



Noise Models and Correction for fMRI

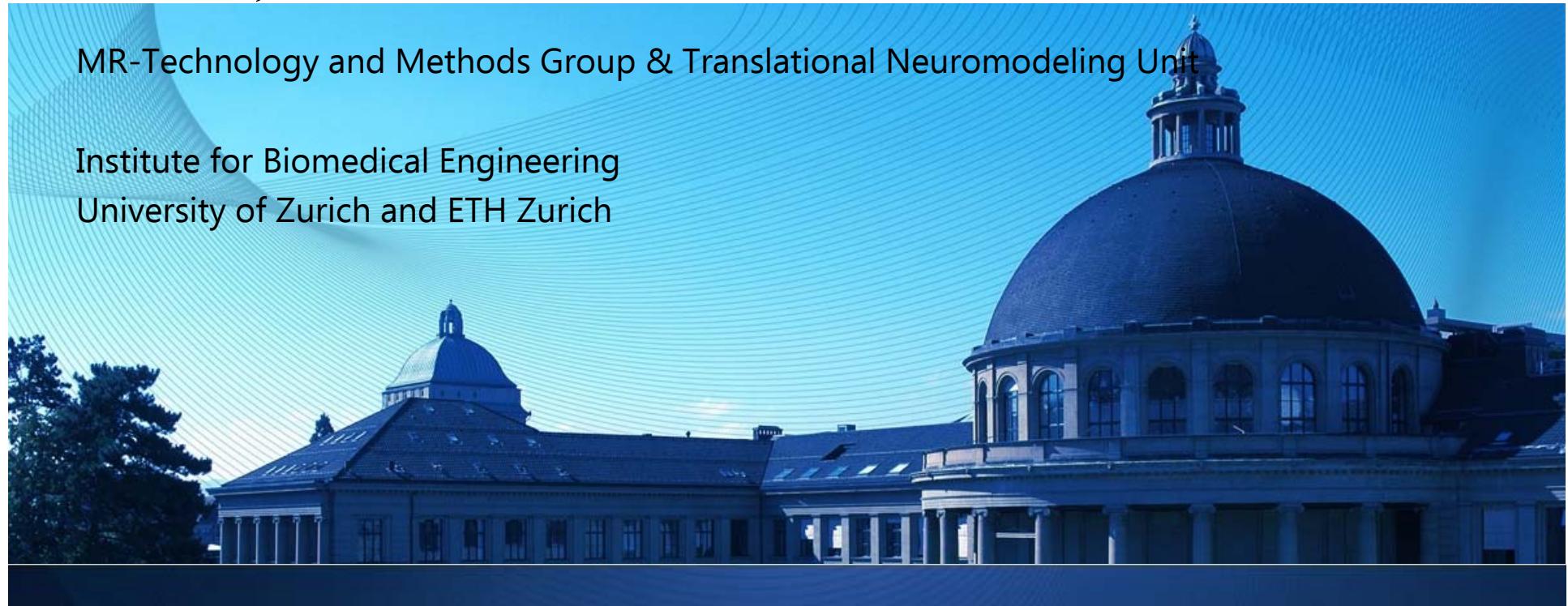
- *an Introduction to the PhysIO Toolbox*

Lars Kasper

Nov 20th, 2018

MR-Technology and Methods Group & Translational Neuromodeling Unit

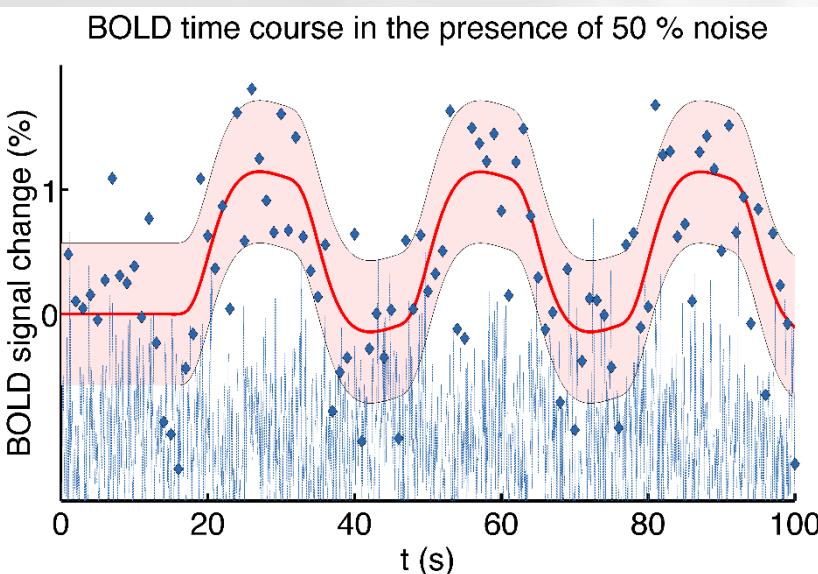
Institute for Biomedical Engineering
University of Zurich and ETH Zurich



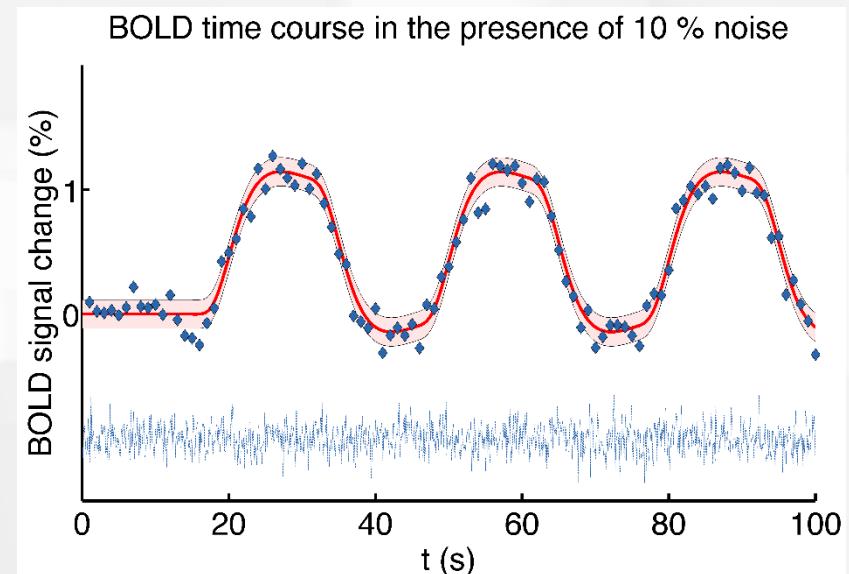
The Goal of Noise Correction



Before



After

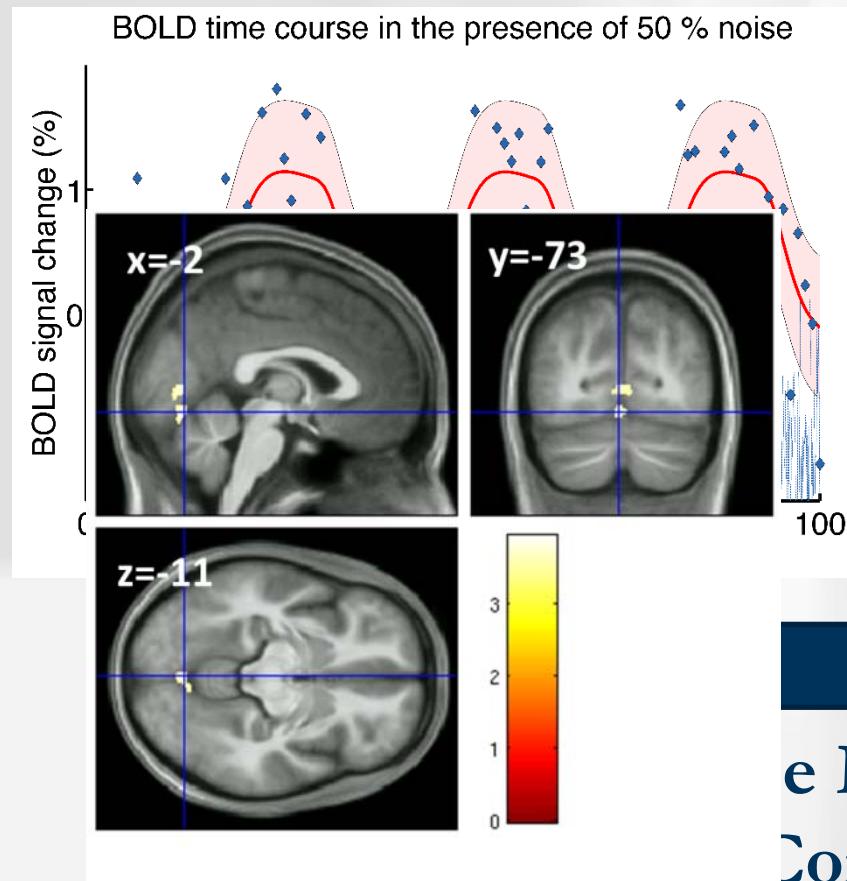


Noise Modeling &
Correction

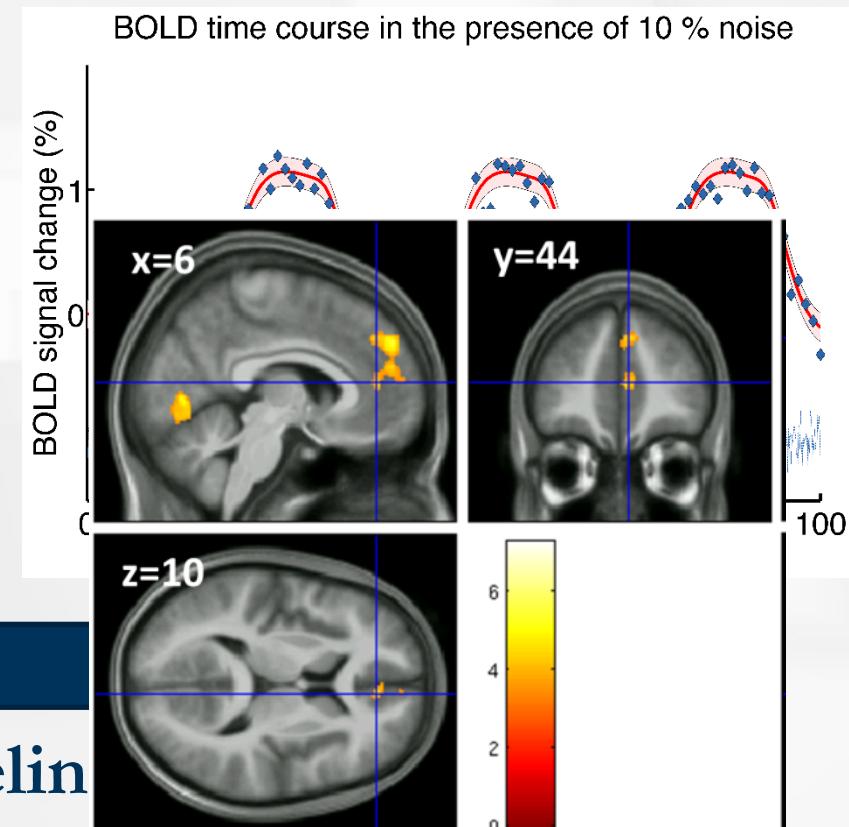
The Goal of Noise Correction



Before

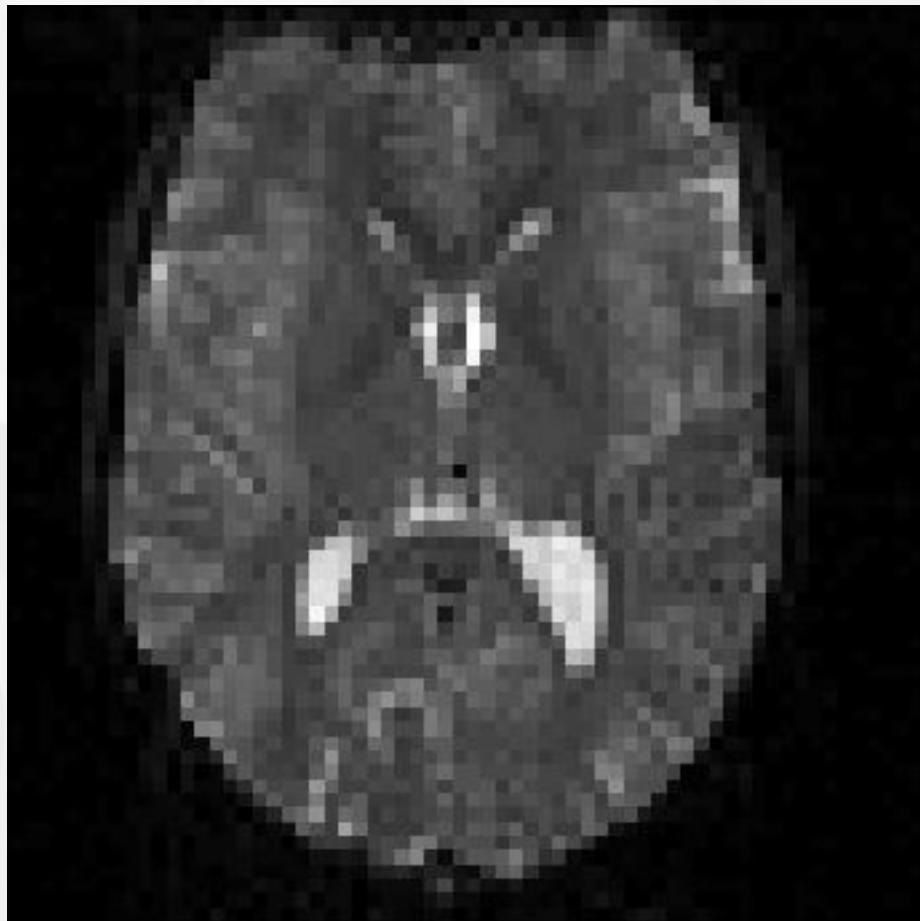
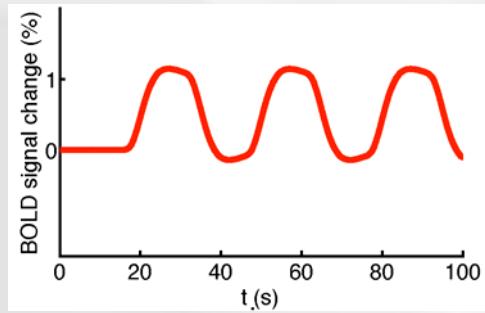


After



e Modeling
Correction

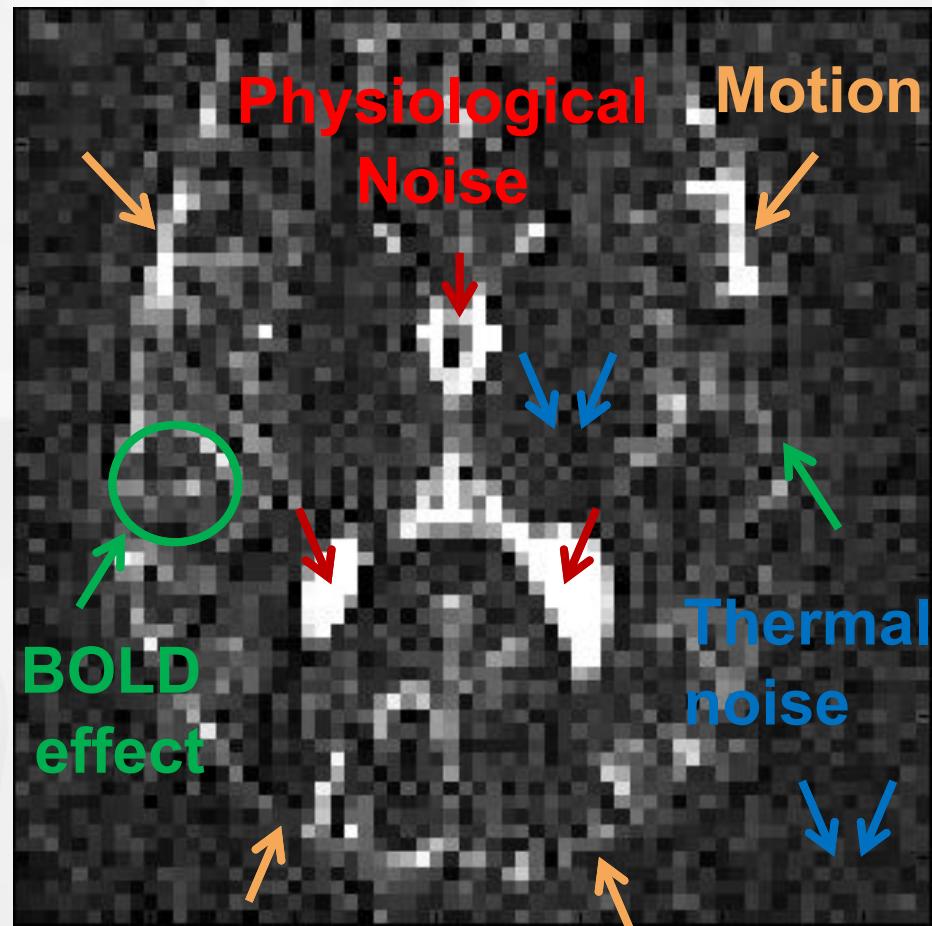
Reminder: fMRI Data is noisy...



fMRI Data is noisy...



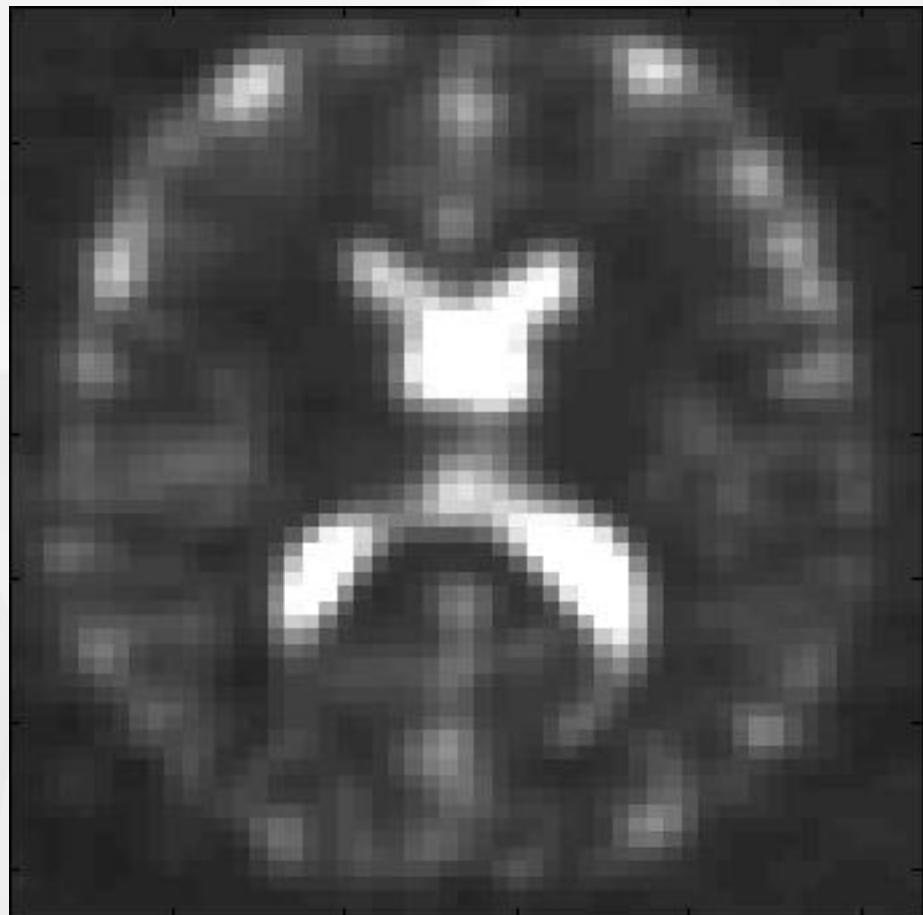
- Interest in fluctuations only: Subtract the mean



Previously...



- How we ended 6 weeks ago (after preprocessing)
- After smoothing... still some fluctuation



Sources of Noise in fMRI



- Acquisition Timing

Temporal Preproc

- Subject Motion

Spatial Preproc

- Anatomical Identity

Spatial Preproc

- Inter-subject variability

Spatial Preproc

- Thermal Noise

Spatial Preproc

- Physiological Noise

Noise Modeling

- Slice-Timing

- Realignment

- Co-registration

- Segmentation

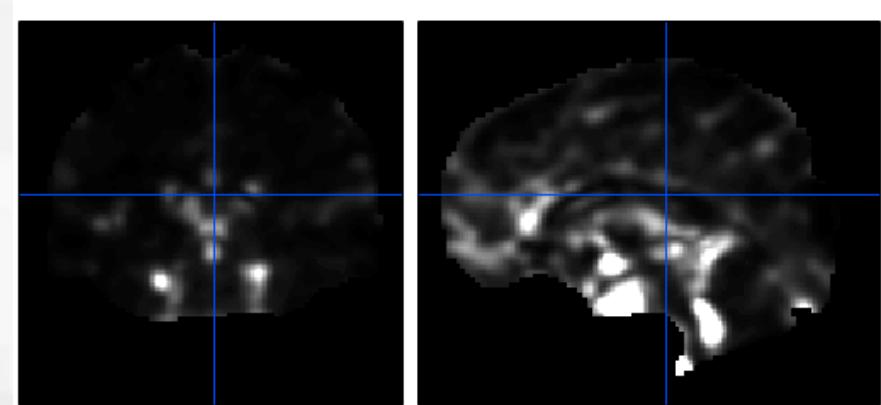
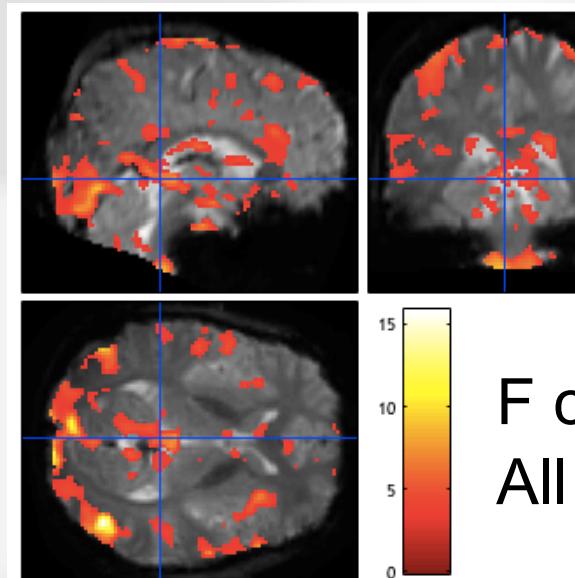
- Smoothing

- PhysIO Toolbox

Previously....(continued)



- ResMS image (cf. GLM lecture)
- Indicates where model incomplete...
- limits sensitivity...



$$\widehat{\sigma}^2 = \frac{(Y - X\beta)^2}{N - p}$$

Outline – Noise Correction



- MRI Time Series Recap and Noise Sources
 - Why de-noising? Structured Noise; Noise Pathways
- Noise Correction Approaches
 - Target: Scanner Drift, Motion, Cardiac/Breathing Cycle
 - Method: Modeling VS Preprocessing
 - Input: fMRI Data VS Peripheral Measures
- Prospects for Improving Group Statistics
- Limitations
 - Degrees of Freedom; Task-related “noise”; Interoception

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fMRI = Acquiring Movies

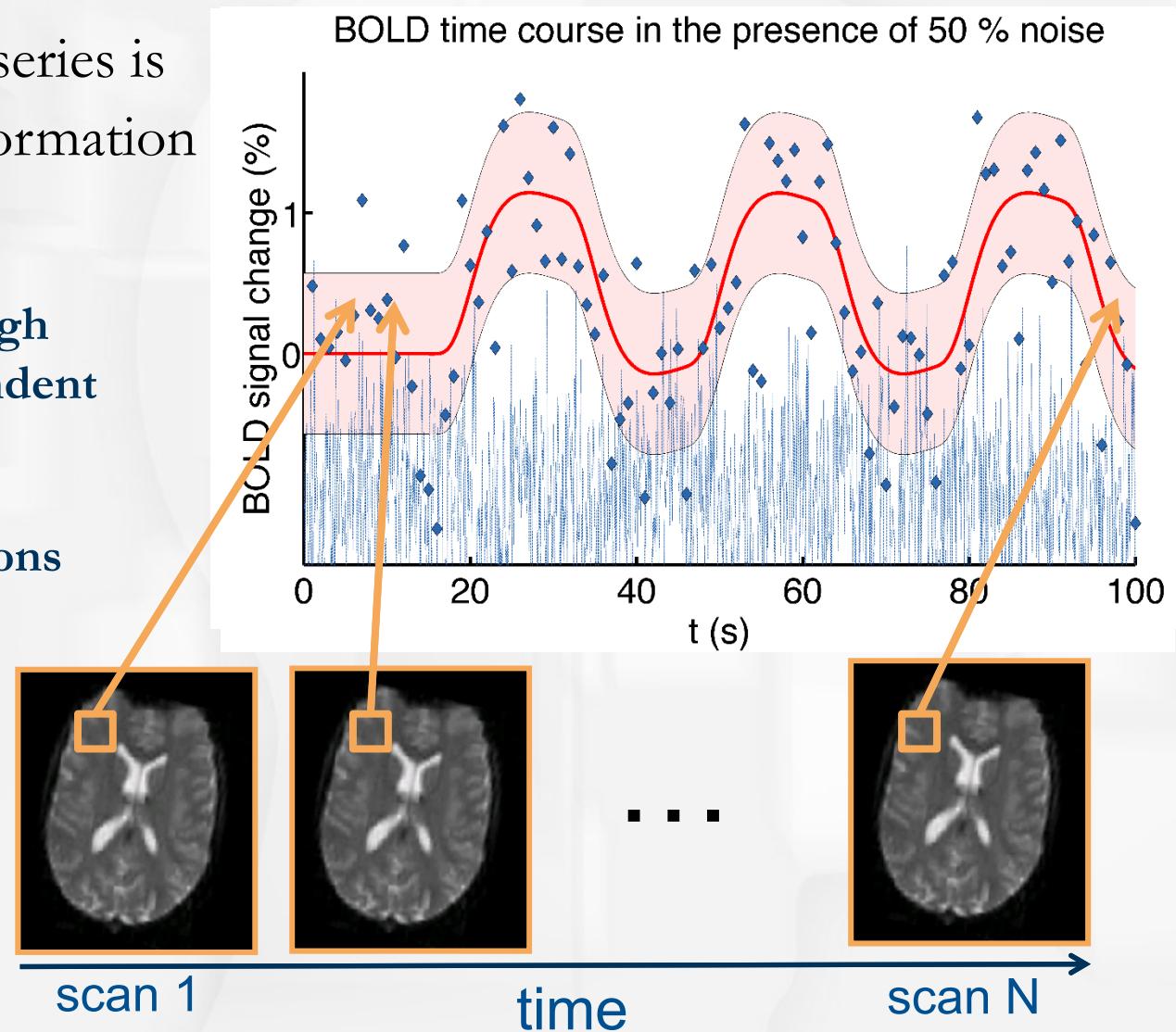


- The Localized Time-series is the Fundamental Information Unit of fMRI

Signal: Fluctuation through Blood oxygen level dependent (**BOLD**) contrast

Noise: All other fluctuations

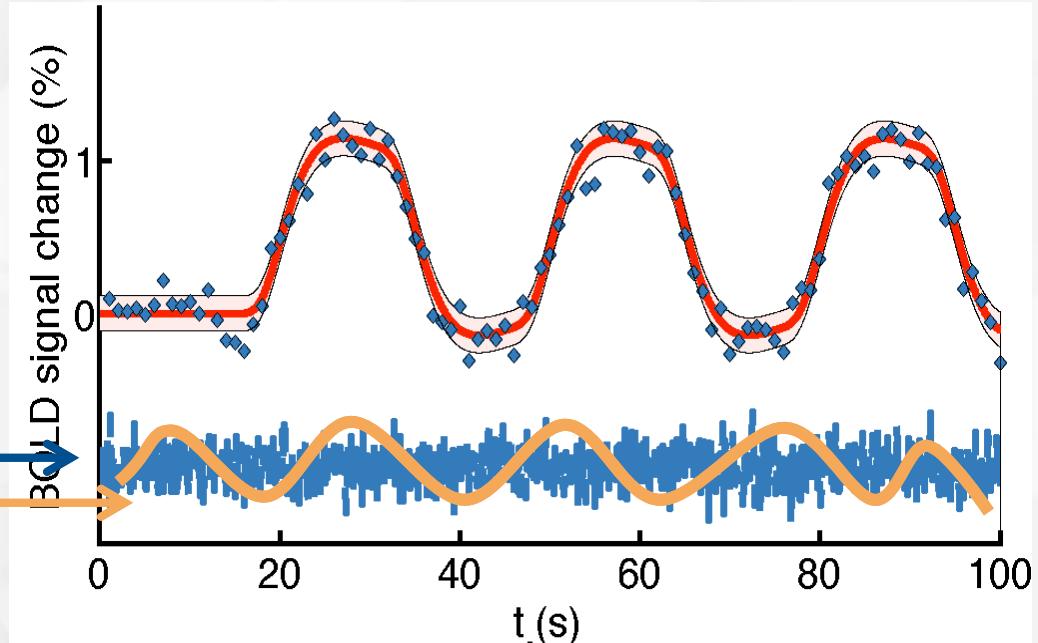
- Run/Session:
Time Series of
Images



Noise Categories & Reduction



- Thermal Noise
 - temporally uncorrelated
 - reduced SNR → risk of false negatives
 - Remedy: Spatial Smoothing
- Noise: All other fluctuations
- “Structured” Noise
 - temporally correlated
 - reduced SNR → risk of false negatives
 - correlated with task → risk of false positives
 - Remedy: Noise modeling (e.g. GLM)



Inference = Signal-To-Noise

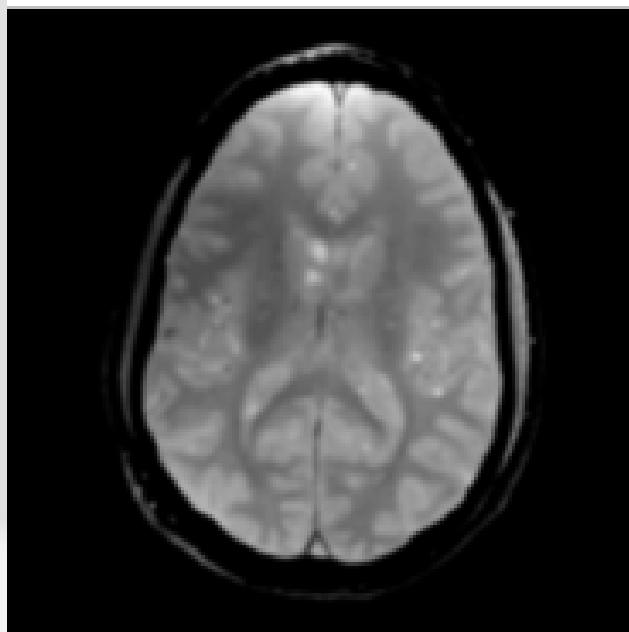
$$t = \frac{\beta}{\sqrt{\hat{\sigma}_\varepsilon^2(X^T X)^{-1}}} = \frac{\beta \|x\|}{\hat{\sigma}_\varepsilon}$$

$$F = \frac{N - M}{M_1} \cdot \frac{(\sigma_s^2 + \sigma_N^2) - \sigma_N^2}{\sigma_N^2}$$

Recap: MR Image Encoding



Image Space (m)



Fourier
Transform
(FT)

In general:
Image
Encoding
 E

k-Space (s)

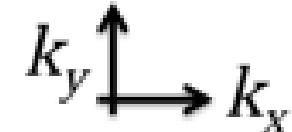
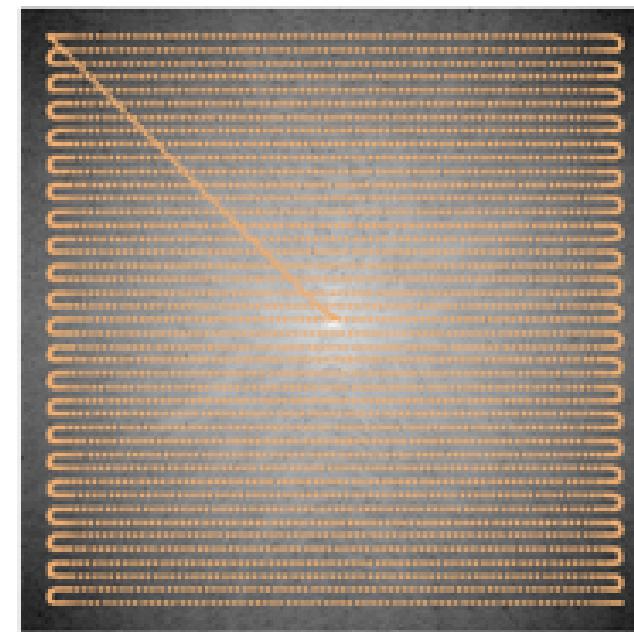
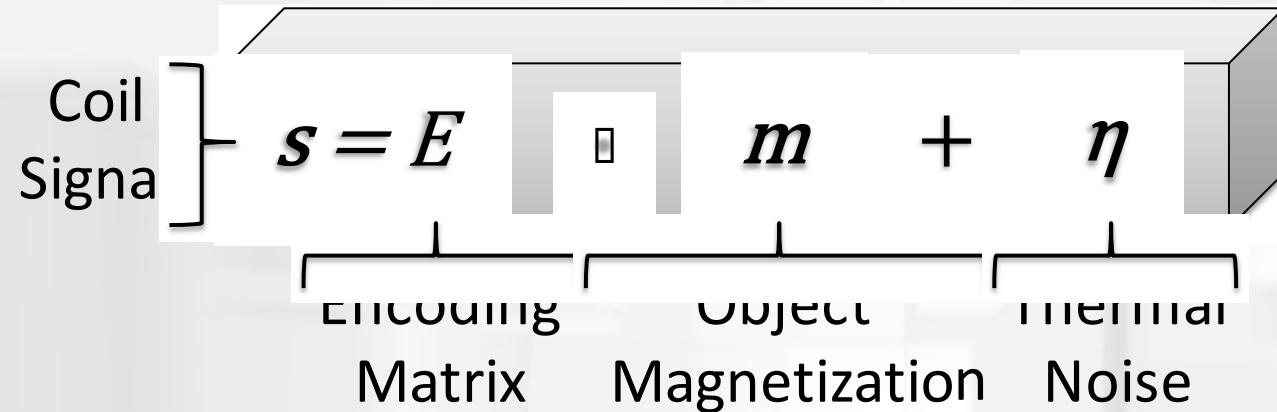
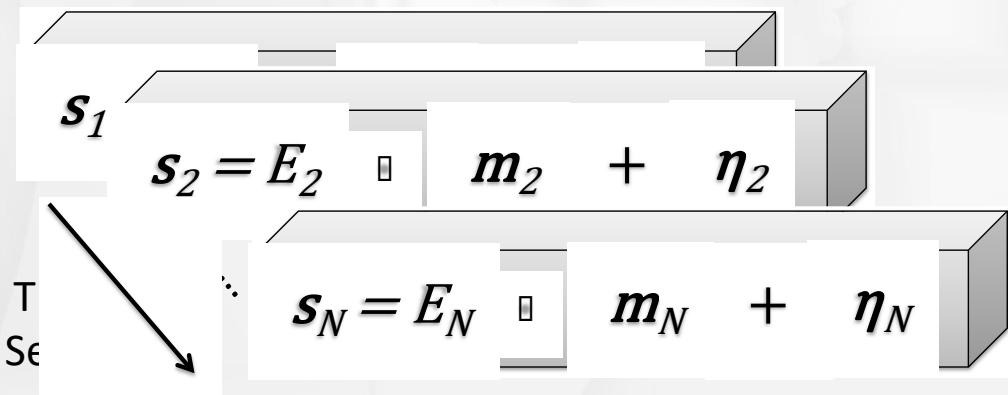


Image Reconstruction & Noise



- Image reconstruction is also a *huge* GLM, $\sim 10^5\text{-}10^6$ rows
 - 3 mm slice, 8 chan: $64^2 \times 8 = 512\text{k}$
 - 1 mm slice, 32 ch: $256^2 \times 32 = 2\text{M}$
- Any change between volumes in encoding matrix (field), object magnetization and thermally induces image noise

$$\hat{m} = (E^H E)^{-1} E^H s$$



What fluctuates?



Noise Sources

Imaged Object

MR System

Entry Points
of Noise

Encoding
Magnetic Fields

Magnetization

Receiver Channels
(Thermal Noise)

Forward Model:
MR Image
Encoding

$$s = E \cdot m + \eta$$

Encoding

Matrix

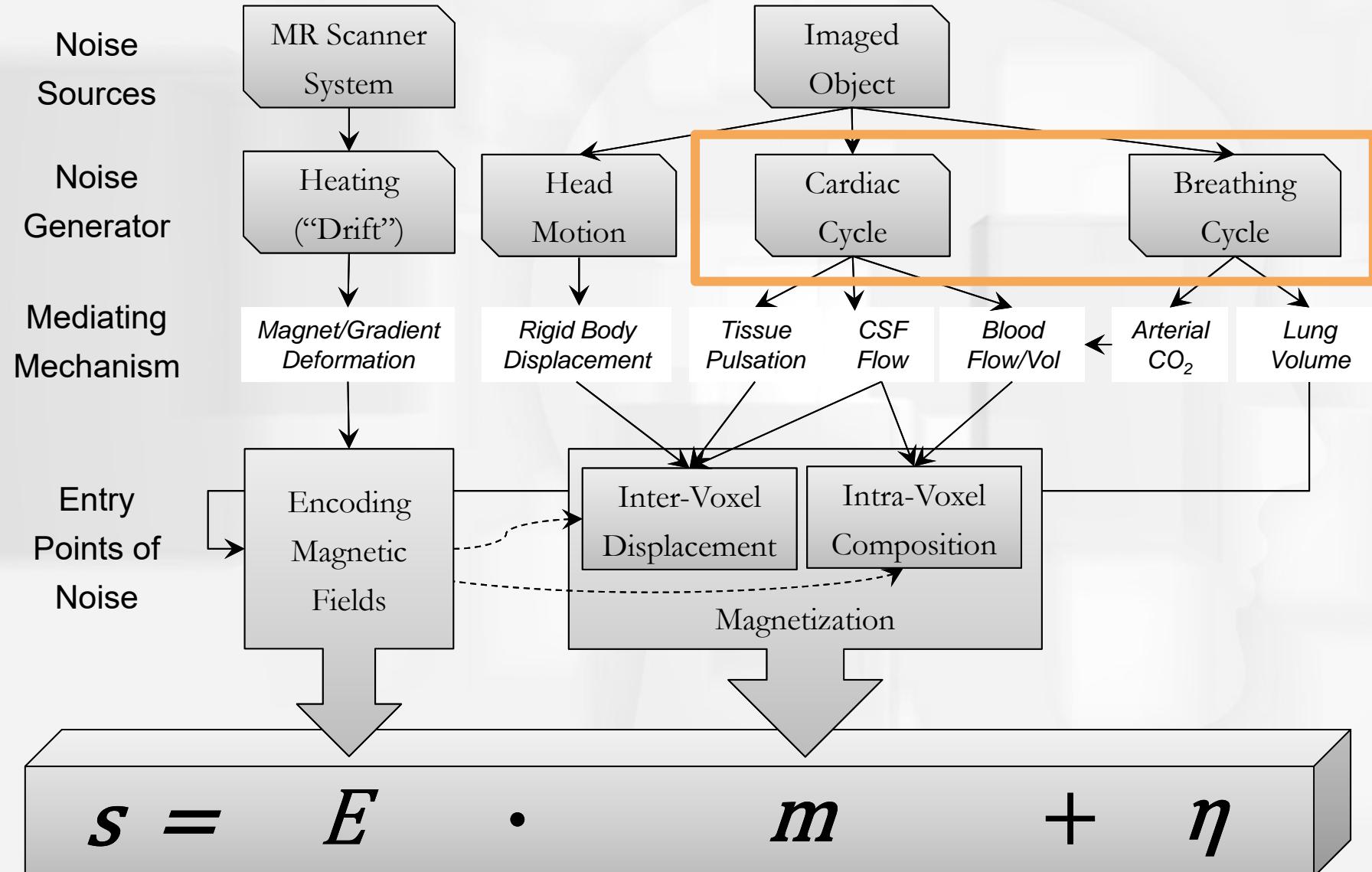
Object

Magnetization

Thermal

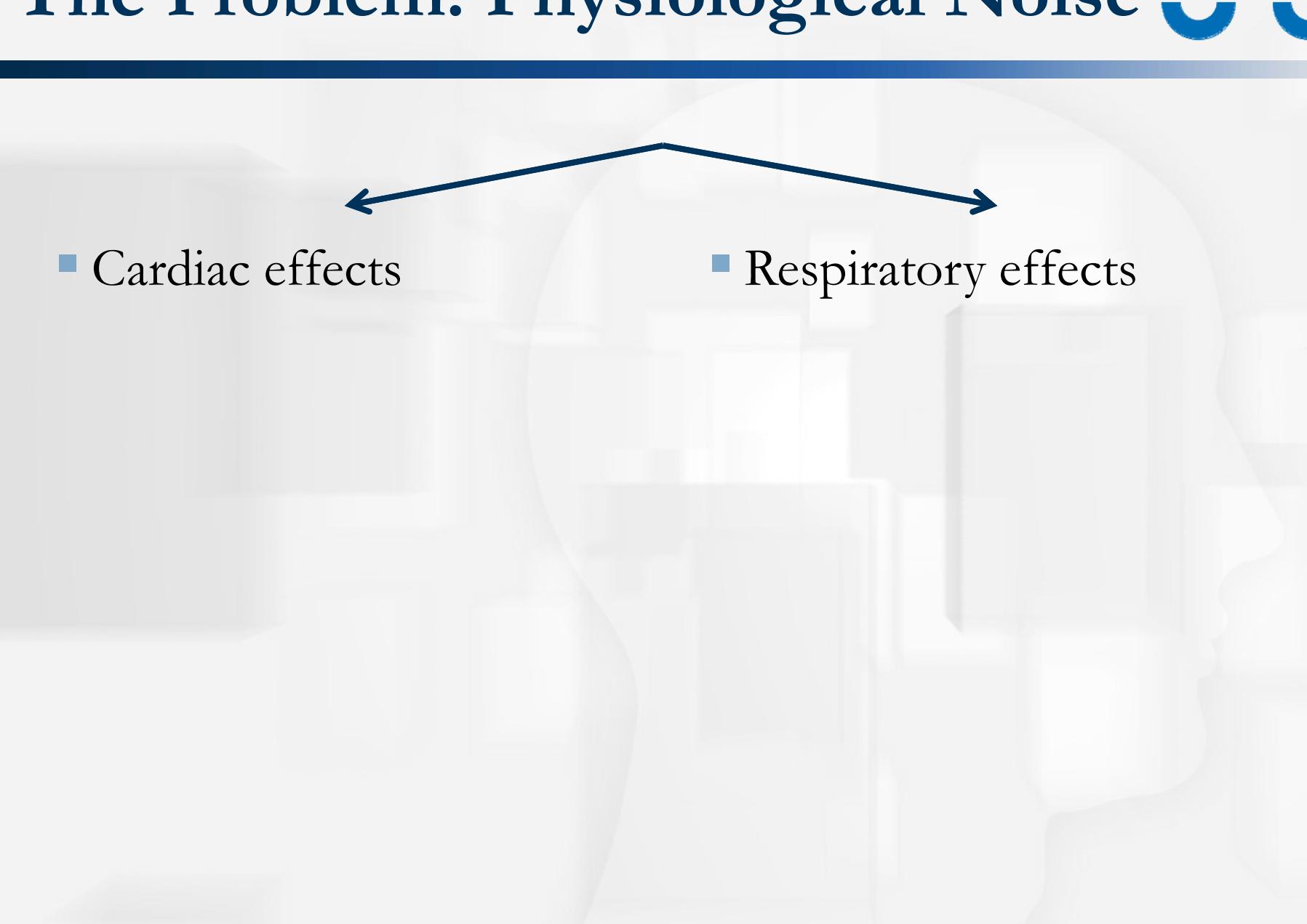
Noise

Structured Noise in MRI



The Problem: Physiological Noise



- 
- Cardiac effects
 - Respiratory effects
- A faint watermark of a human brain scan with a grid overlay is visible in the background.

The Problem: Physiological Noise



Cardiac effects

- Systole:
 - Blood pumped into brain, vessel volume increases: pulsatile vessels
 - CSF pushed down: pulsatile CSF
- Diastole:
 - Vessel volume decreases
 - CSF flows back into “void” brain volume

A Cardiac Cycle in the Brain

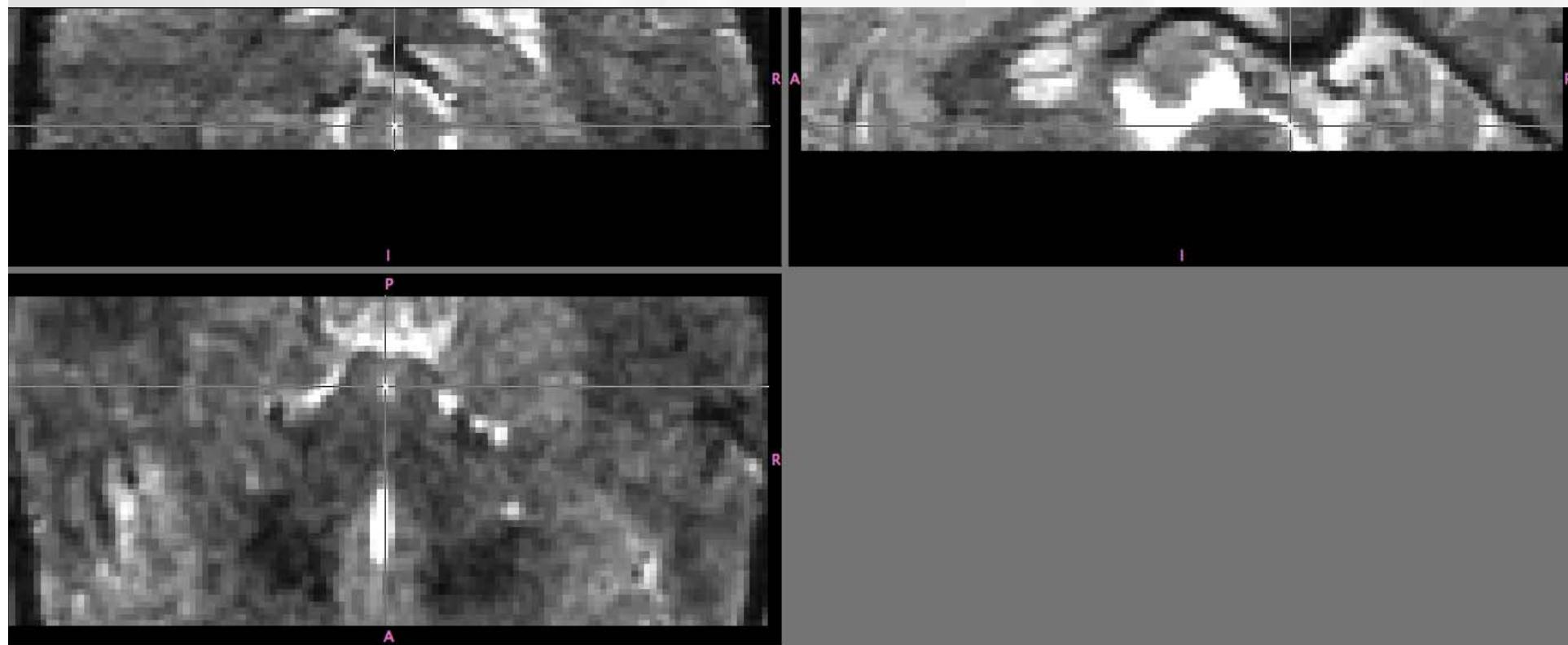


The Problem: Physiological Noise



Triggered High-Resolution fMRI

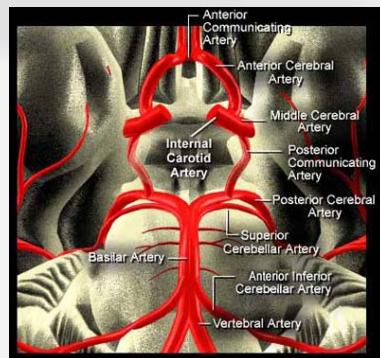
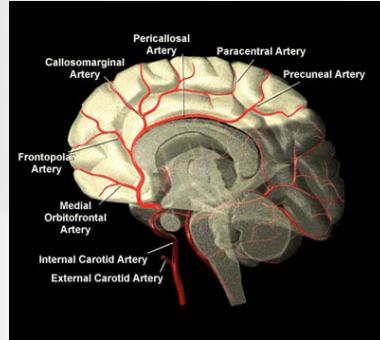
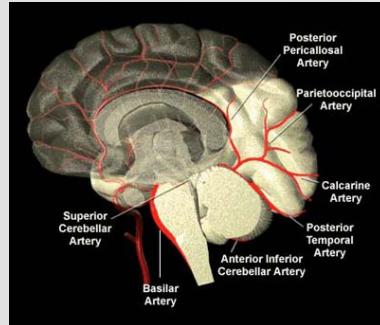
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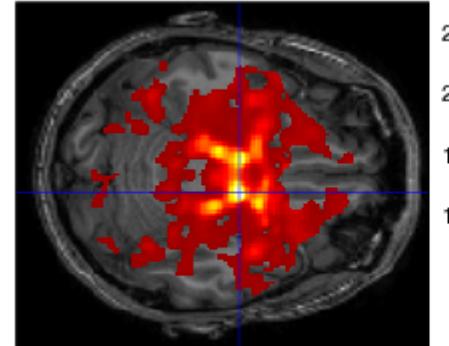
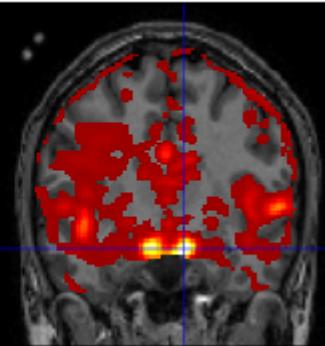
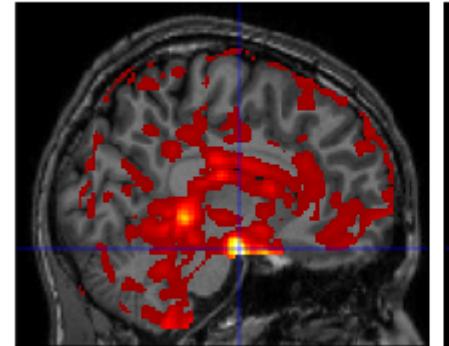
The Problem: Physiological Noise



■ Cardiac effects

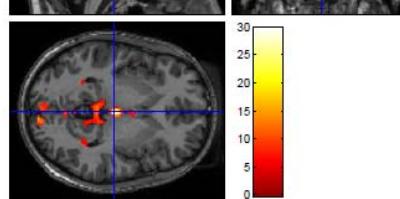
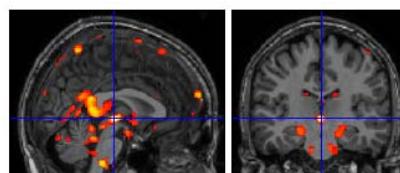
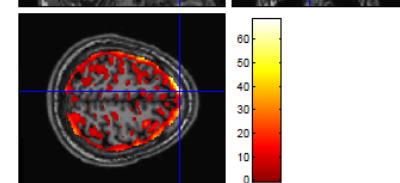
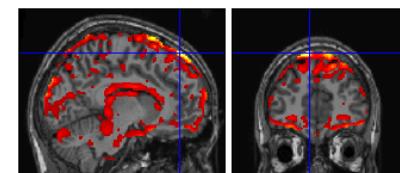
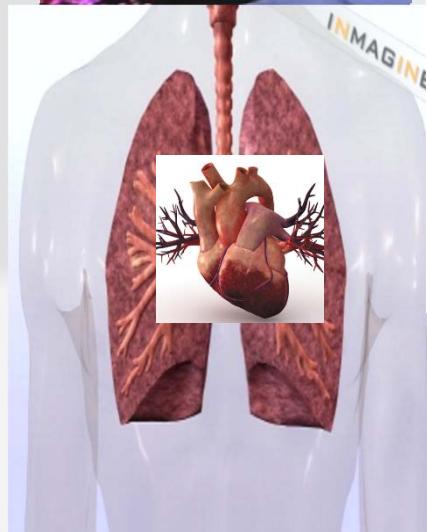
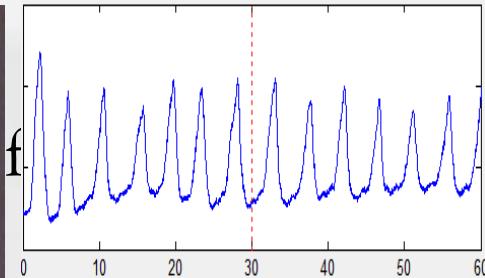


Vessel
Anatomy



Locations
of
Fluctuations

The Problem: Physiological Noise



■ Respiratory effects

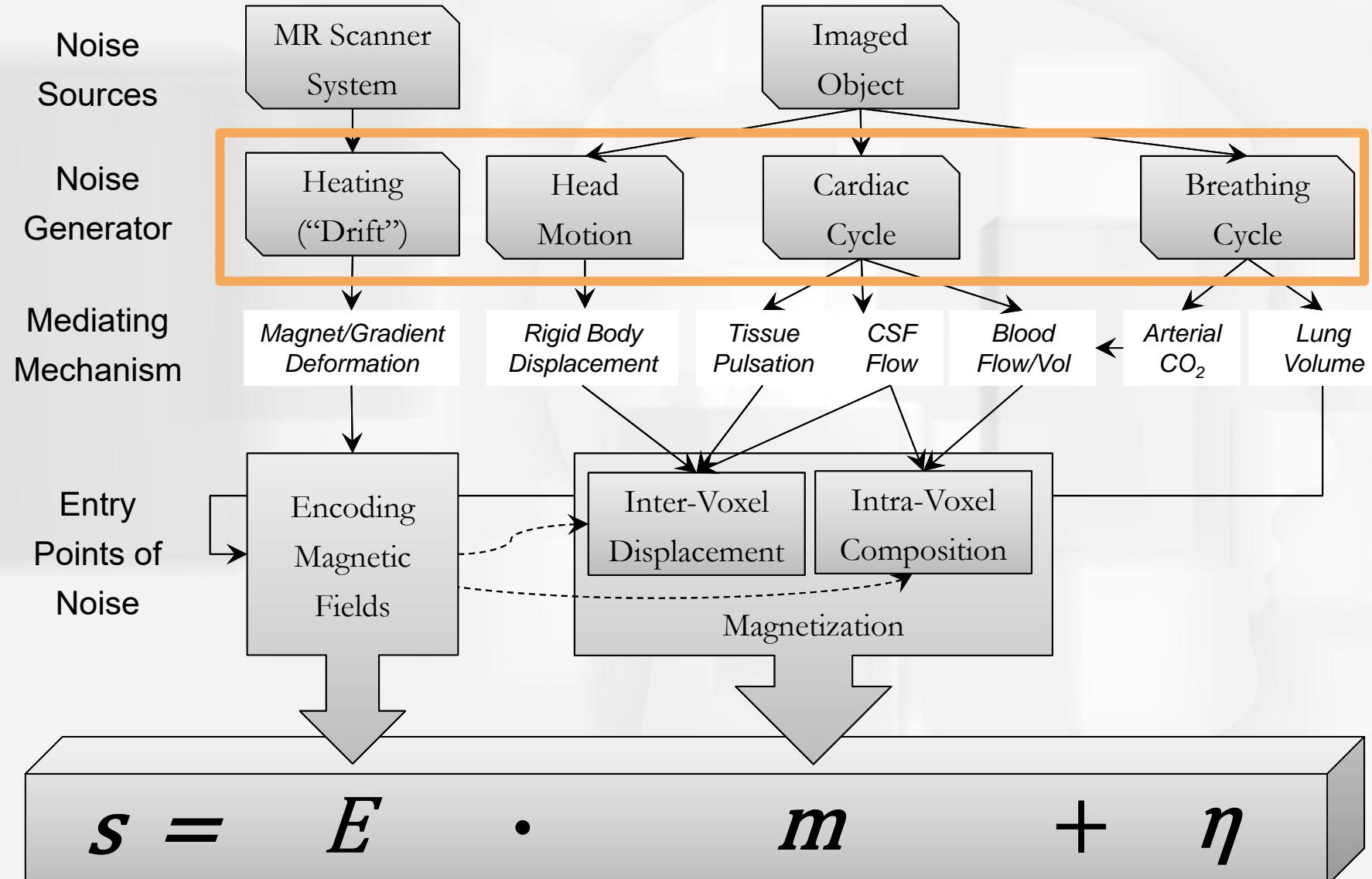
- Chest (&head) moves with respiratory cycle
- Changes in lung volume change encoding magnetic field for MR
 - Geometric distortion/scaling
- Respiratory-sinus arrhythmia
 - Heart beats faster during inhalation

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Noise Correction Targets



Drifts: High-Pass Filtering



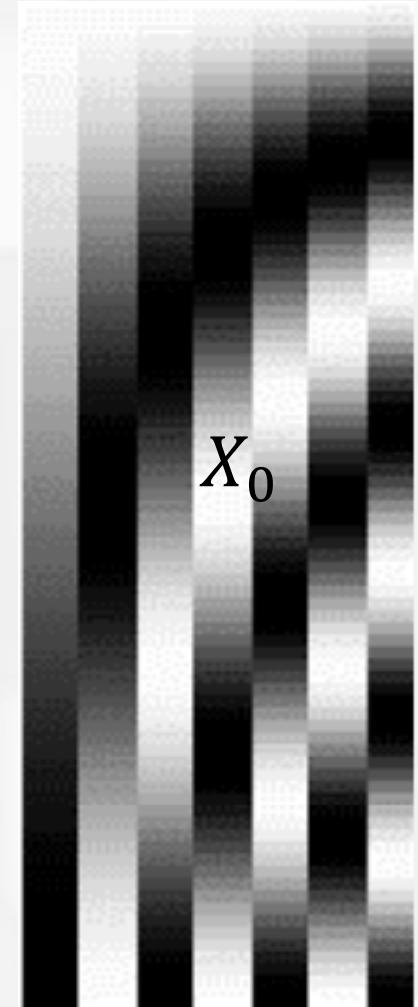
- Discrete Cosine Model (last lecture) of slow oscillations (cycle ≥ 128 s)
- Was: Extra, non-task related columns in design matrix: **nuisance regressors**
- Now: Part of “hidden” preprocessing

- Residual forming Matrix

$$K = \mathbf{I} - X_0(X_0^T X_0)^{-1} X_0^T$$

- With X_0 being the design matrix modeling the confounds
- In fact, GLM in SPM estimates

$$K \cdot \mathbf{y} = K \cdot \mathbf{X} \cdot \boldsymbol{\beta} + K \cdot \boldsymbol{\varepsilon}$$



Modeling VS Preprocessing



- Modeling:
 - Filters, projections (e.g. to independent components) etc. are all linear operations
 - Combination in one design matrix, together with task
 - Simple test of correction efficacy: F-test on nuisance regressors
- Preprocessing:
 - The data y entering the GLM is altered $\Rightarrow y' = X\beta + \varepsilon$
 - For non-linear changes of y or inter-voxel dependencies, alteration outside GLM necessary

The Problem with Preprocessing



- Problem: No inherent measure of efficacy (F-test in GLM), correlation with task regressors undetected
- “Advantage”: No loss of degrees of freedom (sensitivity of F-test)
 - But it is only a hidden loss, statistics for inference is biased, if performed modeling is not incorporated
- Modeling via GLM recommended, if possible
 - Drifts, Motion Regressors
 - RETROICOR, HRV, RVT
 - aCompCor, (ICA)

Motion: Preprocess & Modeling



- Correction for motion artifacts is actually a combination of Preprocessing and modeling
- Preprocessing cannot correct spin-history effects, intra-volume movements (non-rigid!), small partial volume effects
- Preprocessing:
 - Realignment
 - Motion “Scrubbing”
- Modeling (from estimated realignment parameters)
 - Retrospective Modeling: Motion Regressors
 - Motion Censoring

Retrospective Motion Correction



- Best: Avoid subject motion in the first place
- Better: Use Prospective Motion Correction
- Standard: Perform rigid-body realignment, use parameters as nuisance regressors
 - 6 parameters: translation+rotation
 - 12 parameters: include derivatives (for temporal shifts)
 - 24 parameters: include squared regressors
- 24-parameter model known as Volterra expansion

Friston, MRM, 1996

Motion Censoring = “Scrubbing”



- Detect outlier volumes (strong movement, but also spikes, RF flip angle fluctuations)
- Inform the GLM of these bad volumes via stick regressors (zero everywhere else, 1 at volume)
 - Will absorb all variance of that volume
- Problem: Temporal filtering before GLM might create Gibbs ringing of outliers into neighbors
- Alternative: censoring during preprocessing
 - interpolate faulty volume by neighbors

Power, NeuroImage, 2012

Noise Correction Targets

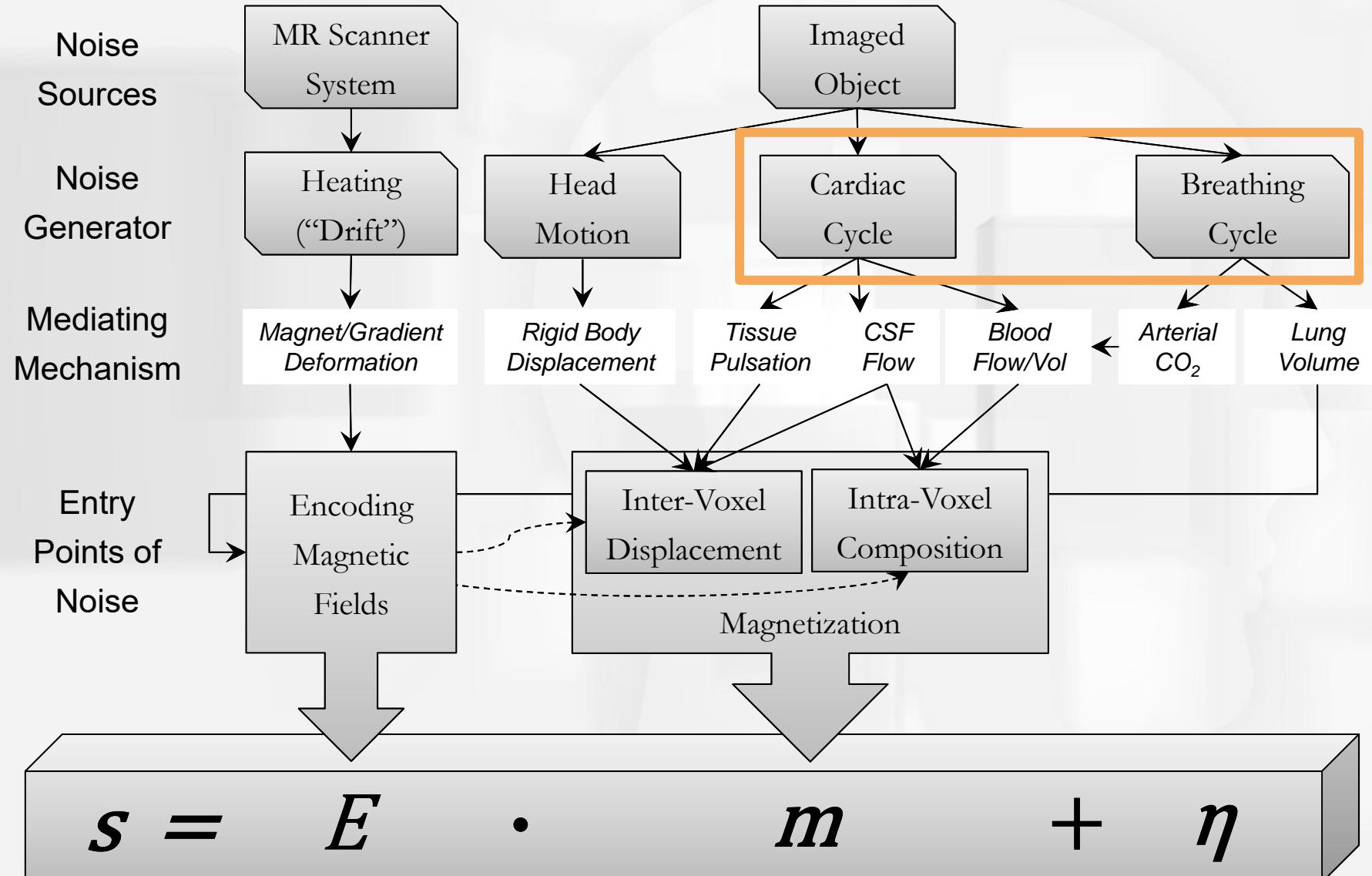
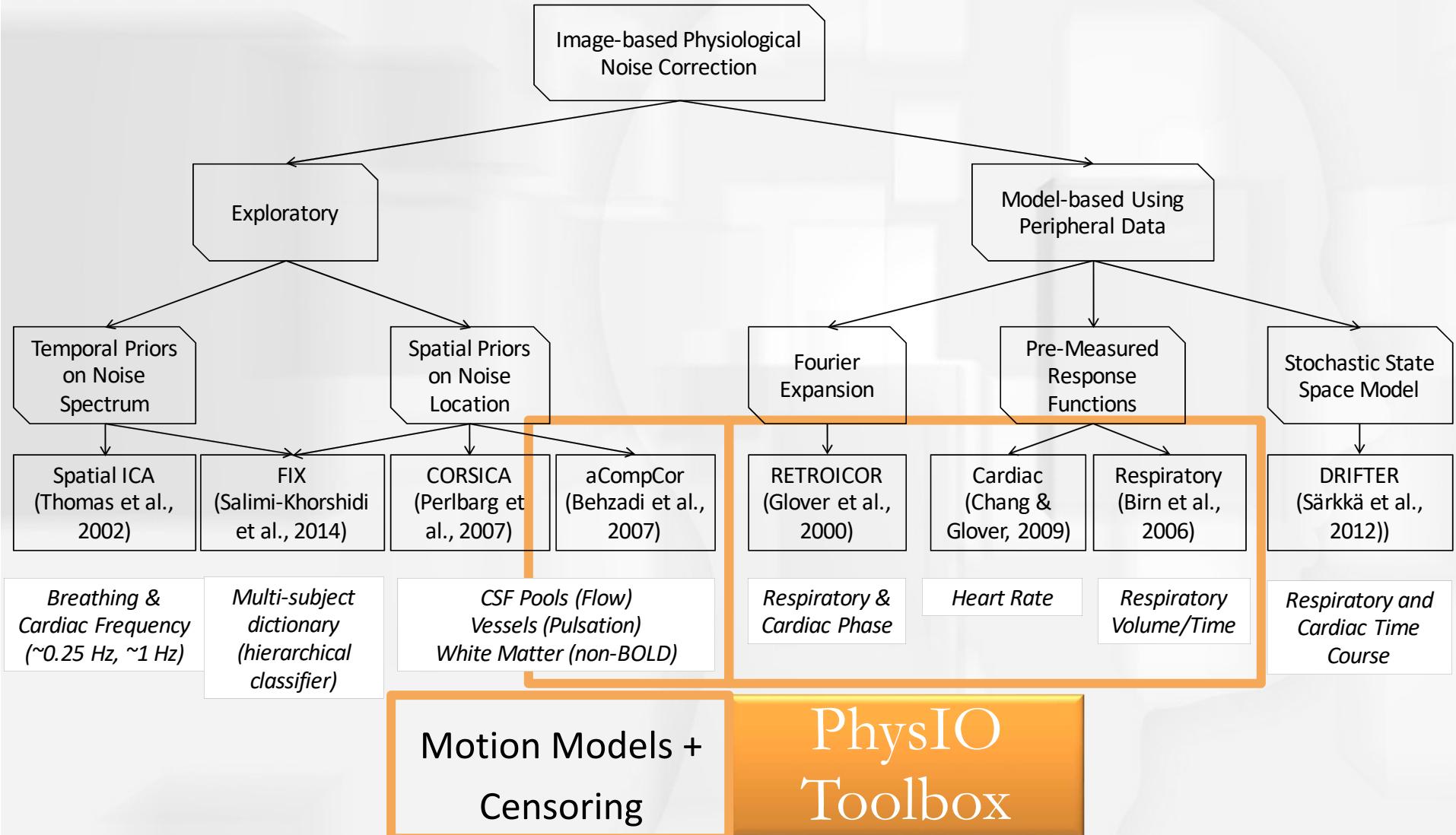
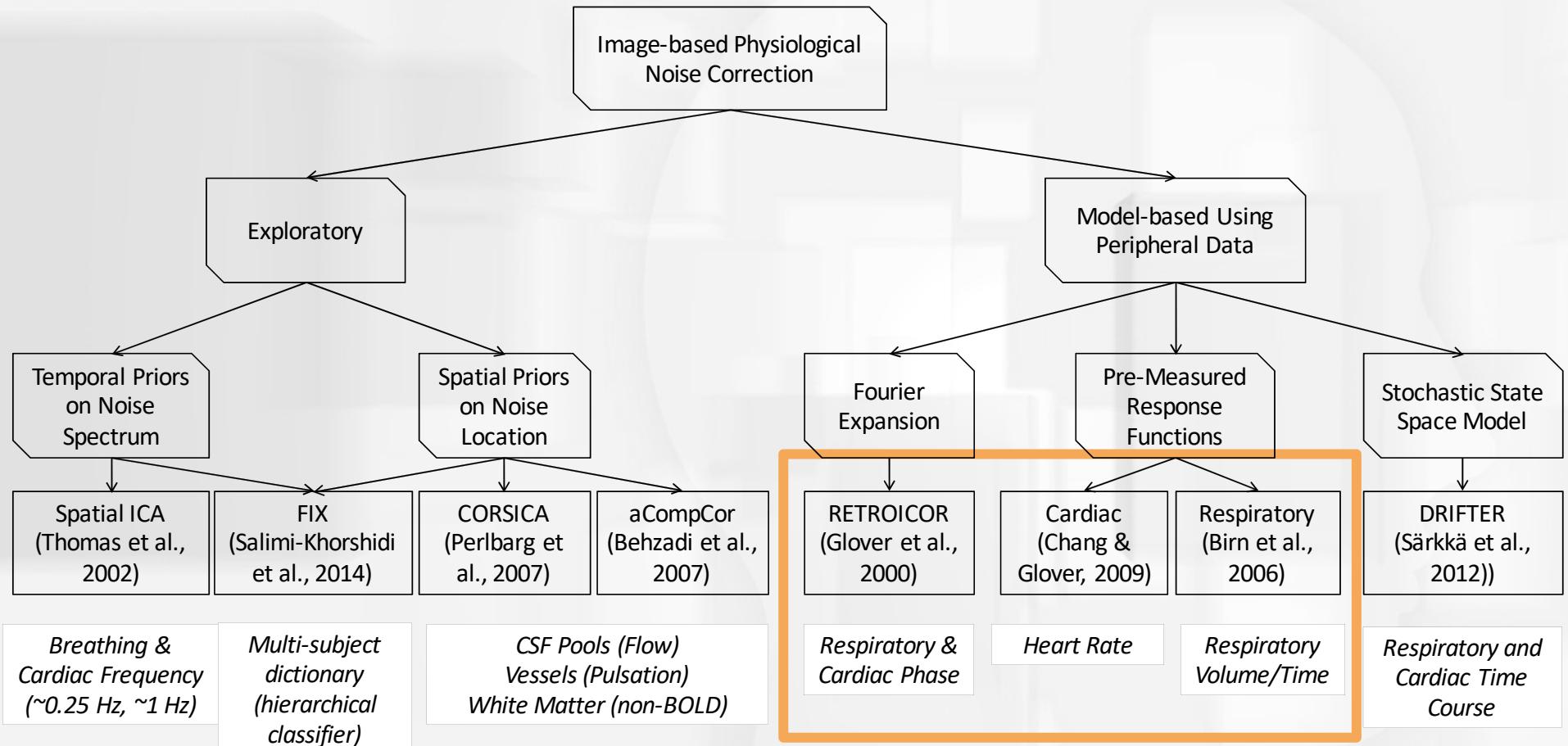


Image-based Noise Correction



Model-based Phys Noise Correction



Noise Modeling



RETROspective
Image CORrection

Cardiac Response
Function

Respiratory
Response Function

- Cardiac/respiratory phase $\varphi_c \quad \varphi_r$
- Fourier expansion (cosine/sine)
- evaluated at 1 time point (slice) per volume = regressor
- Heart Rate
- convolved with CRF
- Resp. Volume per Time
- convolved with RRF

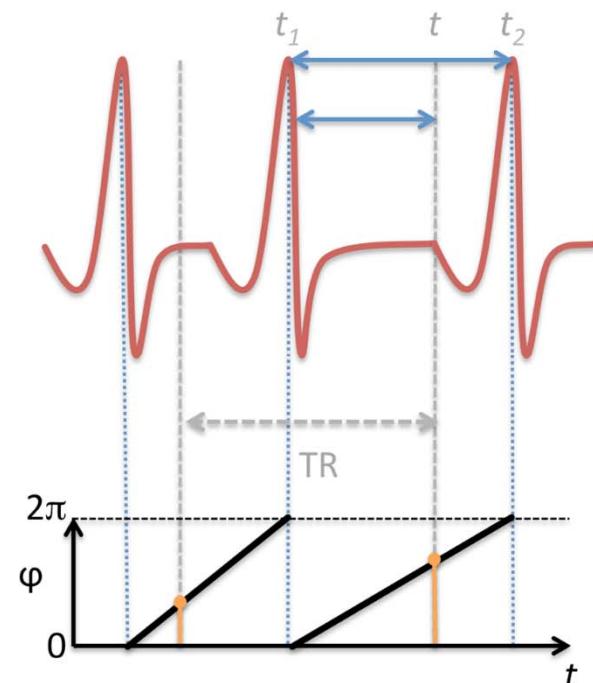
Noise Modeling



RETROspective
Image CORrection

■ Cardiac/resp. response
Function φ_c Respiratory
response Function φ_r

A **Cardiac**

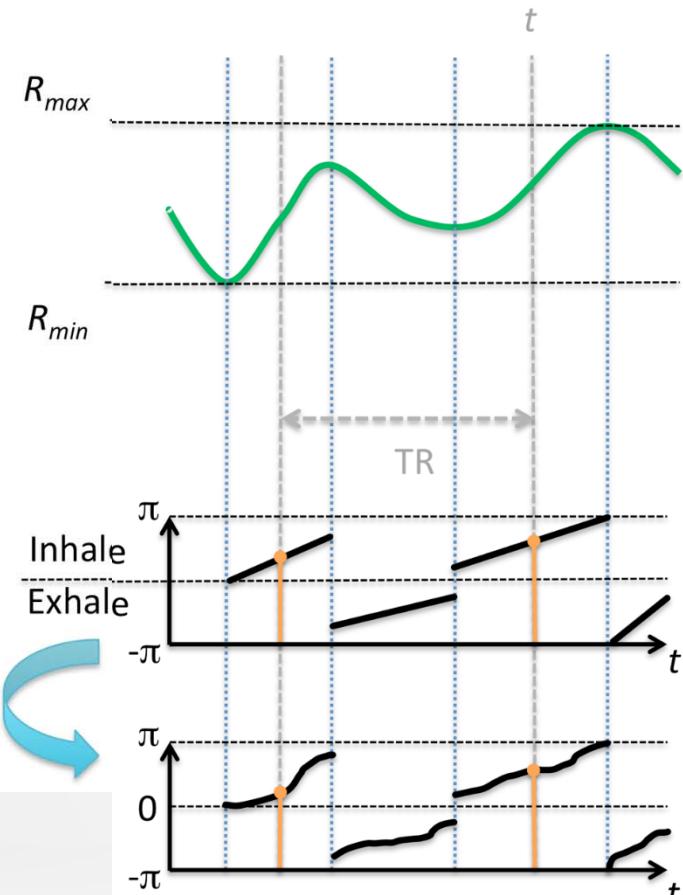


Peripheral
Signal

Estimated
Phase

Estimated Phase
at slice position

B **Respiratory**

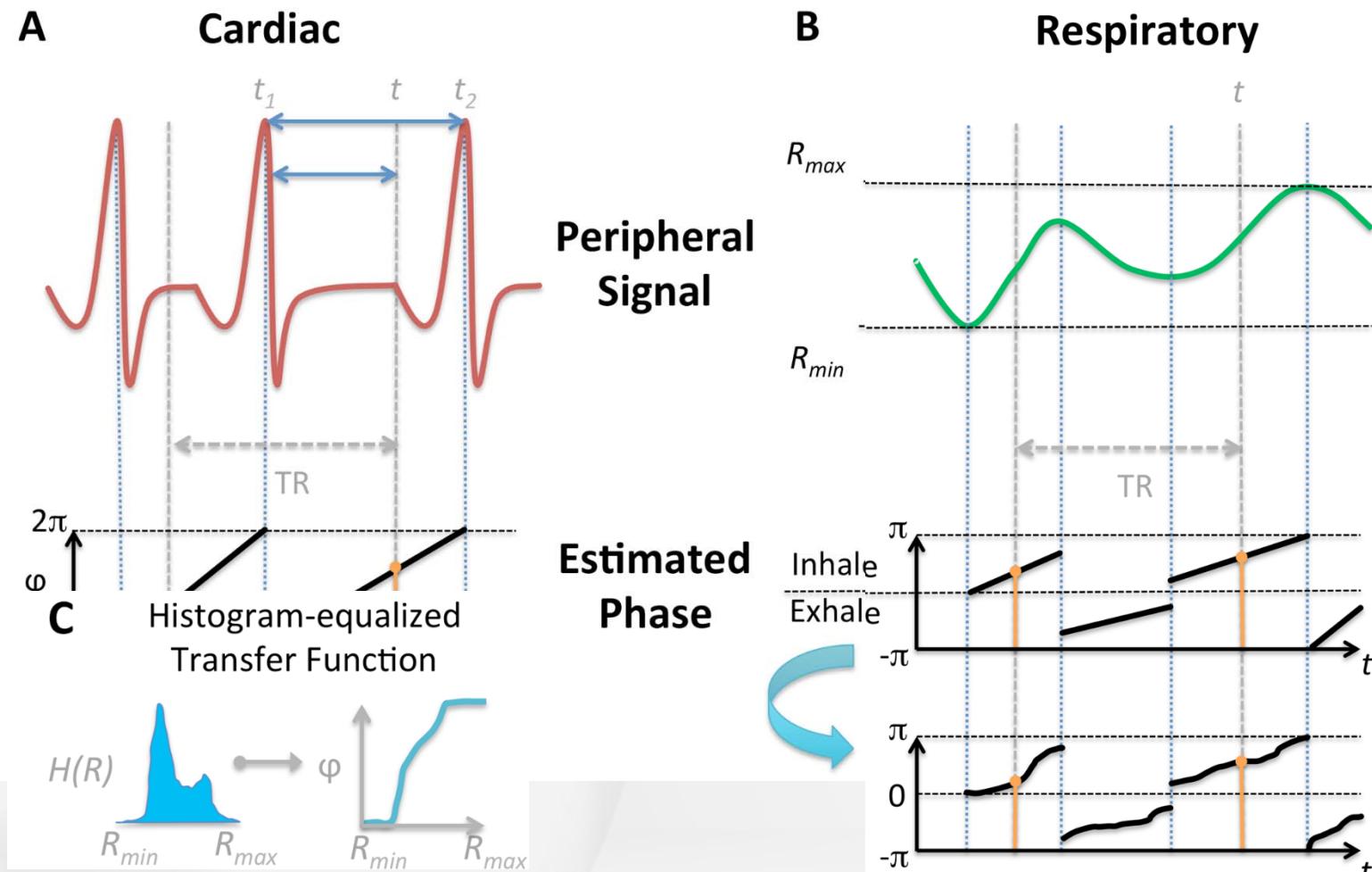


Noise Modeling



RETROspective
Image CORrection

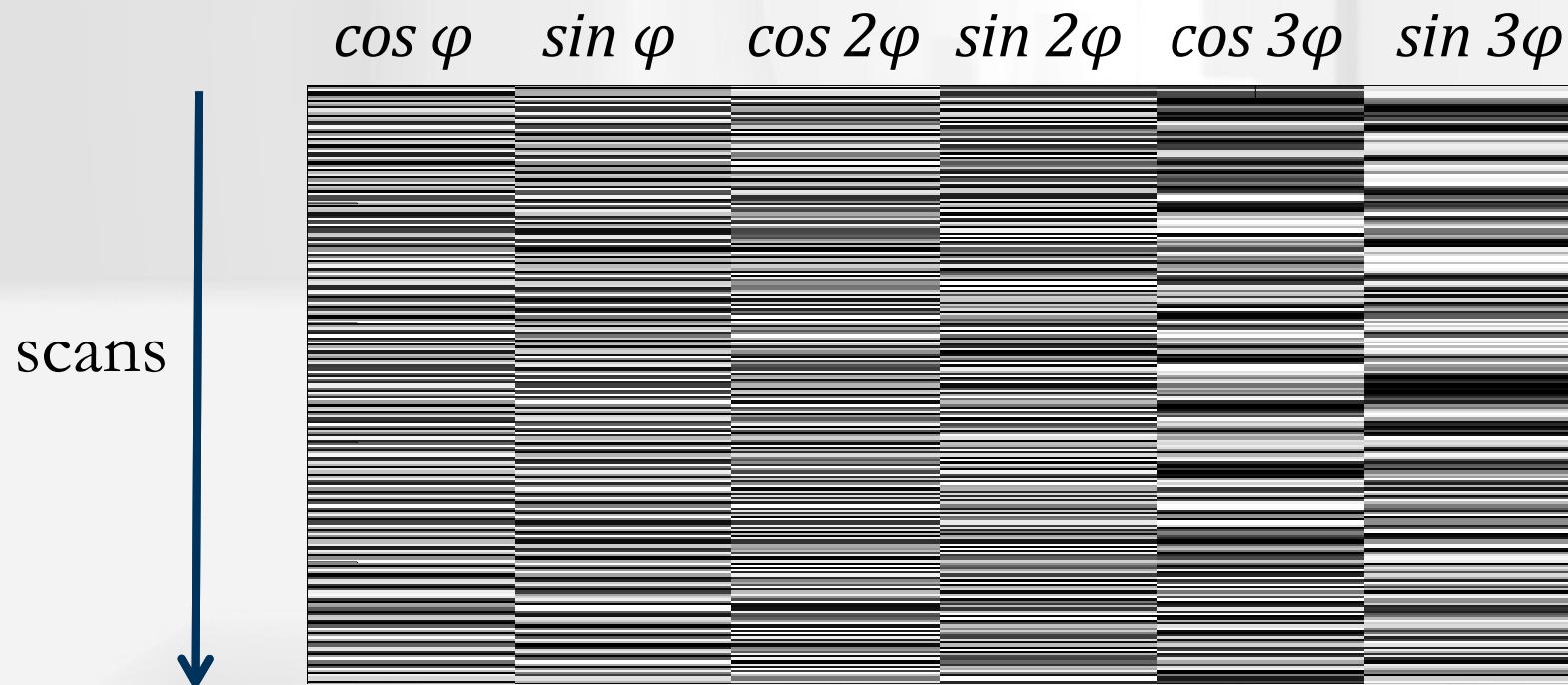
■ Cardiac/ respiratory phase
Function φ_c Respiratory
Function φ_r



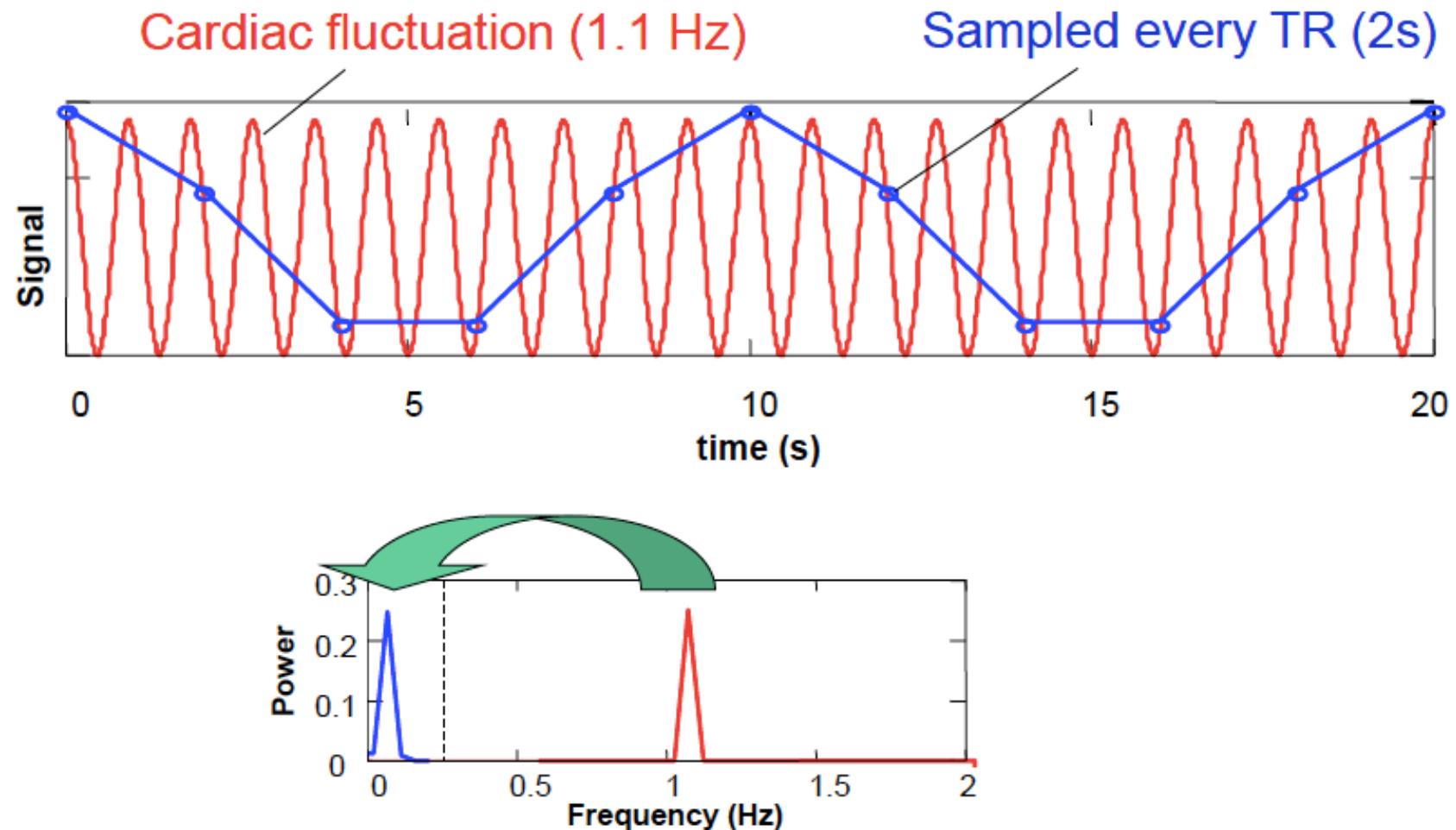
Model: Fourier Phase Expansion



- Cosine and sine to allow for constant phase shifts per voxel
 - Higher model orders to account for under-sampling of physiological frequencies with typical TR in fMRI



Aliasing of Physiology



Courtesy: R. Birn, HBM 2015

Noise Modeling



RETROspective
Image CORrection

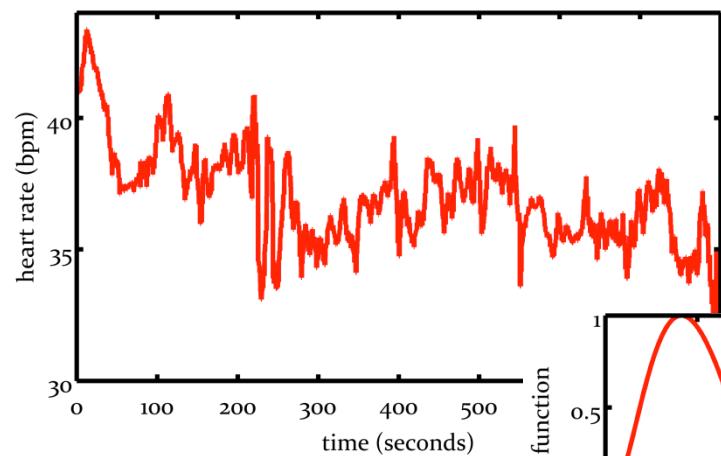
Cardiac Response
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Response Function

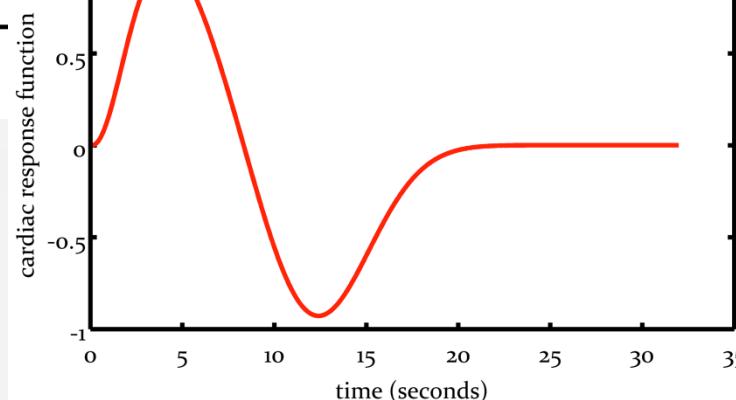
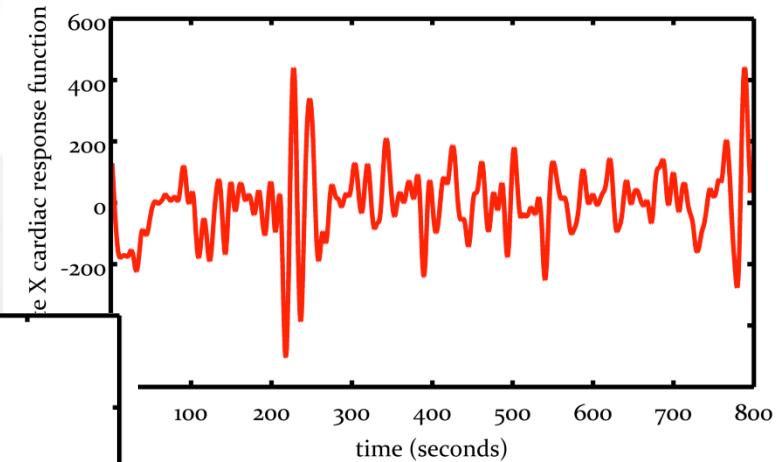
- Heart Rate

- convolved with

- Heart Rate Variability
Response Regressor



CRF



Noise Modeling



RETROspective
Image CORrection

Cardiac Response
Function

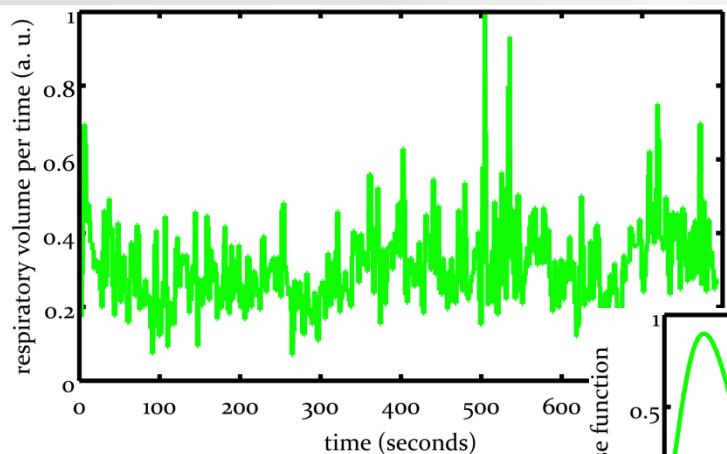
Respiratory
Response Function

- Respiratory

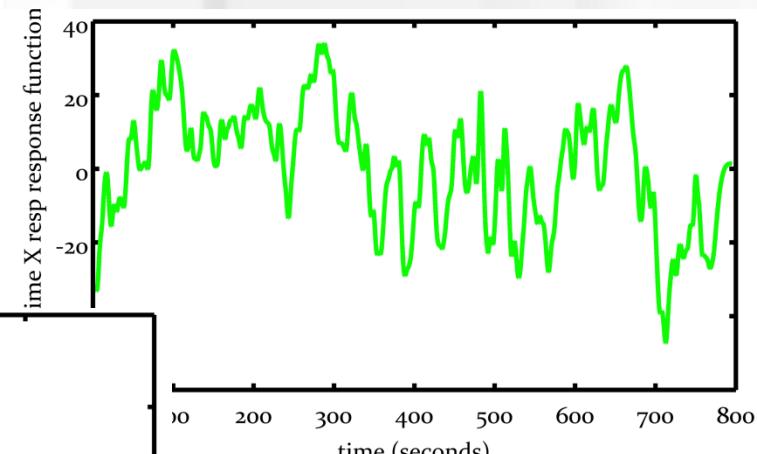
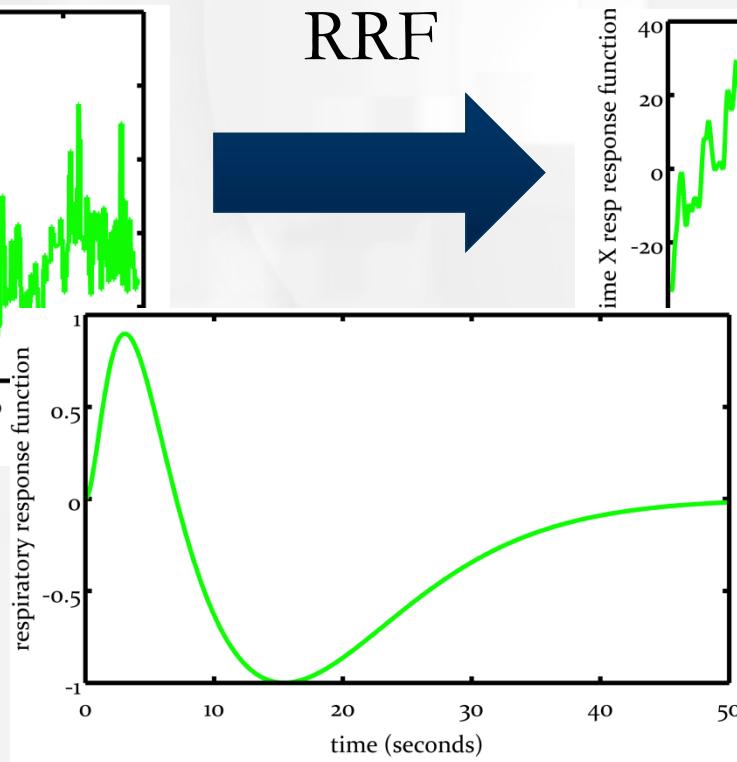
Volume per Time

- convolved with

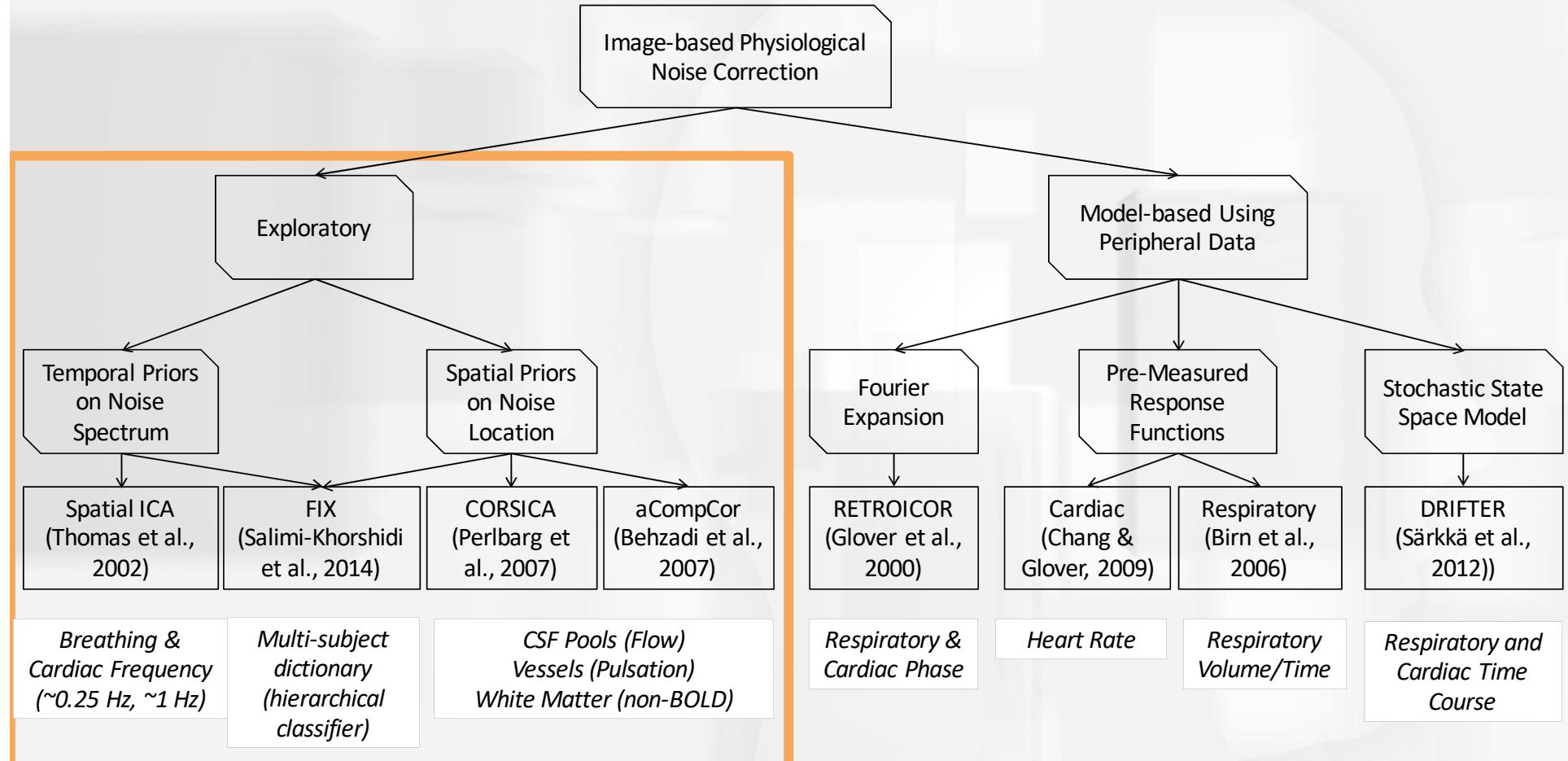
- Respiratory Volume
per Time Regressor



RRF



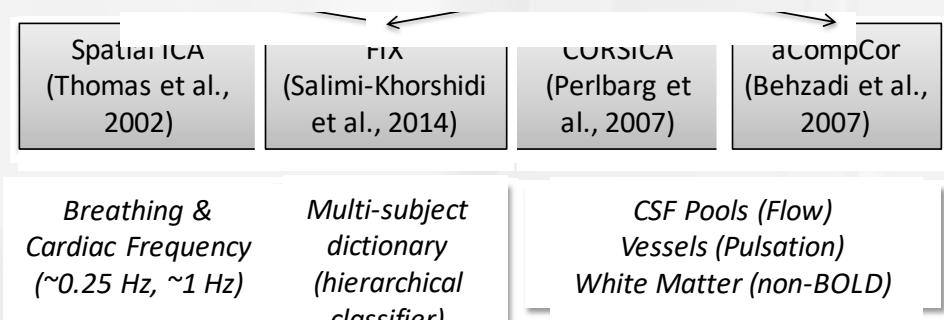
Exploratory Phys Noise Correction



Noise Component Modeling



- Use priors about physiological noise to identify noise components (time series)
 - Spatial Priors: Mechanisms of physiological noise implicate physiological noise in CSF, blood vessels
 - Temporal Priors: Knowledge about typical physiological frequency contents (heart $\sim 1\text{Hz}$, breathing 0.2-0.4 Hz)
 - Note that simple filtering is impossible (cf. aliasing)
 - Population Priors: Use dictionary learning from manually labelled training set of subjects (FIX)



PCA VS ICA

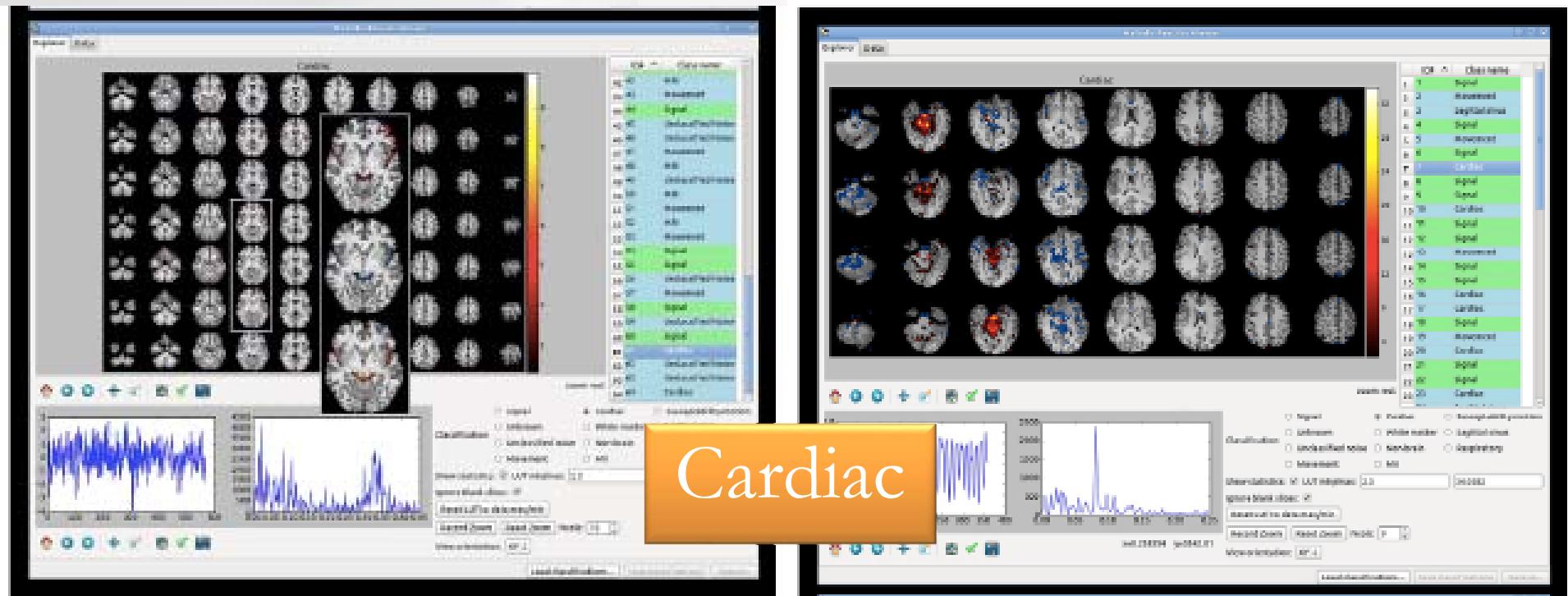


- Methods to extract components (i.e. summarize ROIs/spectra) differ:
 - Maximum variance time series: Principal Component Analysis (PCA) from region of interest (aCompCor, Behzadi 2007)
 - Maximally independent time courses/sites: spatial/temporal ICA, FSL MELODIC, FIX
- aCompCor is basically identical to a seed-based correlation analysis in resting-state fMRI
 - Here: seed is in region-of-no-interest and correlated time series regressed out
 - See previous talk (resting state analysis) for more details

Preprocessing Techniques



- FSL MELODIC, FIX



Other Physiological Corrections



- Non-linear models
 - DRIFTER: Kalman Filter, Bayesian, *Joint* Stochastic State-space model of peripheral physiology and BOLD
- Identify noise via task test-retest reproducibility
 - PHYCAA: e.g. via high-freq. autocorrelation, anatomy
 - GLMDenoise: PCA of noise regressors
- MEICA: Multi-Echo ICA
 - Use diff. TE-images to decompose proton density from T2* changes

Särkkä, *NeuroImage*, 2012

Churchill, *NeuroImage*, 2012/13

Kay, *Front. Neurosc.*, 2013

Olafsson, *NeuroImage*, 2015

Outline – Noise Correction



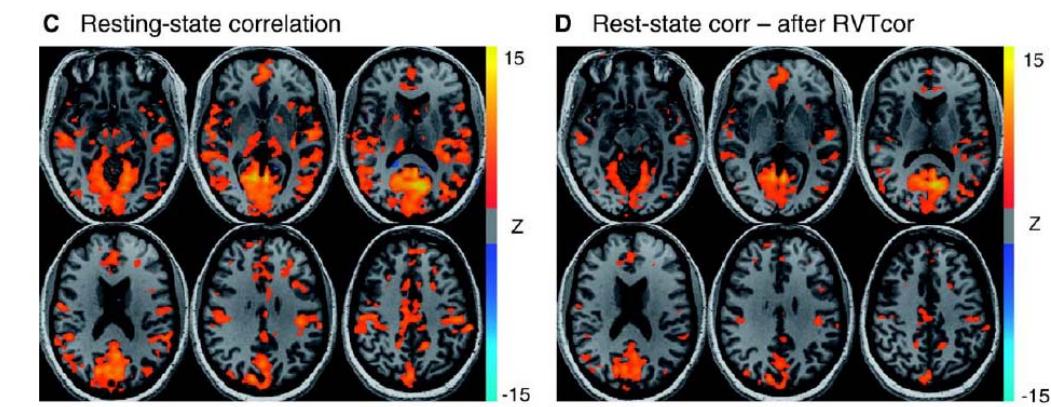
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When? – Literature Evidence



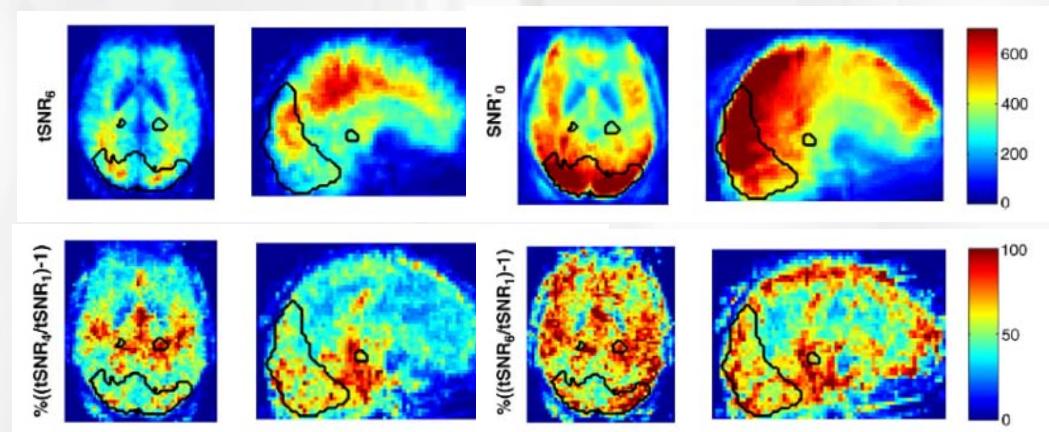
■ Resting-state:

- Birn, R. M. "The Role of Physiological Noise in Resting-state Functional Connectivity." *NeuroImage* 62, 2012
- Birn, R. M., et al. "Separating Respiratory-variation-related Fluctuations from Neuronal-activity-related Fluctuations in fMRI." *NeuroImage* 31, 2006



■ Task-based:

- Hutton, C., et al. "The Impact of Physiological Noise Correction on fMRI at 7 T." *NeuroImage* 57, 2011:



All these methods, but...

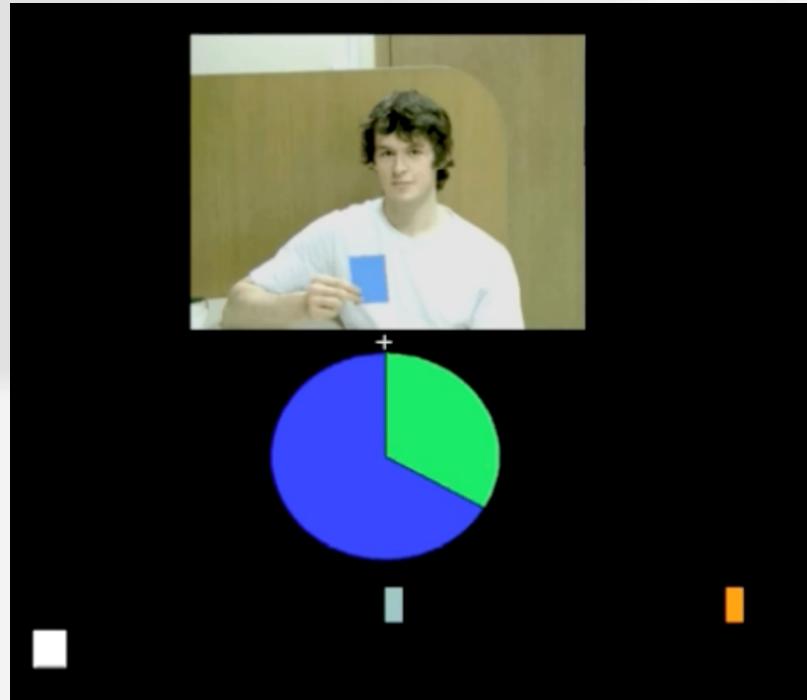


- Physiological noise correction not a default pre-processing step in task-based fMRI
- Reasons
 - Impact on group level fMRI
 - no reports for non-trivial paradigms
 - Existing Toolboxes lack...
 - robust, automatic implementation
 - dealing with variable peripheral data quality

Paradigm: Learning from Advice



- Hierarchical learning of trustworthiness of advisor over time
- Contrasts: Prediction and Prediction Error about advice



recommendations of adviser were **veridical** (pre-recorded videos from behavioural study)

volatility of advice (changing intentions of adviser through incentive structure)

interactive, gender-matched (40 male subjects)

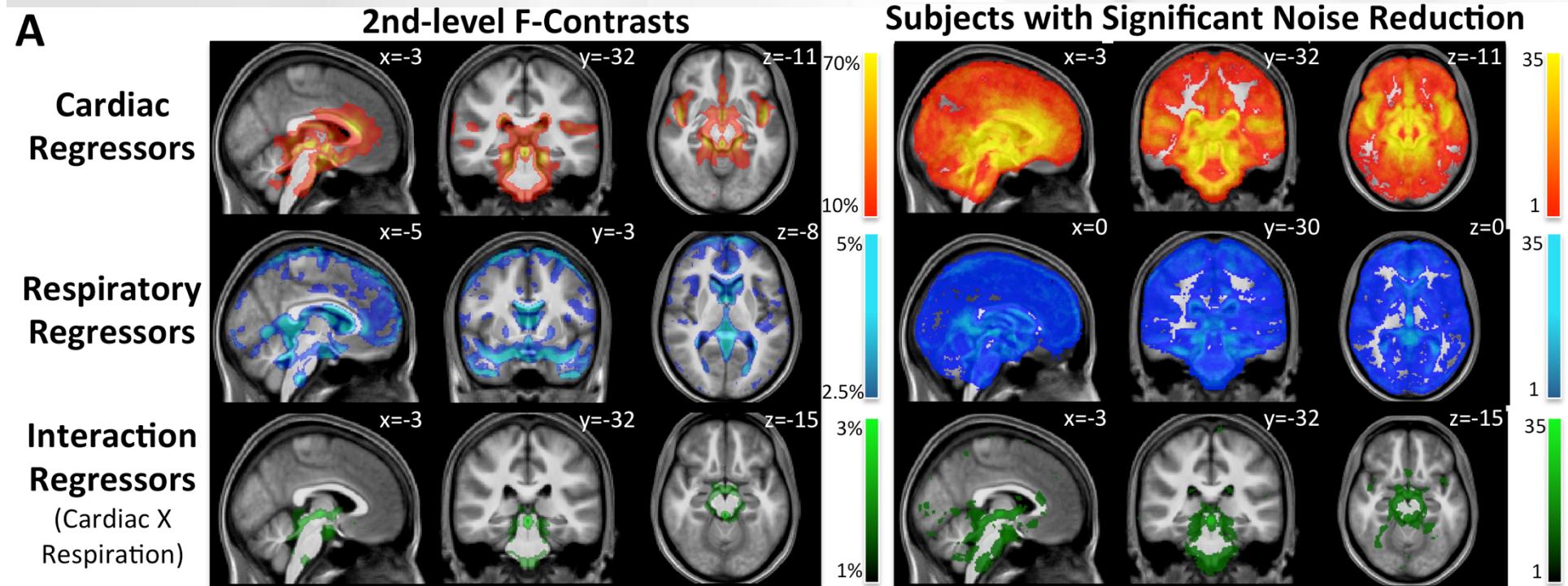
fMRI design: Philips Achieva 3T
TR/TE 2500/36ms, 2 x 2 x 3 mm³

Diaconescu et al, 2014, PLoS Comp. Biol.

Group Level Impact PhysIO



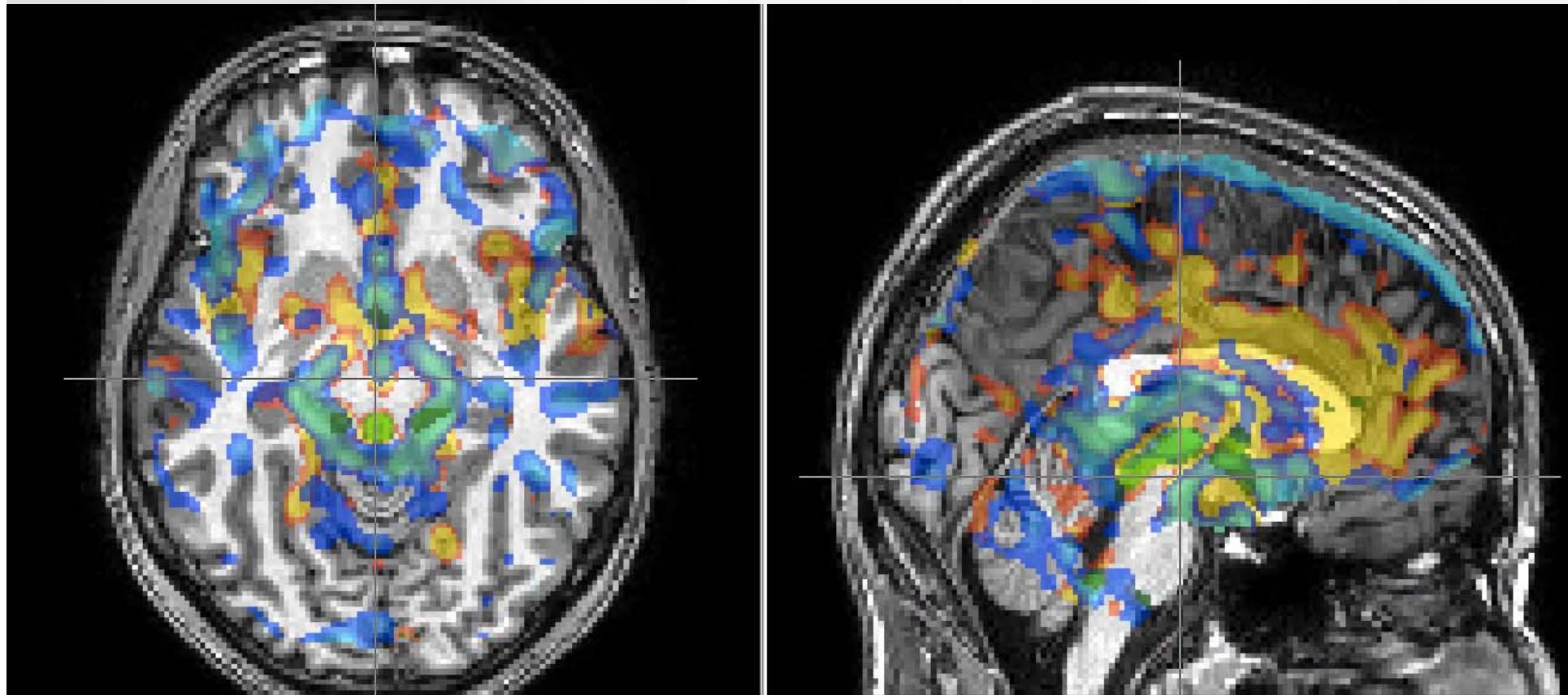
- Andreea Diaconescu (TNU): Social Learning Experiment 2012-2014, (N=35)
- F-contrast: Where does physiological noise model explain significant variance?



Relevance for Neuromodulation



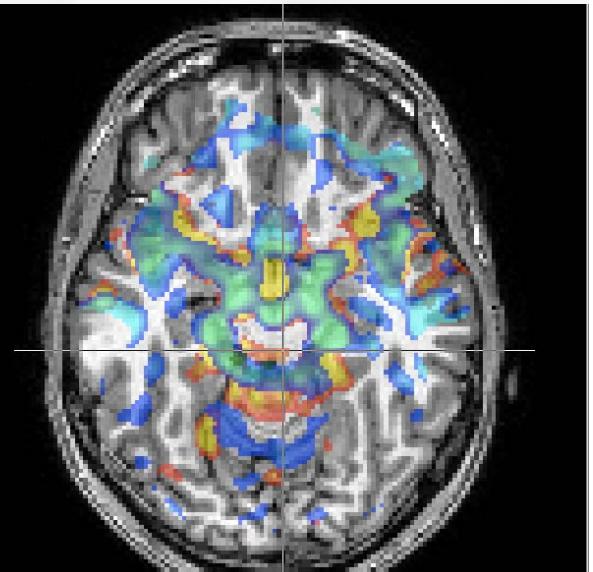
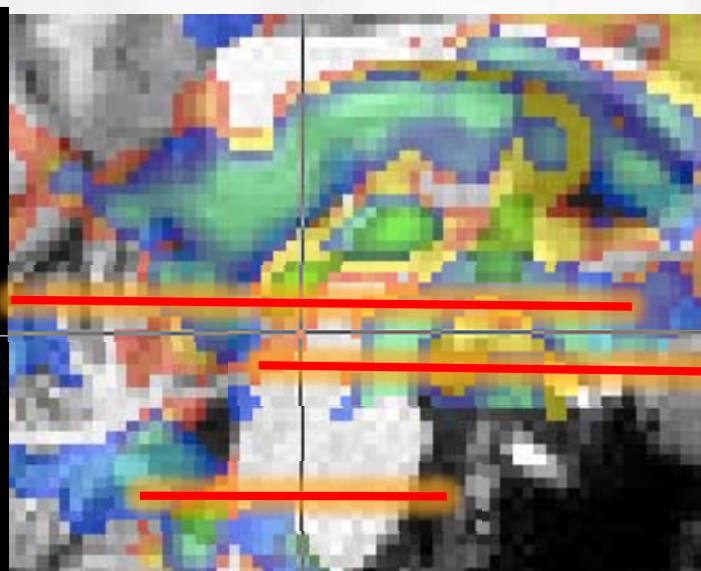
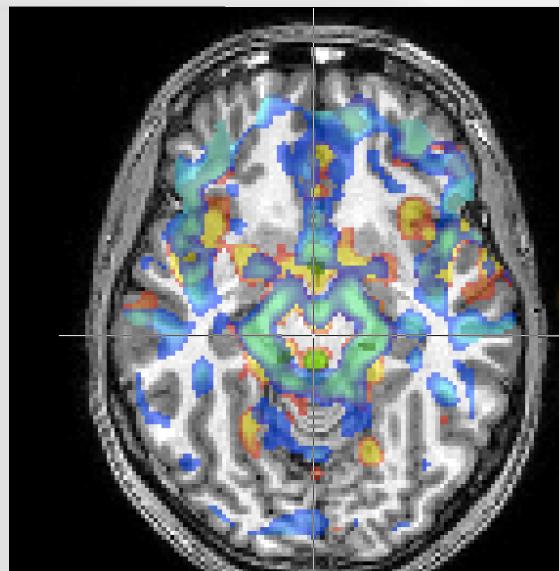
- cardiac (red), respiratory (blue), cardXresp (green)



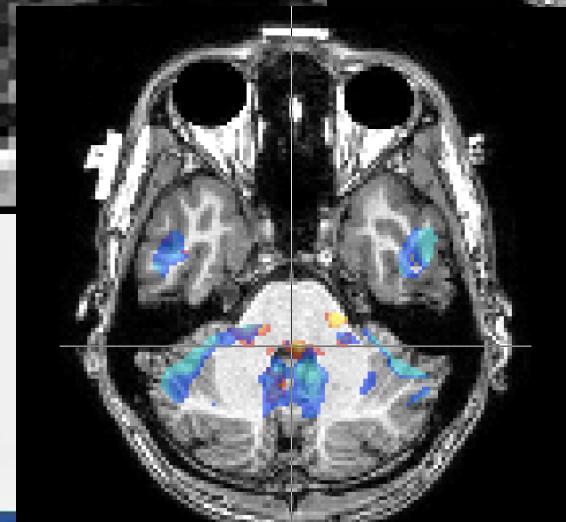
Relevance for Neuromodulation



- VTA (DA)



- Raphe Nuclei (5-HT)



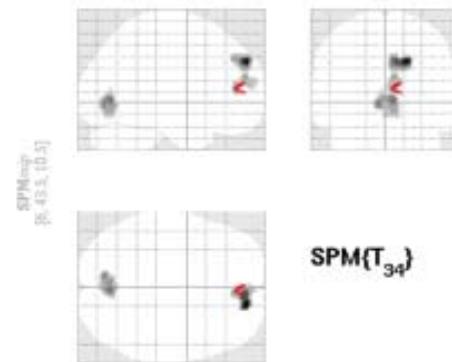
- Locus coeruleus (NA)

Effects on Group Contrasts

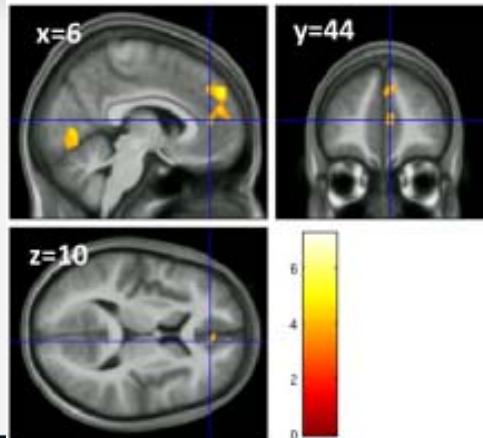


Higher Sensitivity

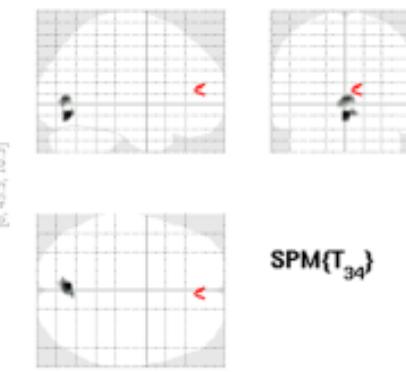
With
PhysIO



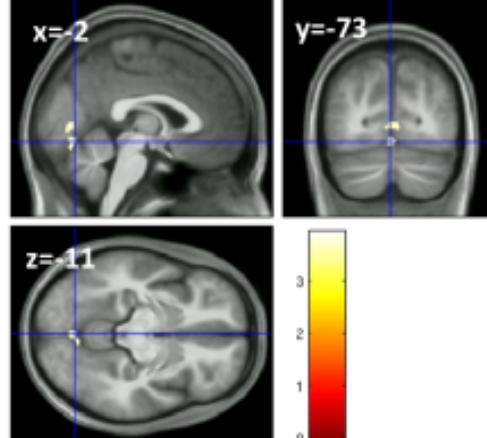
Peak-level p < 0.05 corrected



Without
PhysIO

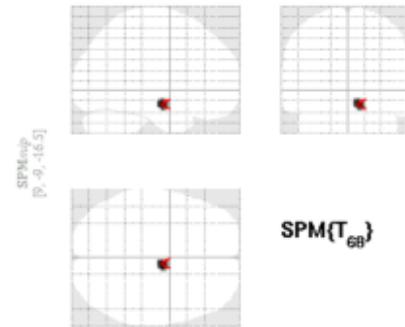


Cluster level p < 0.05 FWE, k >100

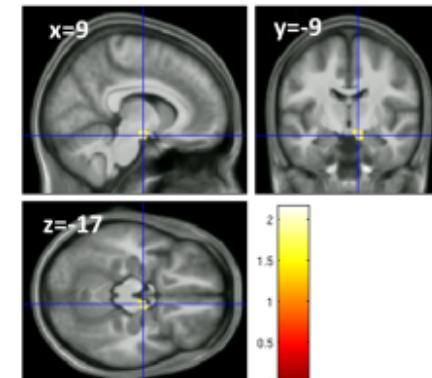


False Positives

NoPhysIO > PhysIO



Peak level p < 0.02 uncorrected

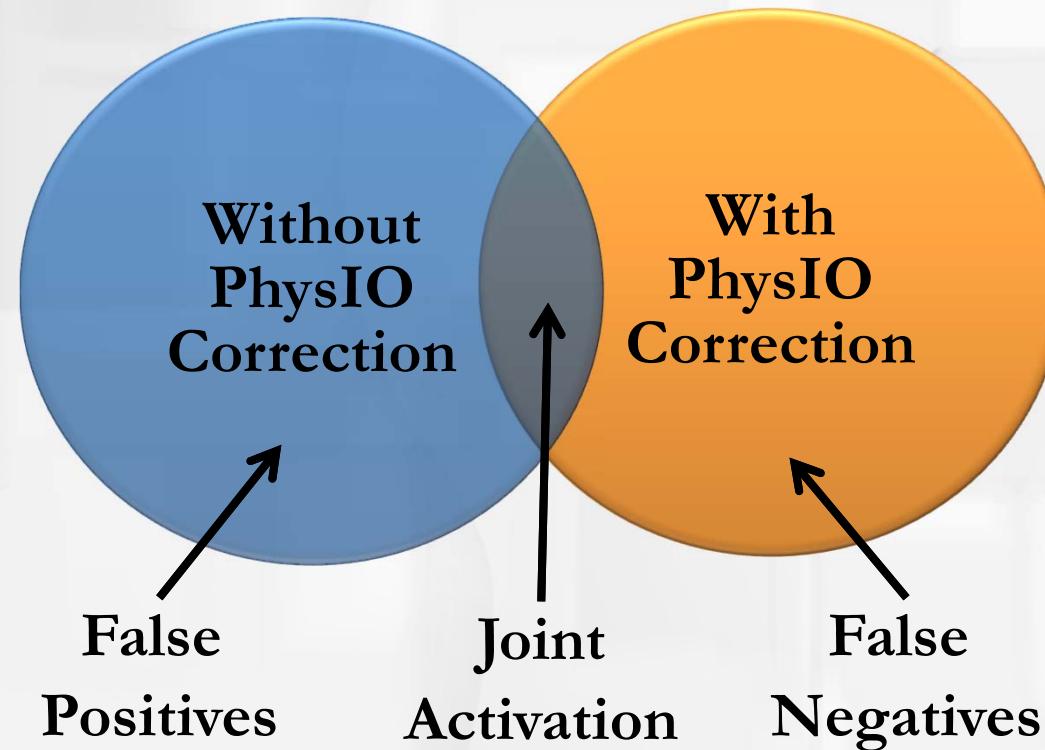


2nd level t-contrast
Social Prediction Error

Venn-Diagramme Cluster Analysis



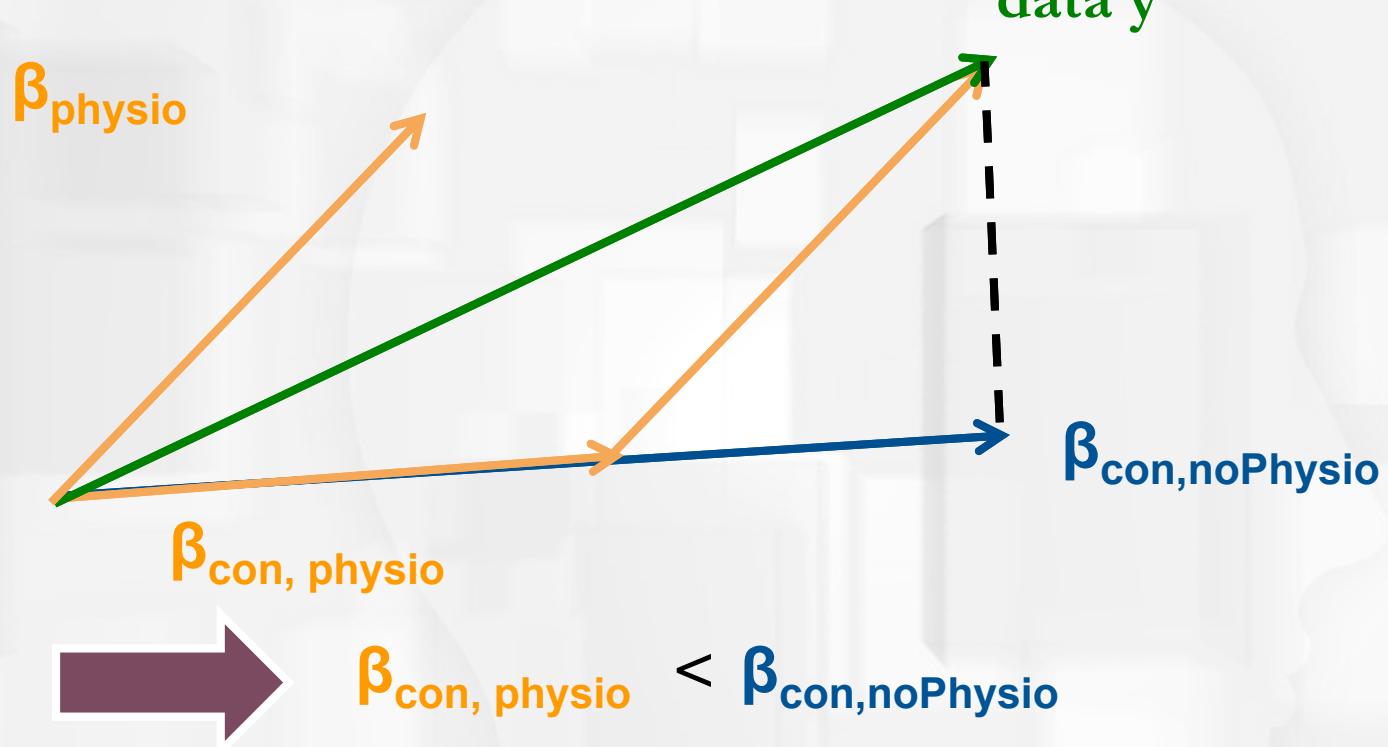
Significant Clusters



Noise modeling impact on task?



$$y = X_{\text{con}}\beta_{\text{con}} + X_{\text{physio}}\beta_{\text{physio}}$$



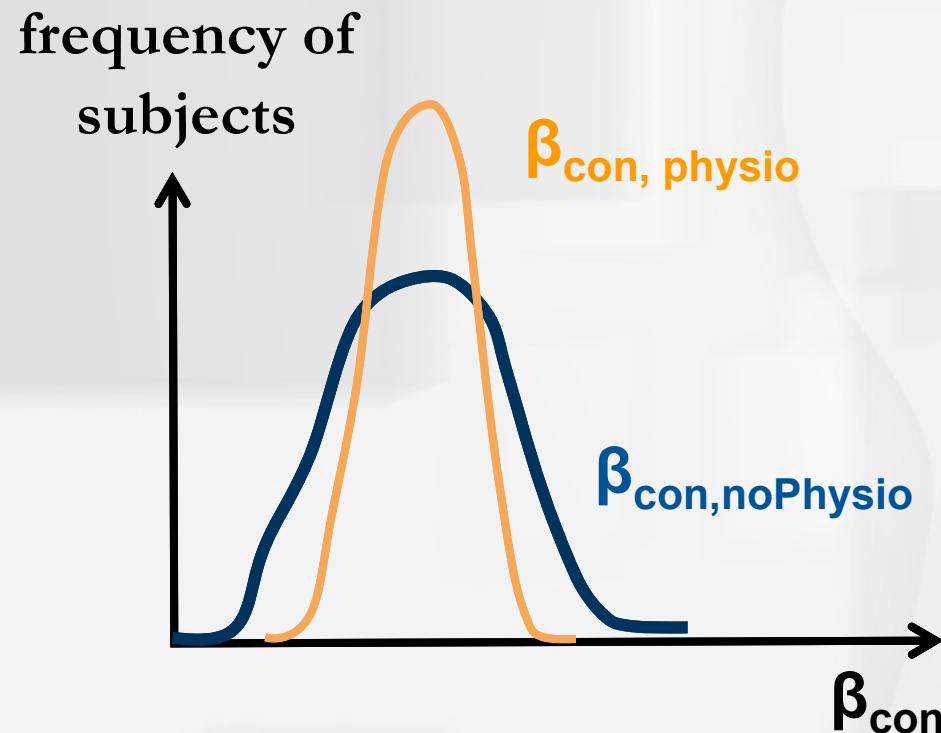
- Phys noise correction can change parameter estimates for regressors of interest (correlation!)
- Thereby change distribution of $\beta \Rightarrow$ Mean? Variance?

Group Effect: Correlated Regressors

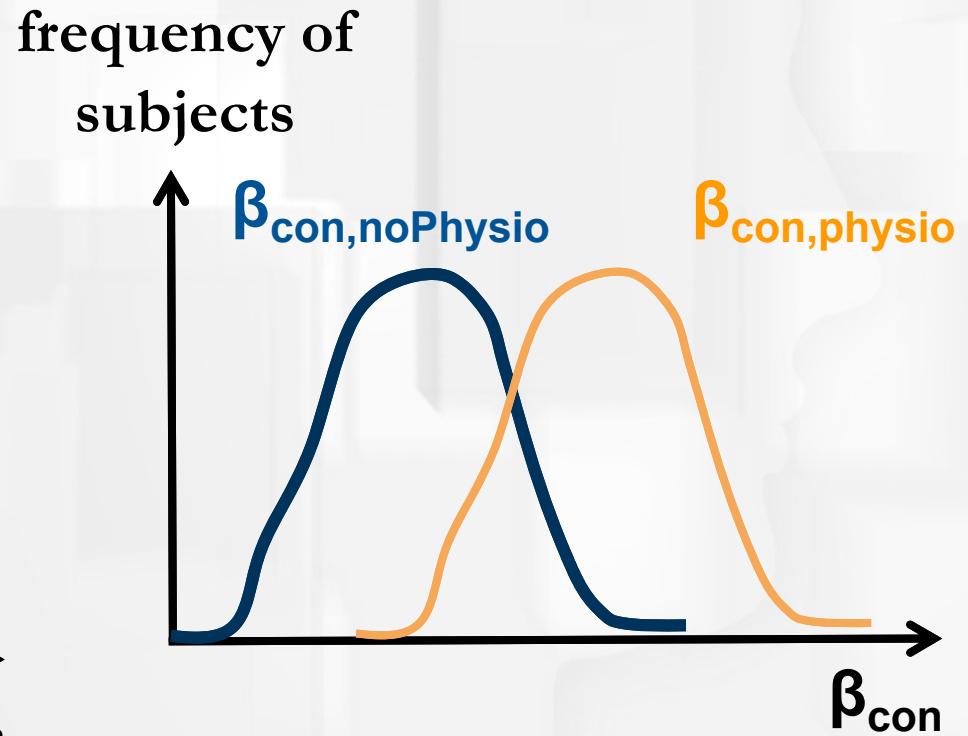


- Two mechanisms imaginable

Reduced inter-subject variance



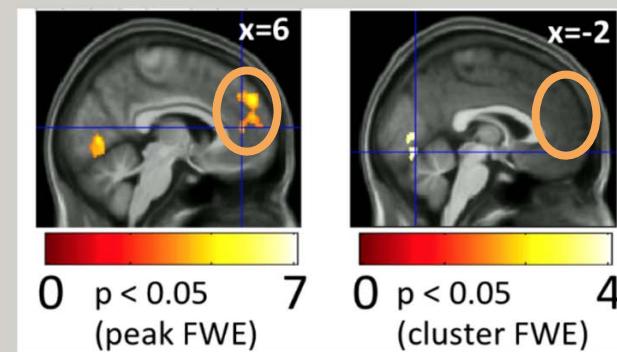
Increased inter-subject mean estimates



The Corrective Mechanism



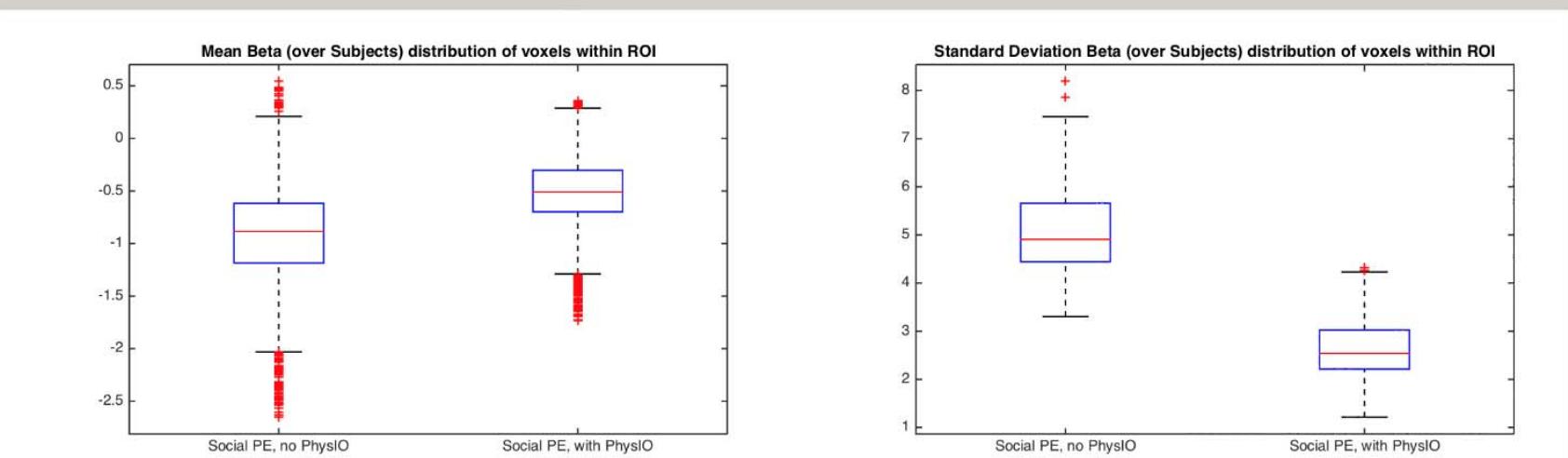
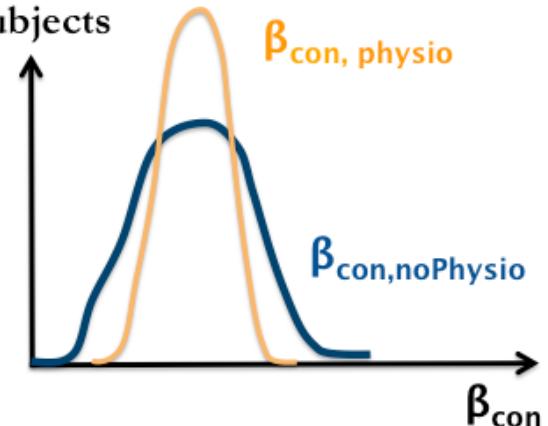
Social Pred. Error



Mean

Reduced inter-subject variance

frequency of subjects



Outline – Noise Correction



- MRI Time Series Recap and Noise Sources
 - Why de-noising? Structured Noise; Noise Pathways
- Noise Correction Approaches
 - Target: Scanner Drift, Motion, Cardiac/Breathing Cycle
 - Method: Modeling VS Preprocessing
 - Input: fMRI Data VS Peripheral Measures
- Prospects for Improving Group Statistics
- **Limitations**
 - Degrees of Freedom; Task-related “noise”; Interoception

Limitations of Noise Modeling



- Degrees of freedom, sensitivity reduced by too many ineffective regressors
 - F-test informative
- Intrinsic correlations of functional areas of interoception and peripheral physiology
 - E.g. Amygdala, Insula, ACC
 - Controversial reading:
[fMRI of the Amygdala: All In Vein? – Neuroskeptic](#)
 - Alternative: Masking, Pure anatomical priors removing CSF, angiography (vessels)

Conclusion



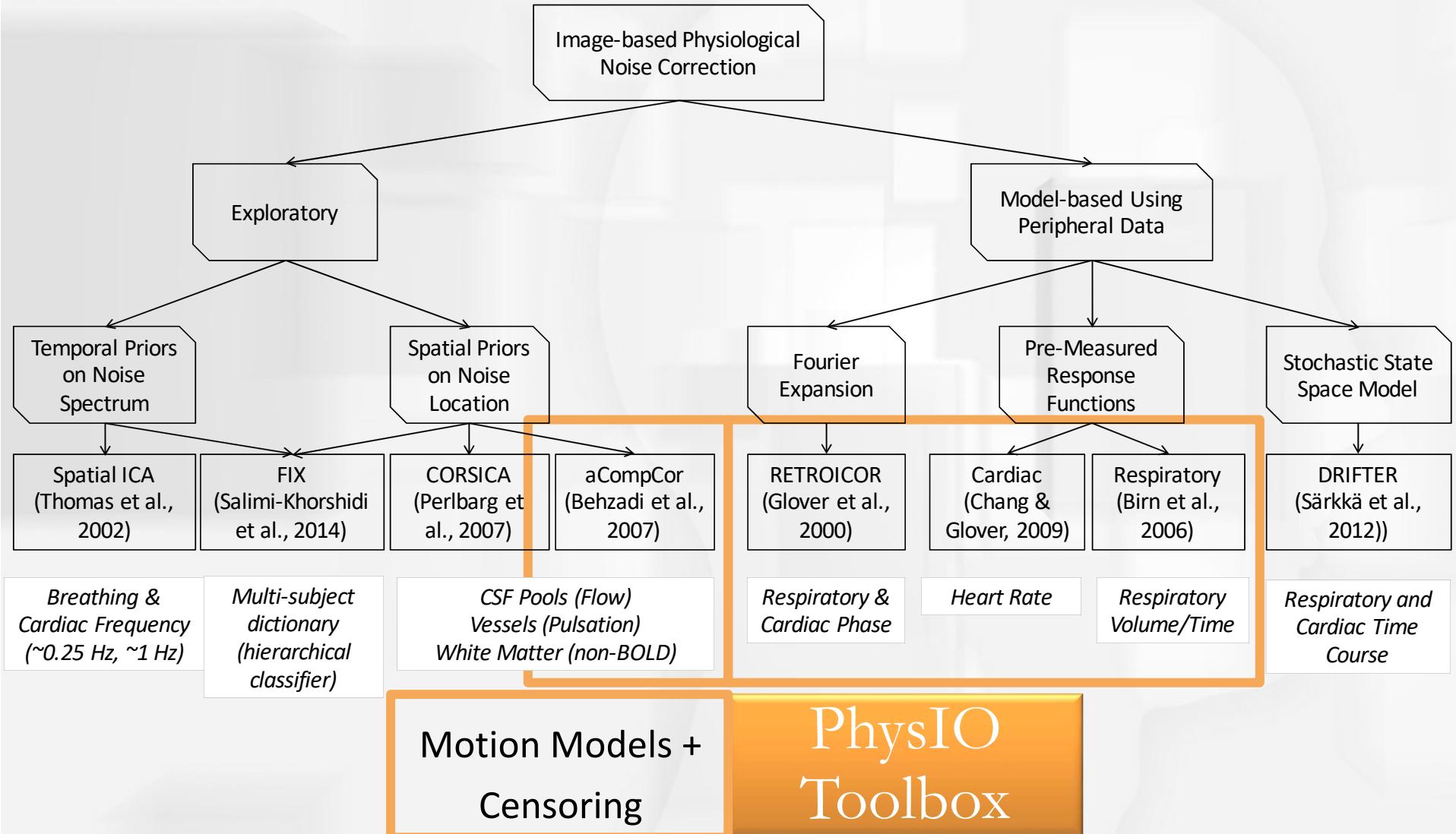
- MRI Time Series and Physiological Noise
- Image-Based Correction in the GLM
- Noise Modeling Prospects: Group FX
- The PhysIO Toolbox
- Structured noise through cardiac/resp cycle (70%)
- Nuisance regressors from Fourier expansion, response functions
- Increase group sensitivity (low inter-subject variability), fewer false positives
- Correction in SPM/Matlab in practice => **NOW!**

Practical Session



- **Demo: The PhysIO Toolbox for Physiological Noise Correction in fMRI**
 - Features and Workflow
 - Image-based physiological noise correction in the GLM
 - RETROICOR, HRV, RVT
 - Noise-ROIs
 - Practical Demo (SPM Batch)
 - Estimating different Models
 - Understanding the Preprocessing Plots
 - Automatic Model Assessment, Diagnostics on Contrast

Image-based Noise Correction

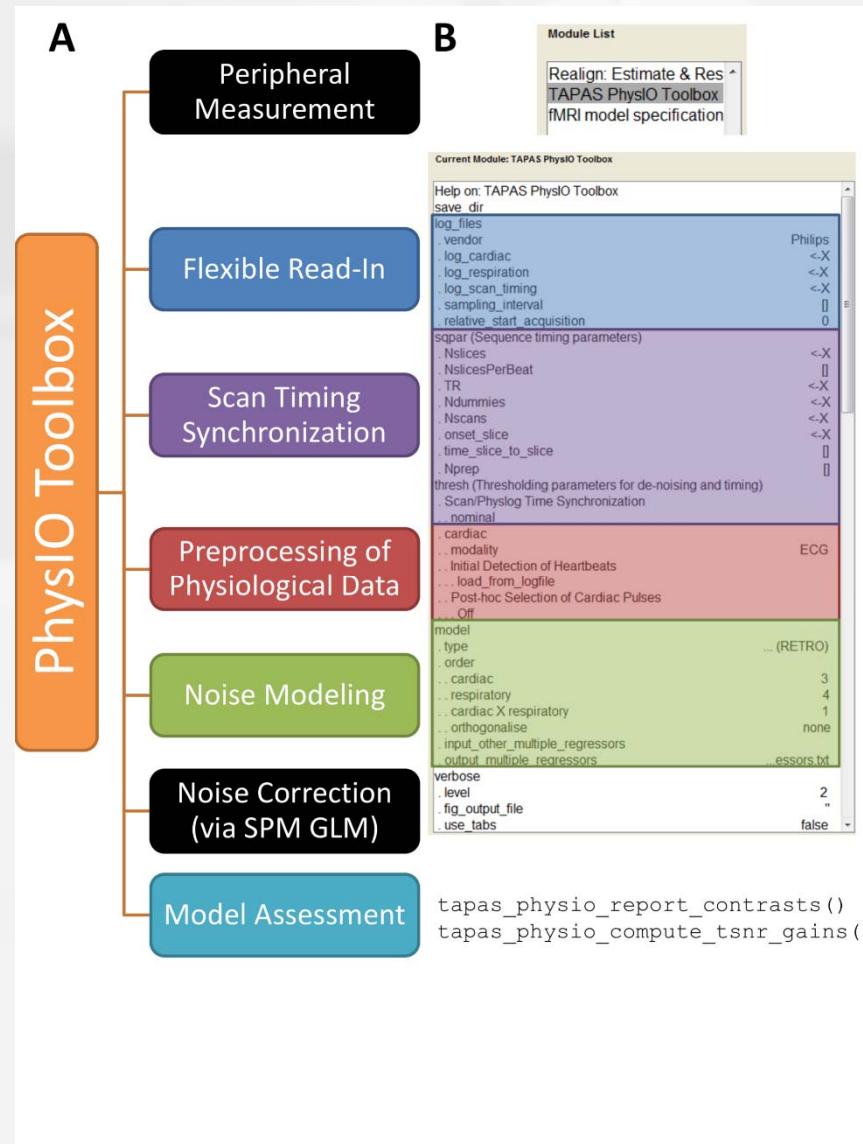


The PhysIO Toolbox

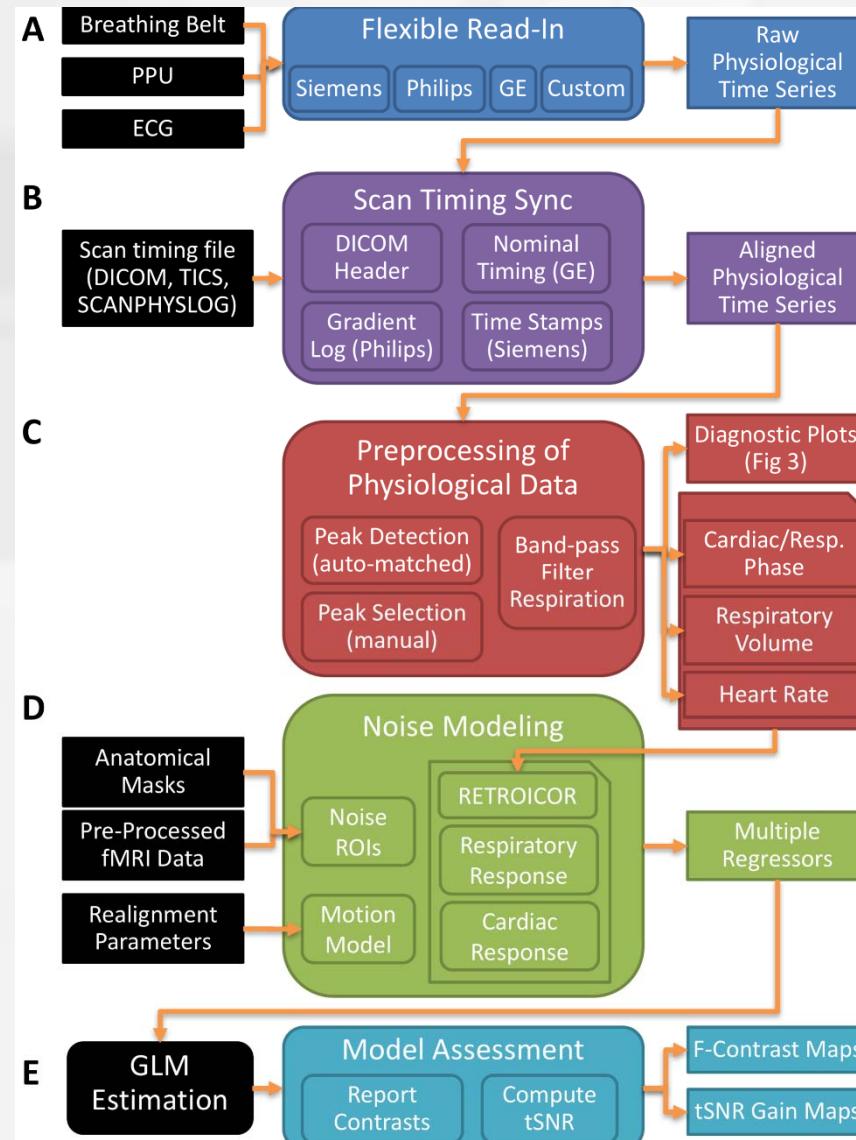


- Developed at the Translational Neuromodeling Unit (TNU) since 2008
 - Lead programmer: Lars Kasper (TNU)
 - Contributors: Jakob Heinze (TNU), Steffen Bollmann (KiSpi Zurich)
- Part of the TNU «TAPAS» software suite
- Used at the TNU, in Zurich and beyond by ~50 researchers
 - Iglesias 2013, Neuron; Kasper 2014, NeuroImage; Bollmann 2014, PhD Thesis; Sulzer 2013, NeuroImage; Hauser 2014, NeuroImage; Grueschow 2015, Neuron
- Download & Example Data:
 - <https://www.tnu.ethz.ch/en/software/tapas.html>
 - <https://www.tnu.ethz.ch/en/software/tapas/data.html>

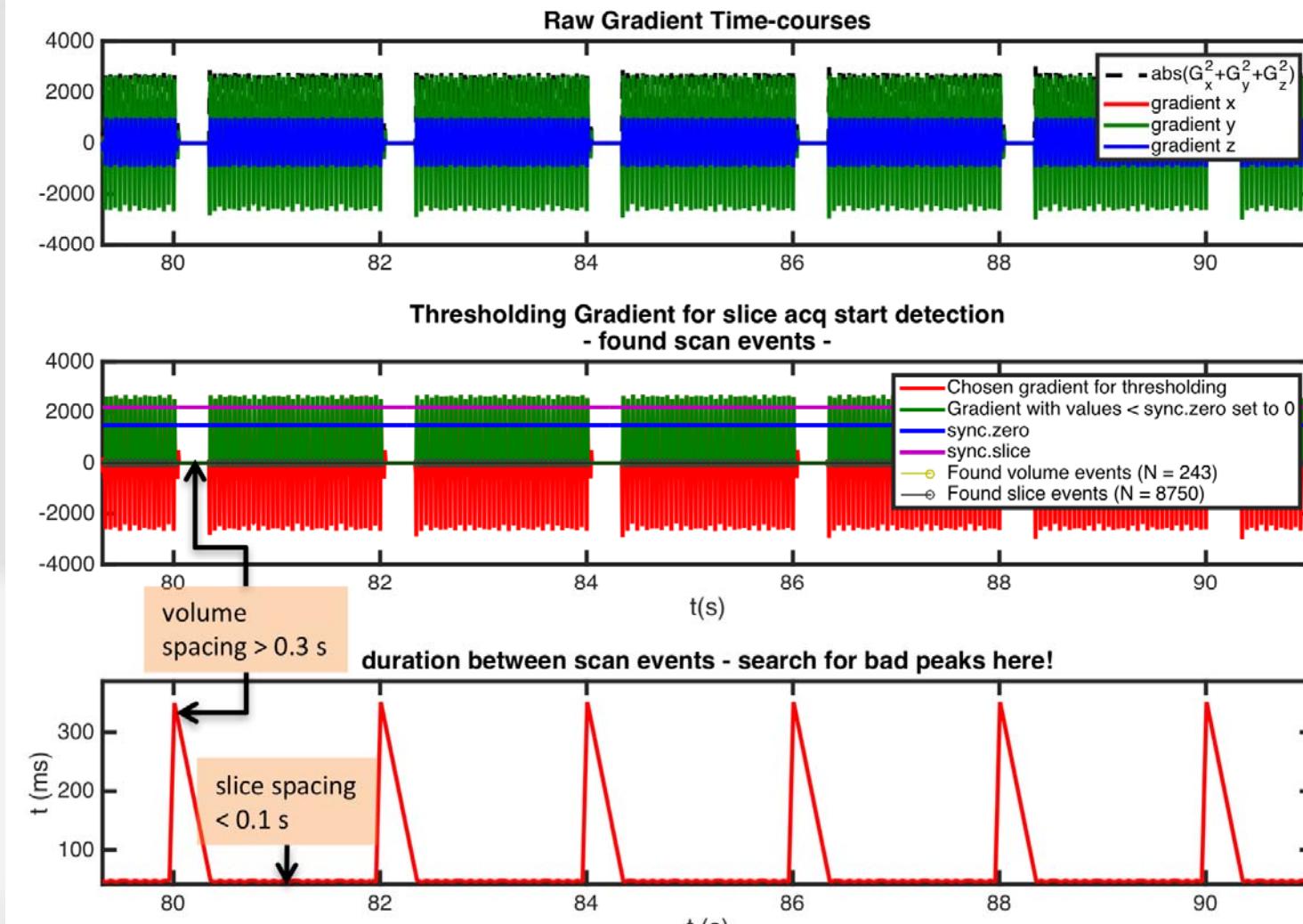
Workflow of the PhysIO Toolbox



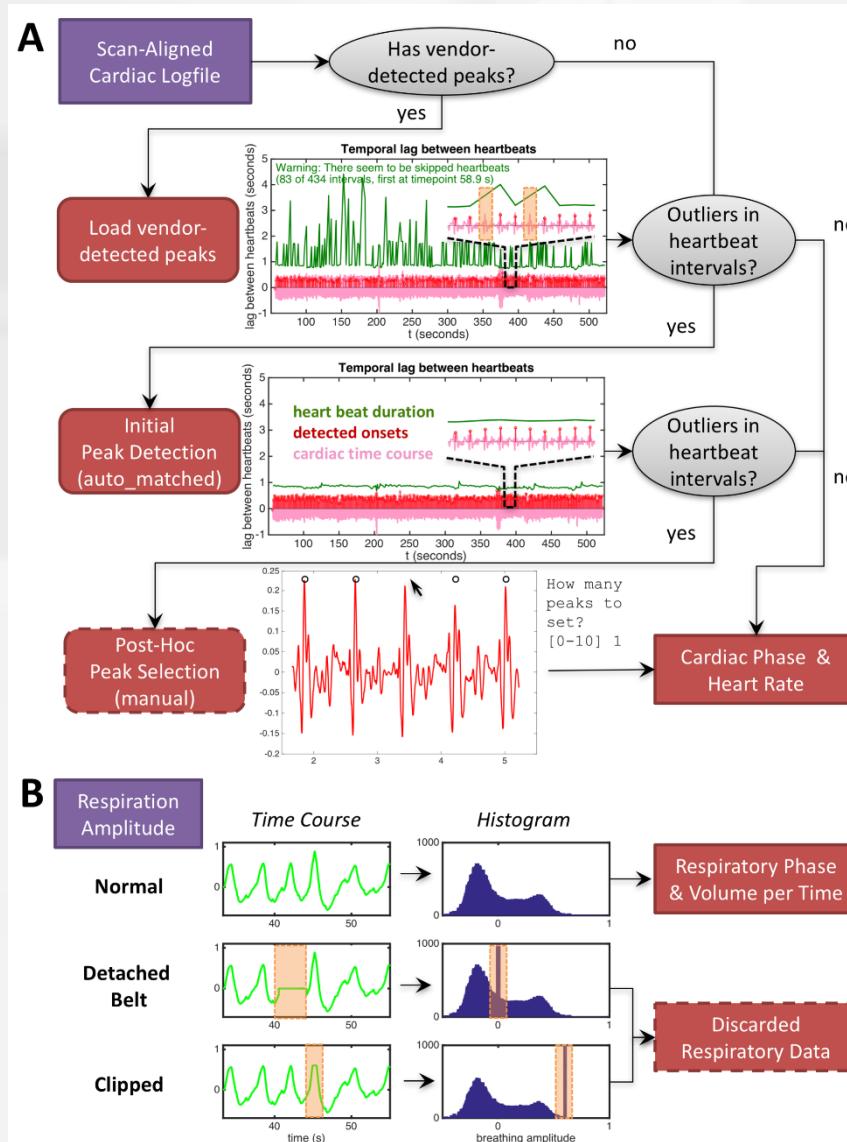
Flowchart of Noise Correction



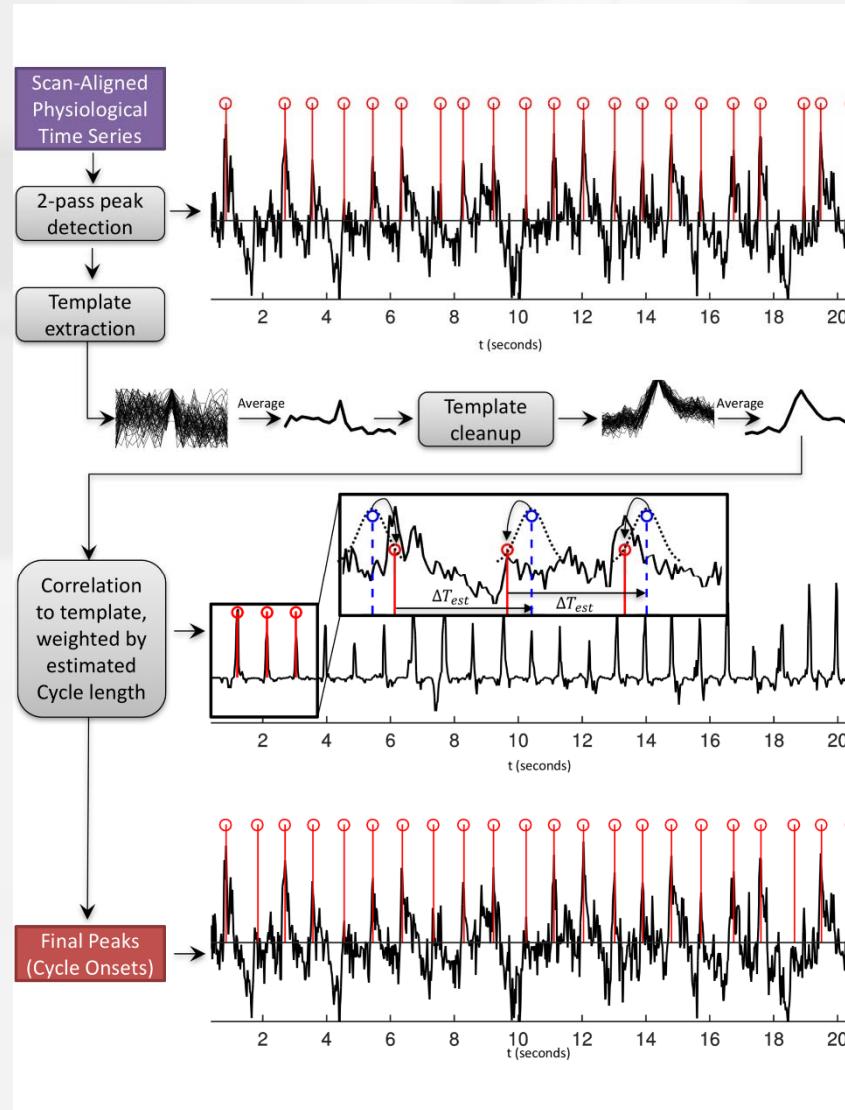
Scan Sync with Philips Gradients



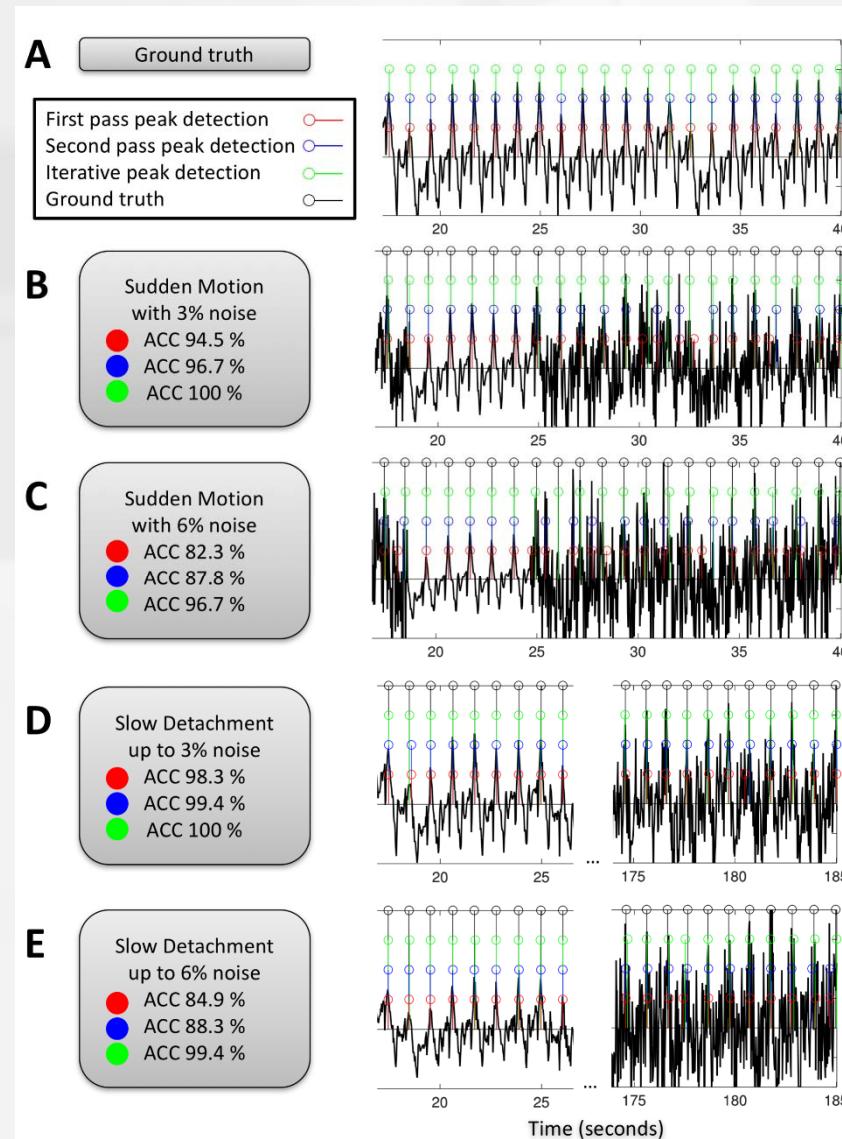
Data Preprocessing Overview



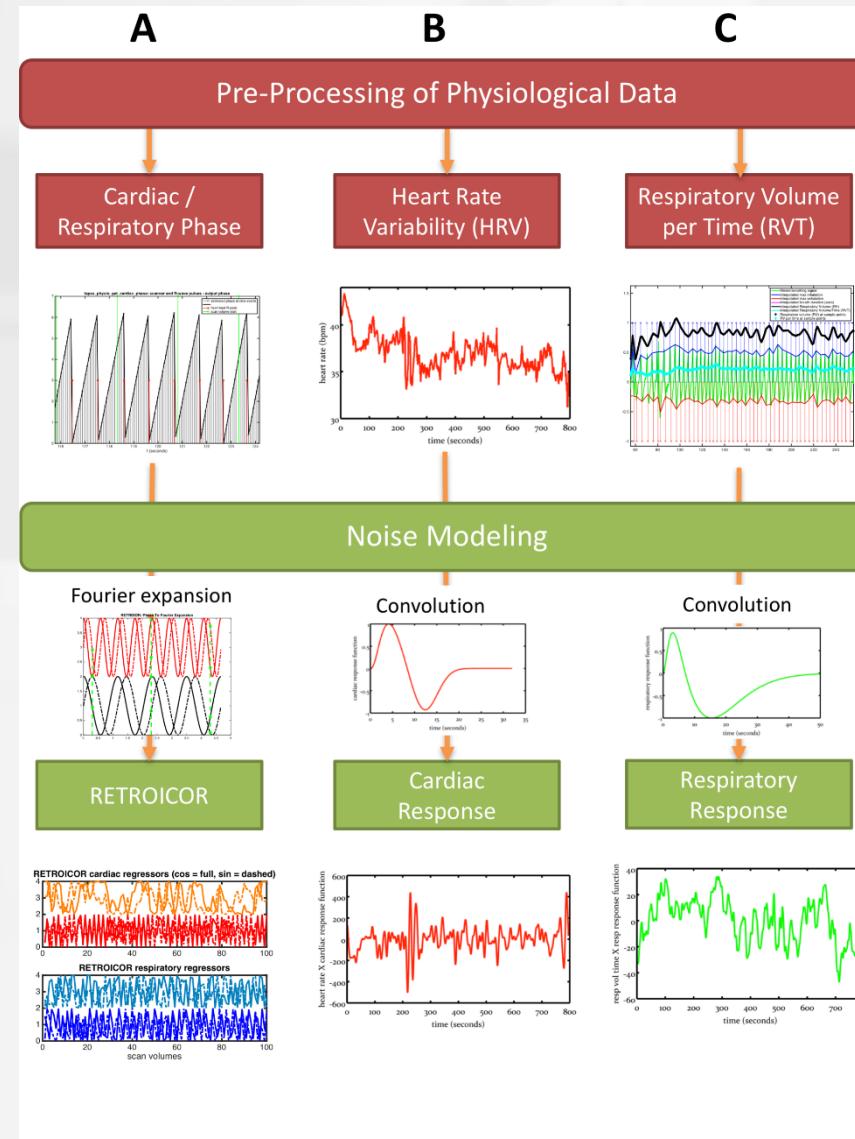
Preprocessing: Peak Detection



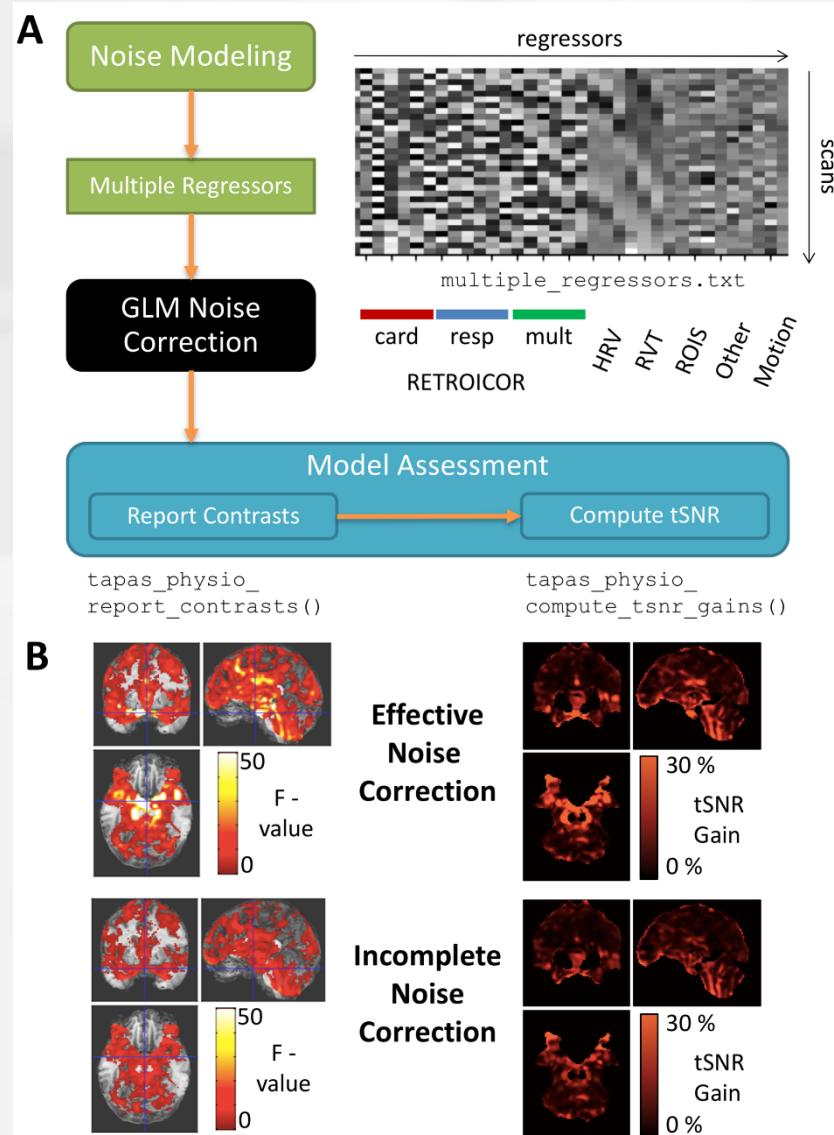
Peak Detection: Robustness



Noise Modeling



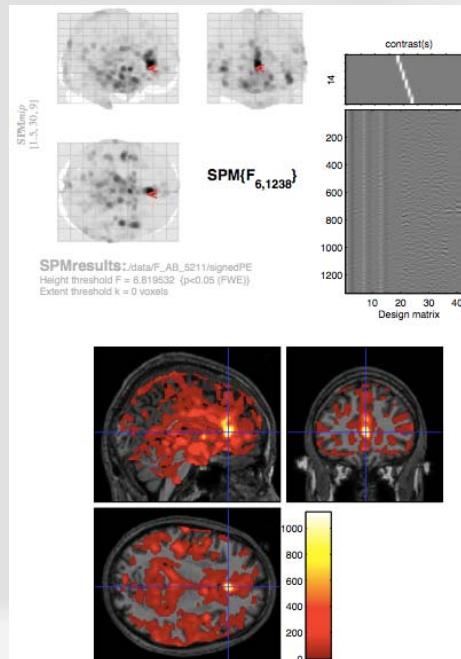
Diagnostics: Model Assessment



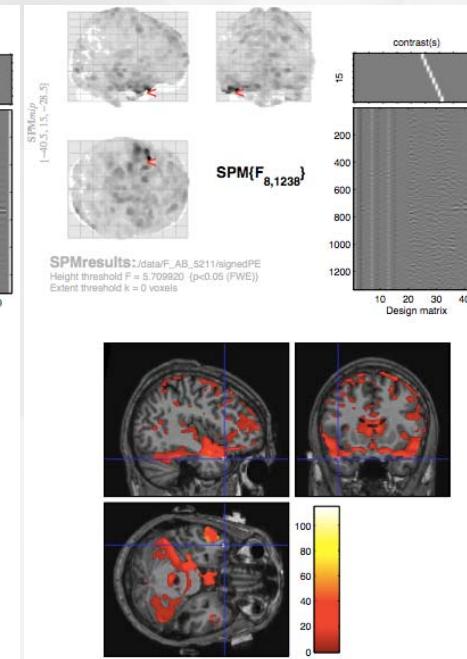
Model Check: SPM F-contrasts



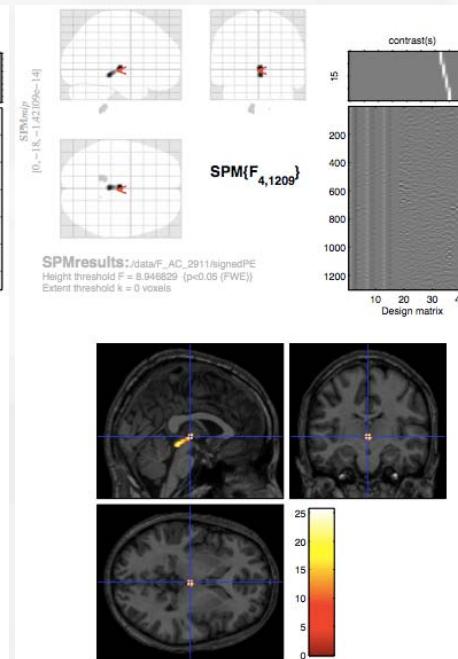
Cardiac regressors



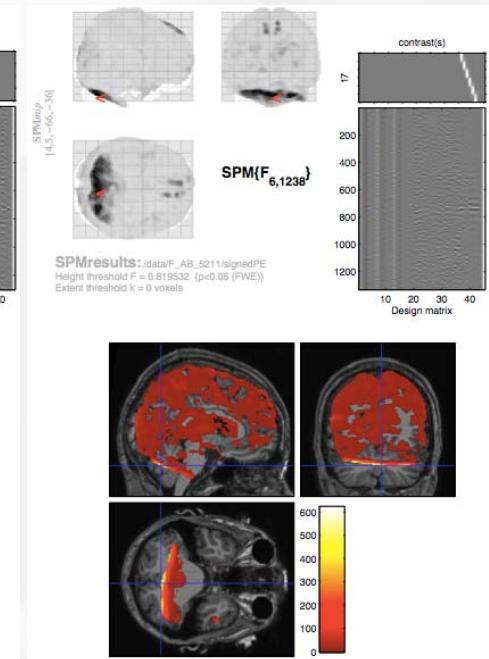
Respiratory regressors



Cardiac x Respiratory



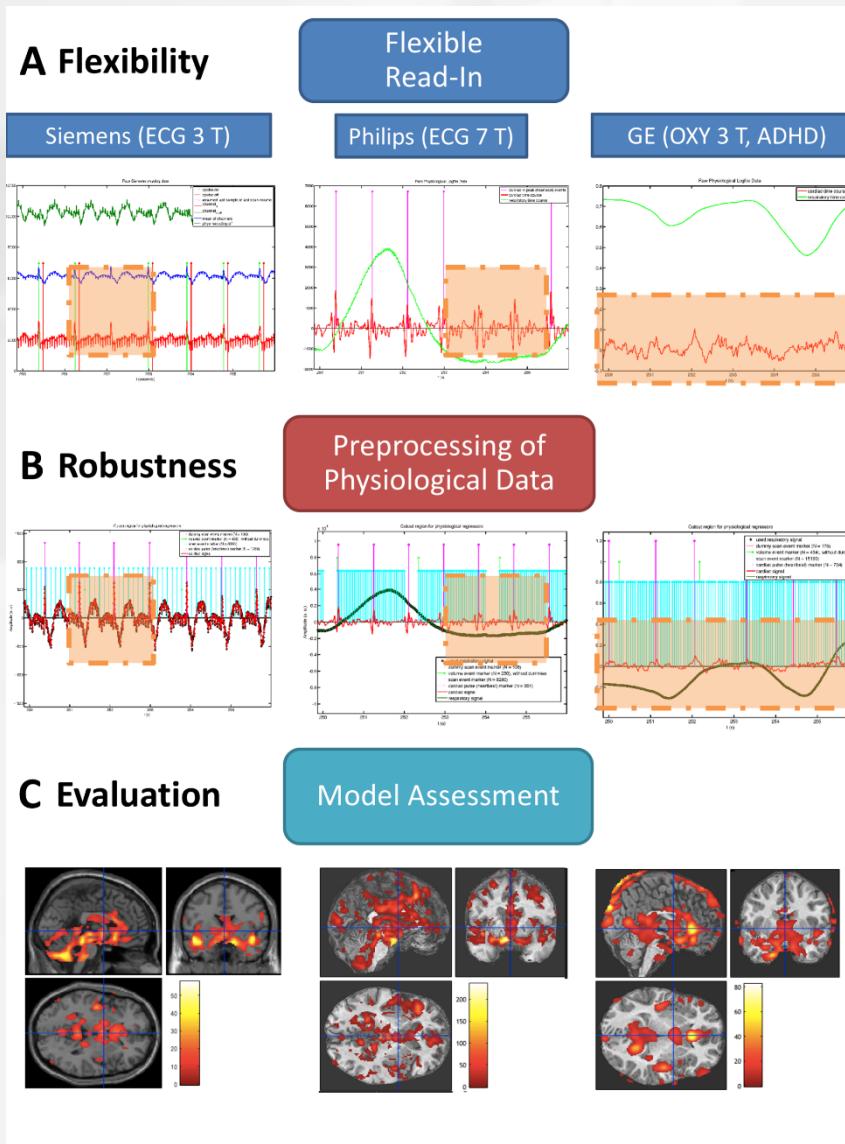
Movement regressors



Finally:

- Check Influence of Physiological Noise (Correction) on Data
- SPM
- F-contrast on 1st and second level

Flexibility: Scanner vendors

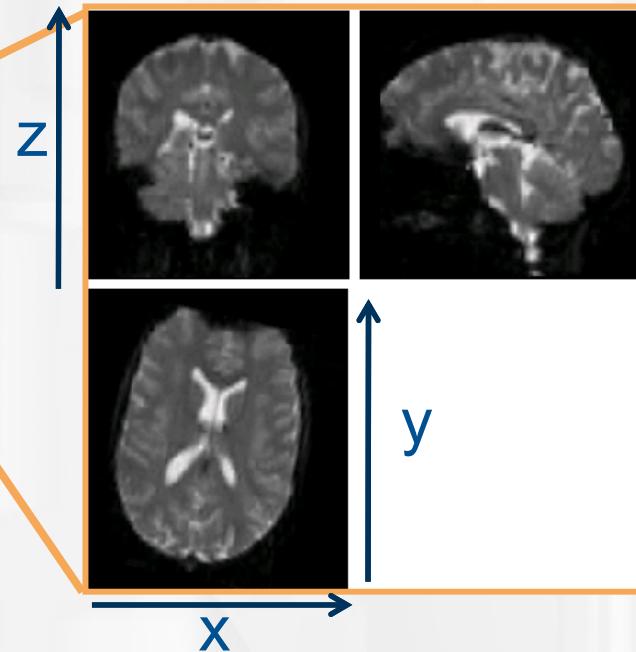


References



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- **Josephs**, O., Howseman, A.M., Friston, K., Turner, R., 1997. “Physiological noise modelling for multi-slice EPI fMRI using SPM.” Proceedings of the 5th Annual Meeting of ISMRM, Vancouver, Canada, p. 1682
- **Kasper, L.**, Bollmann, S., Diaconescu, A.O., Hutton, C., Heinze, J., Iglesias, S., Hauser, T.U., Sebold, M., Manjaly, Z.-M., Pruessmann, K.P., Stephan, K.E., 2016. The PhysIO Toolbox for Modeling Physiological Noise in fMRI Data. *Journal of Neuroscience Methods* *accepted*. doi:10.1016/j.jneumeth.2016.10.019

fMRI = Acquiring Movies



- ...of three-dimensional Blood Oxygen-Level Dependent (BOLD) contrast images

- Run/Session:
Time Series of
Images

