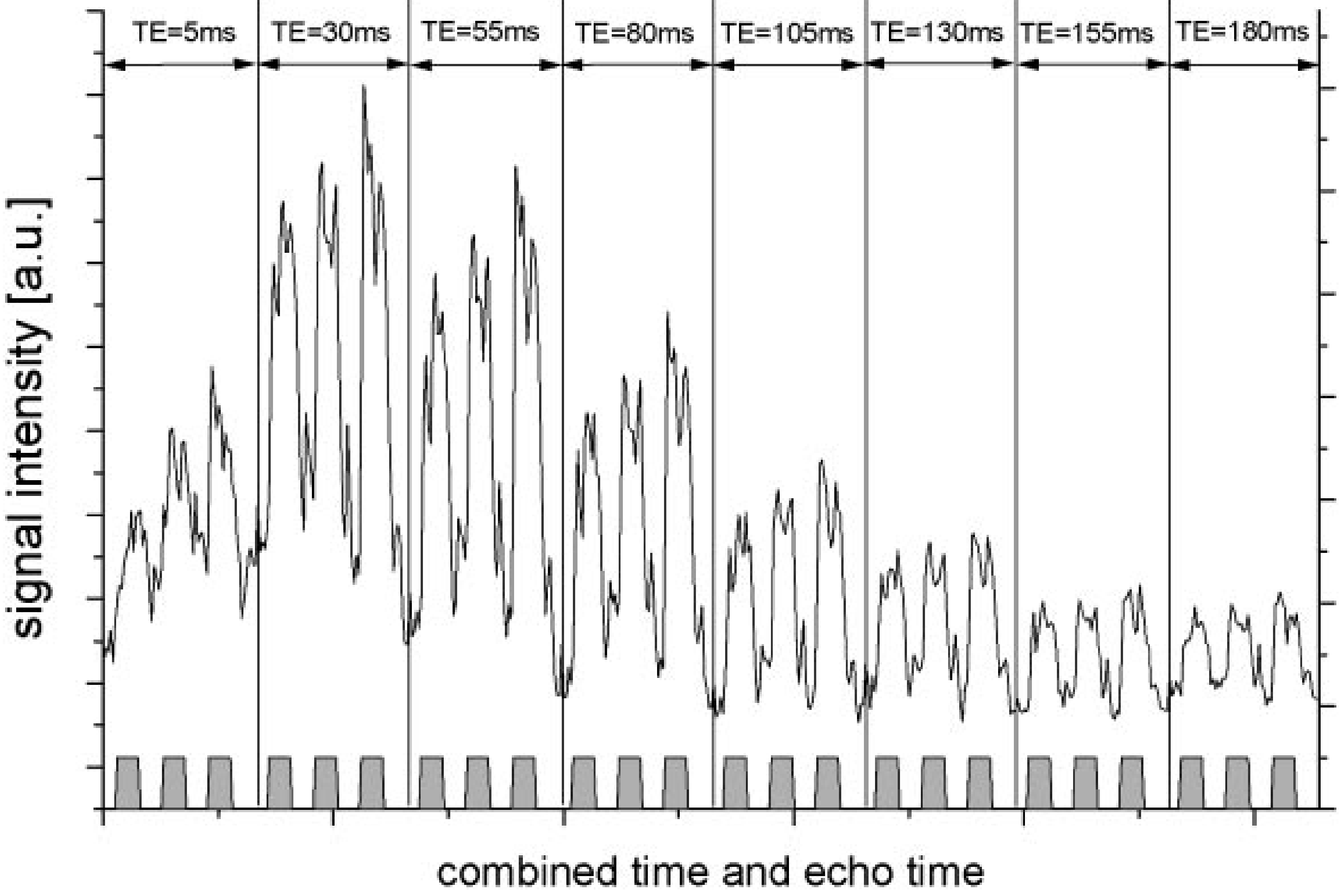


Based on the physical properties of the data

- Distortion correction through field mapping (Not covering)
- Calibration scans (Mentioned in the last lecture)
- Multi-echo fMRI approaches

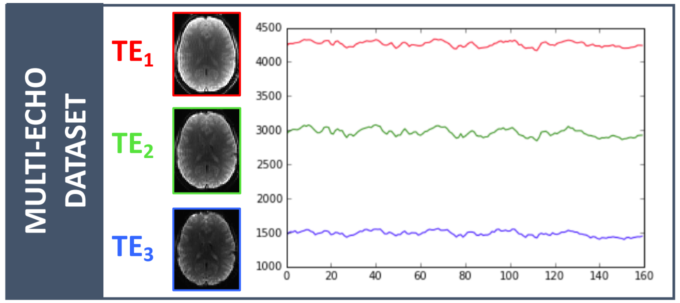
Using multi-echo fMRI to increase confidence that responses are BOLD

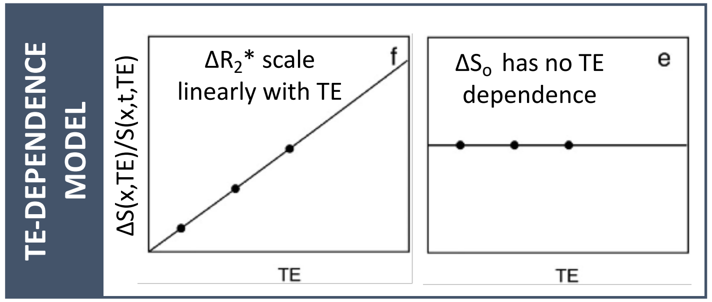
Average across active voxels in a figure tapping task at 3T



Barth et al NMR Biomed 2001, p484

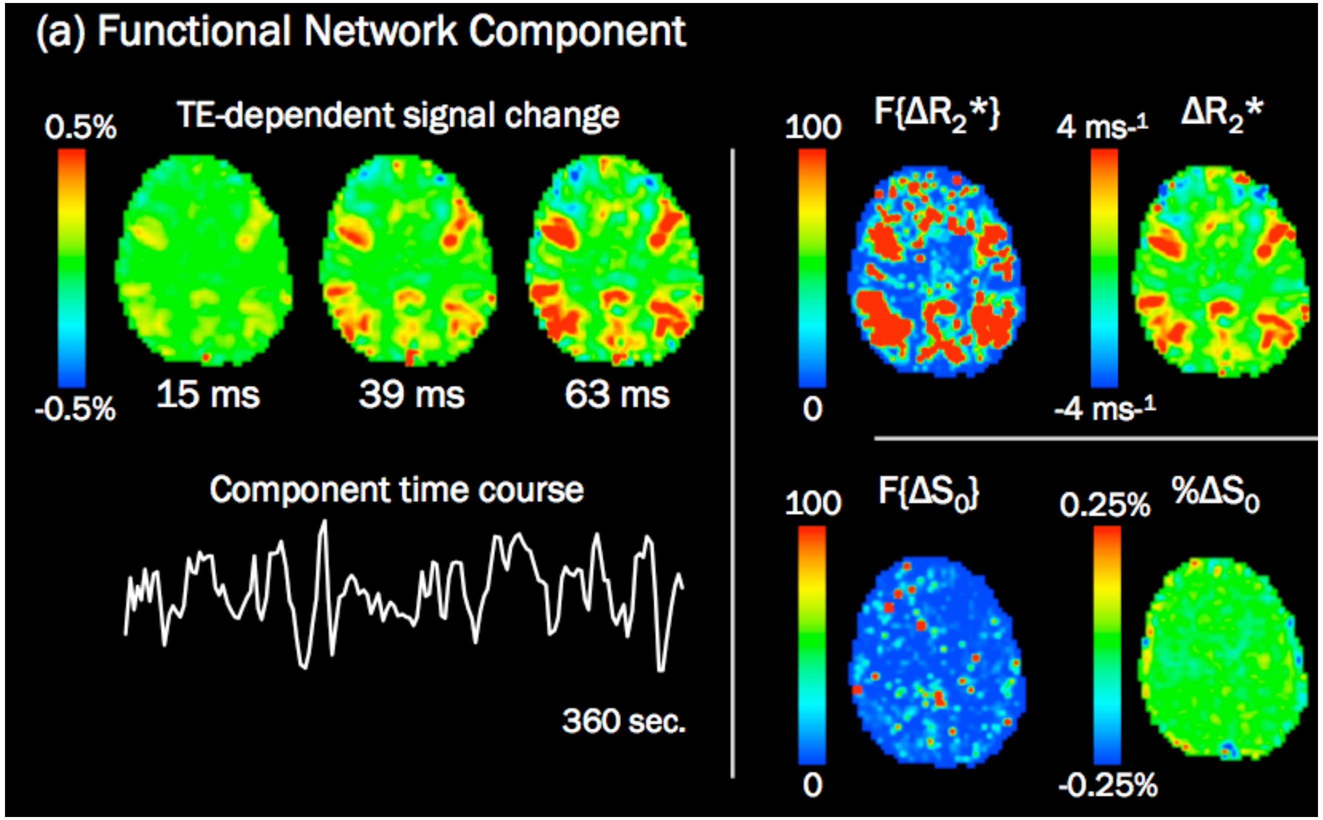
ME-ICA Denoising





TIMESERIES OF INTEREST

ICA Representative Timeseries



$$\kappa = \sum_{AllVoxels} z_v^2 F_{v,R_2^*}$$

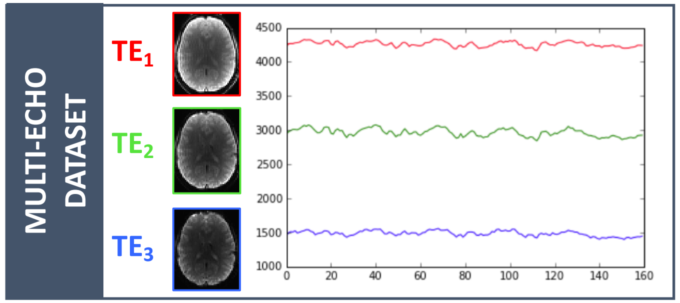
$$\rho = \sum_{AllVoxels} z_v^2 F_{v,S_o}$$

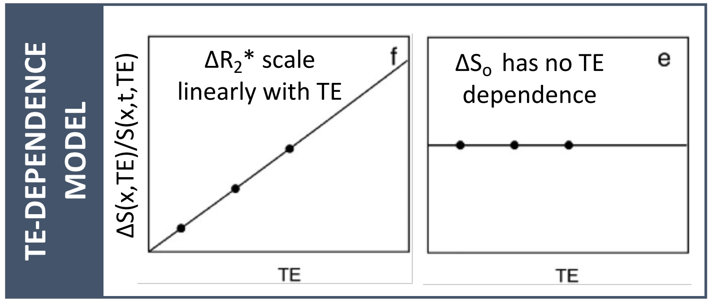
Kappa (κ) = 210

Rho (ρ) = 10

Kundu et al., NeuroImage 2012

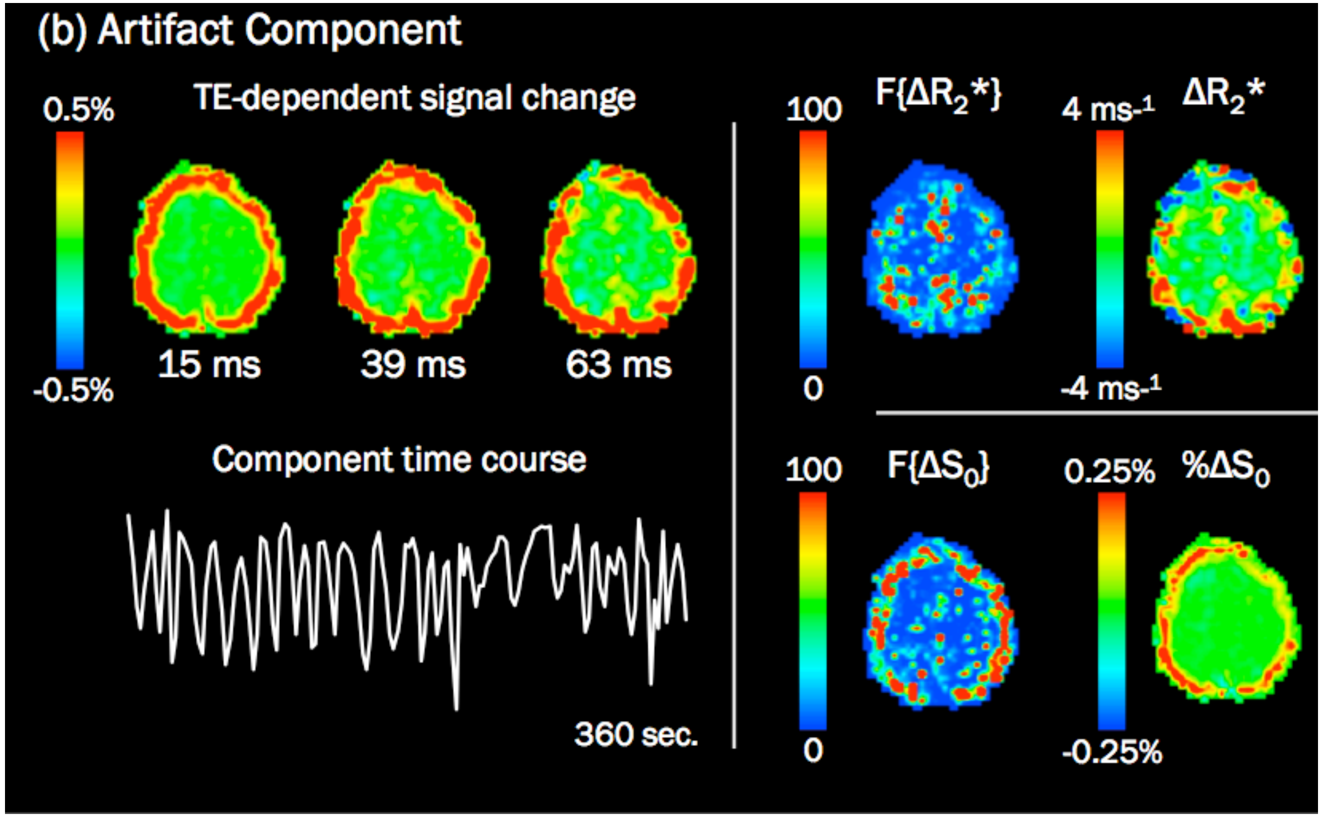
ME-ICA Denoising





TIMESERIES OF INTEREST

ICA Representative Timeseries

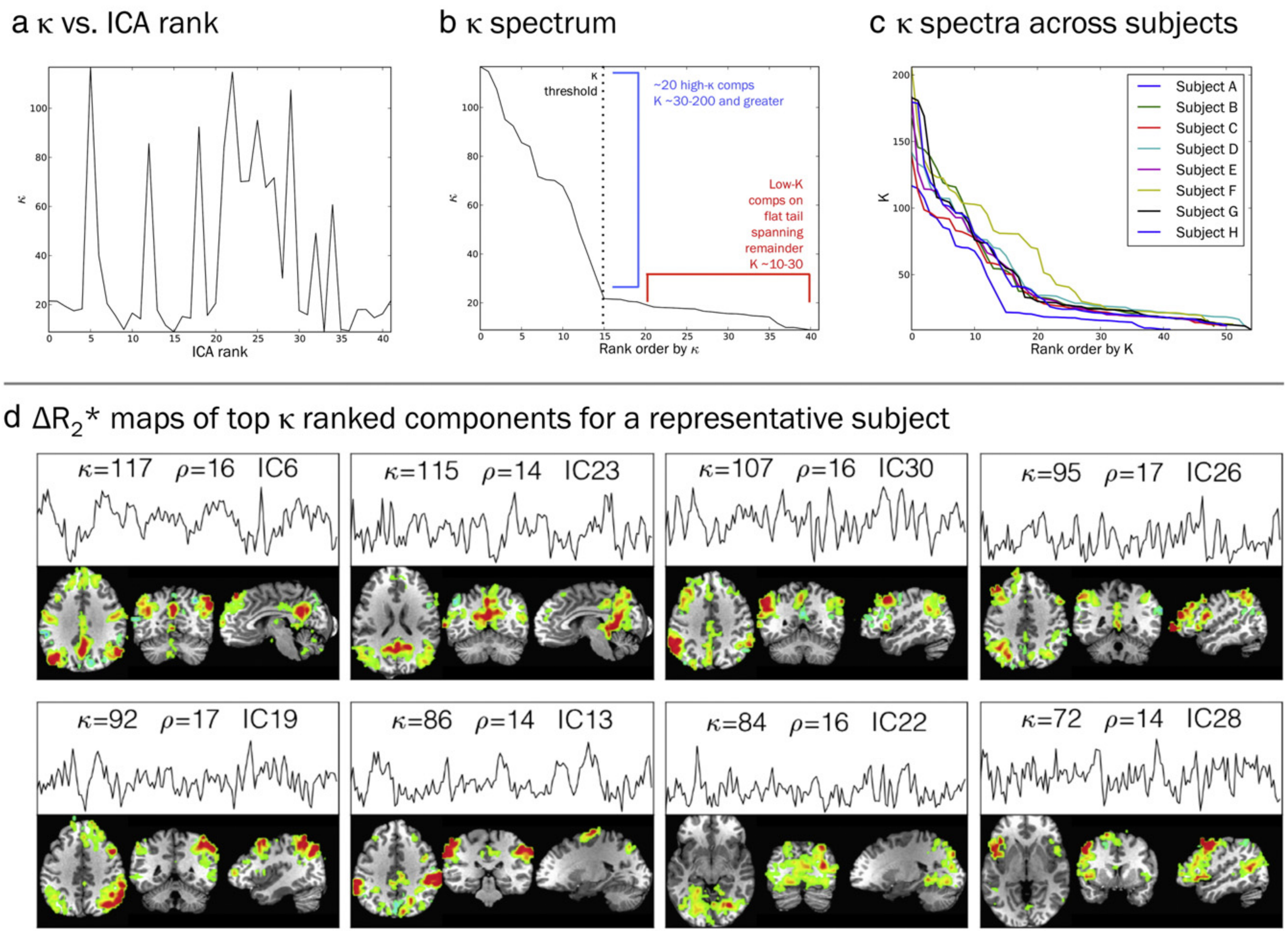


Kappa (κ) = 32

Rho (ρ) = 81

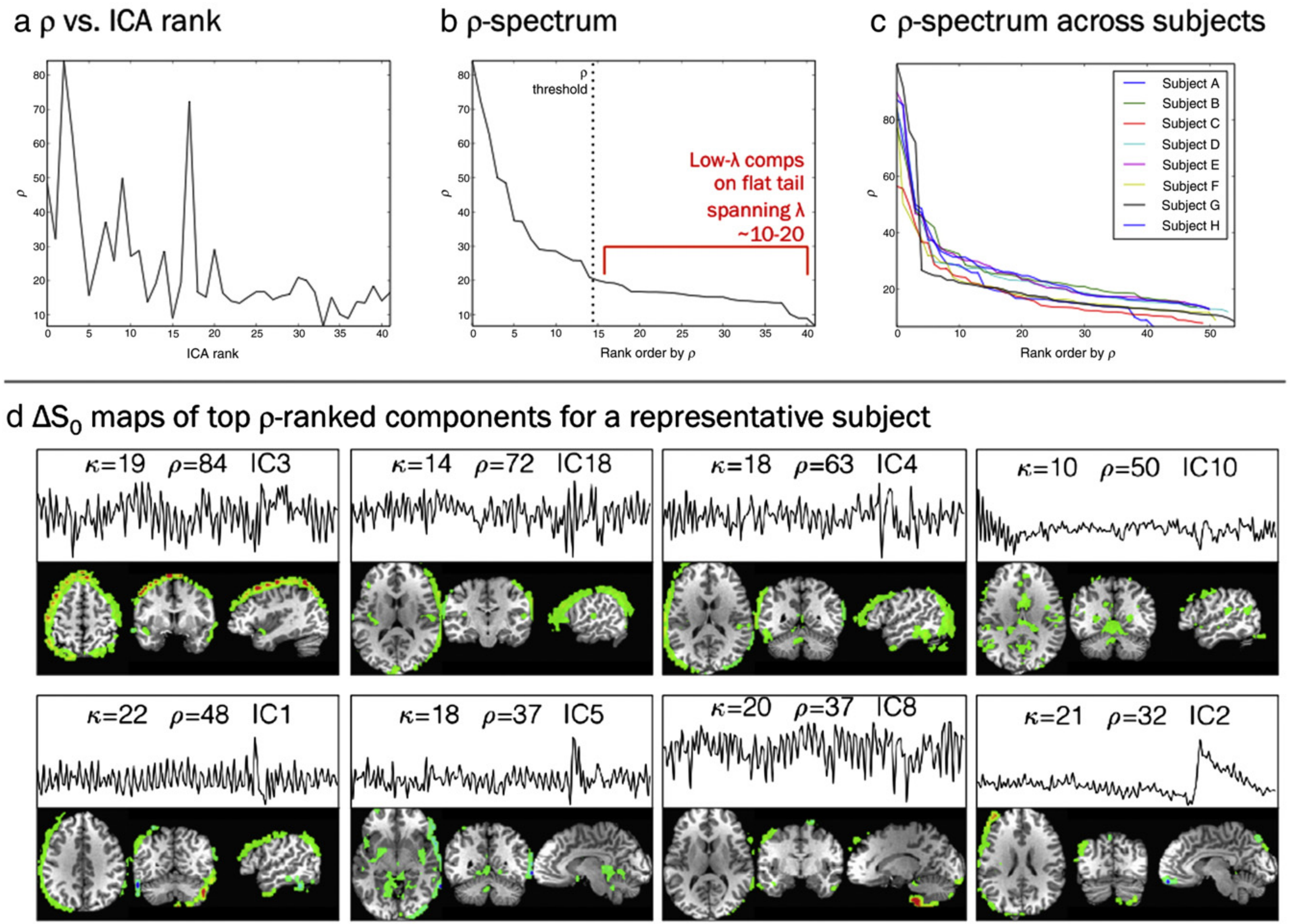
Kundu et al., NeuroImage 2012

ME-ICA Denoising



Kundu et al., NeuroImage 2012

ME-ICA Denoising



Kundu et al., NeuroImage 2012

ME-ICA is just one method for using multi-echo fMRI for denoising

+ It has been shown to empirically remove multiple noise sources
+ Potentially can retain difficult non-noise signals, like slow neural changes
- As an ICA method it is still dependent on what is or isn't in each ICA component
- Some noise signals, like respiration, are BOLD weighted
- Optimal algorithm is still being developed
- Still rests on making models of what is or isn't likely to be BOLD

Other approaches are in use or under development

Avoid analyses that are sensitive to biased noise

- When comparing populations with a clear head motion differences, use caution with methods that are really sensitive to head motion
  - Global functional connectivity measures?
- When comparing populations with a neurovascular coupling differences, use caution with methods that are really sensitive to neurovascular coupling
  - Over-reliance on the response peak magnitudes or response shape of a single region

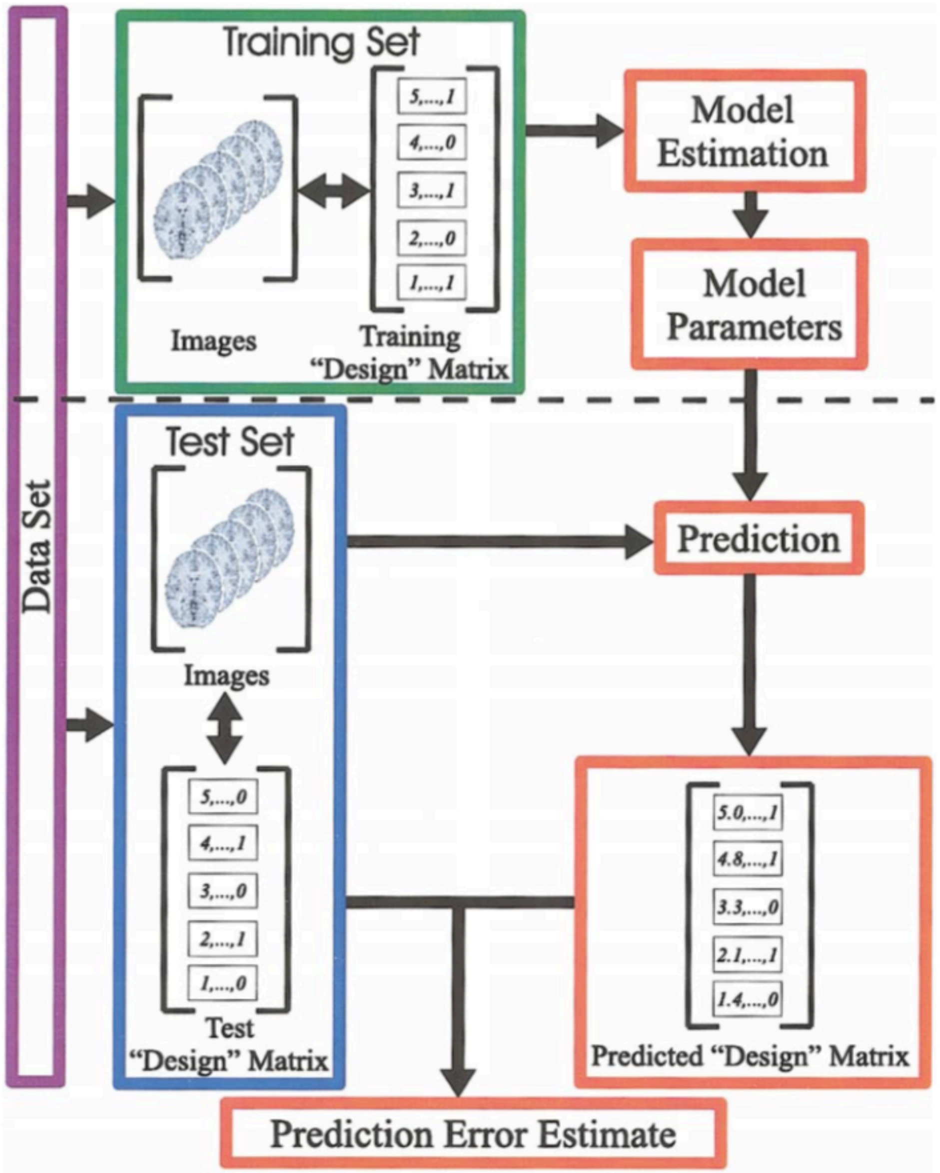
Avoid analyses that are sensitive to biased noise

NPAIRS Data Analysis Framework
Strother et al NeuroImage 2002

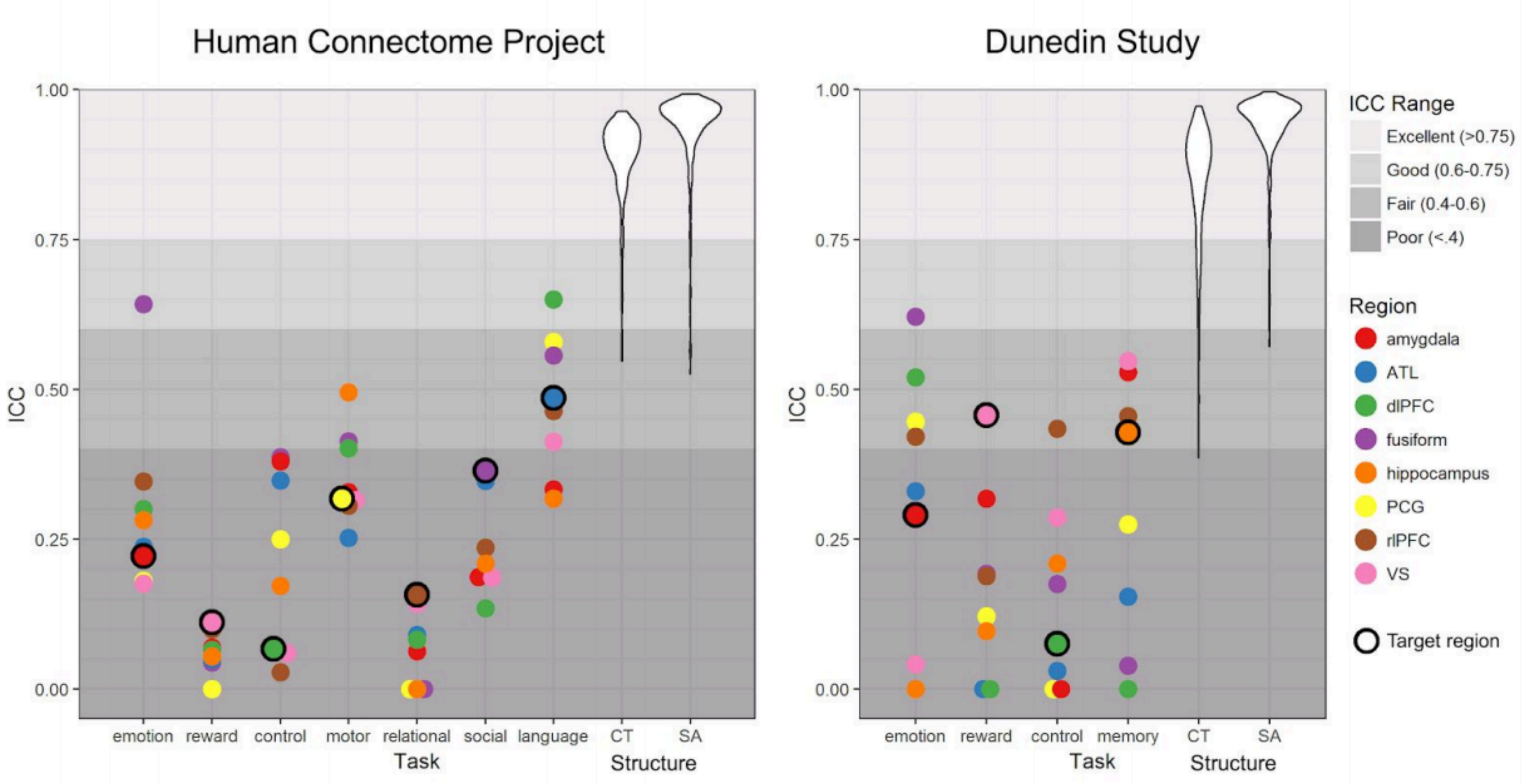
Review: Churchill et al NeuroImage 2017

Also

Nipype:
Neuroimaging in Python
Pipelines and Interfaces



Avoid analyses that are sensitive to biased noise



Poor test re-test reliability measures
Elliott et al https://www.biorxiv.org/content/10.1101/681700v1

Pre-print focuses on problems, but it could also be a basis for a framework for testing what data/analysis factors matter

More Resources

- OHBM Education Course 2017
  “Advanced Methods for Cleaning up fMRI Time-Series”
  https://www.pathlms.com/ohbm/courses/5158/sections/7788

- NeuroImage Special Issue. Volume 154, July 2017
  Cleaning up the fMRI time series: Mitigating noise with advanced acquisition and correction strategies
  https://www.sciencedirect.com/journal/neuroimage/vol/154