Noise Models and Correction for fMRI

- *an Introduction to the PhysIO Toolbox*

Lars Kasper

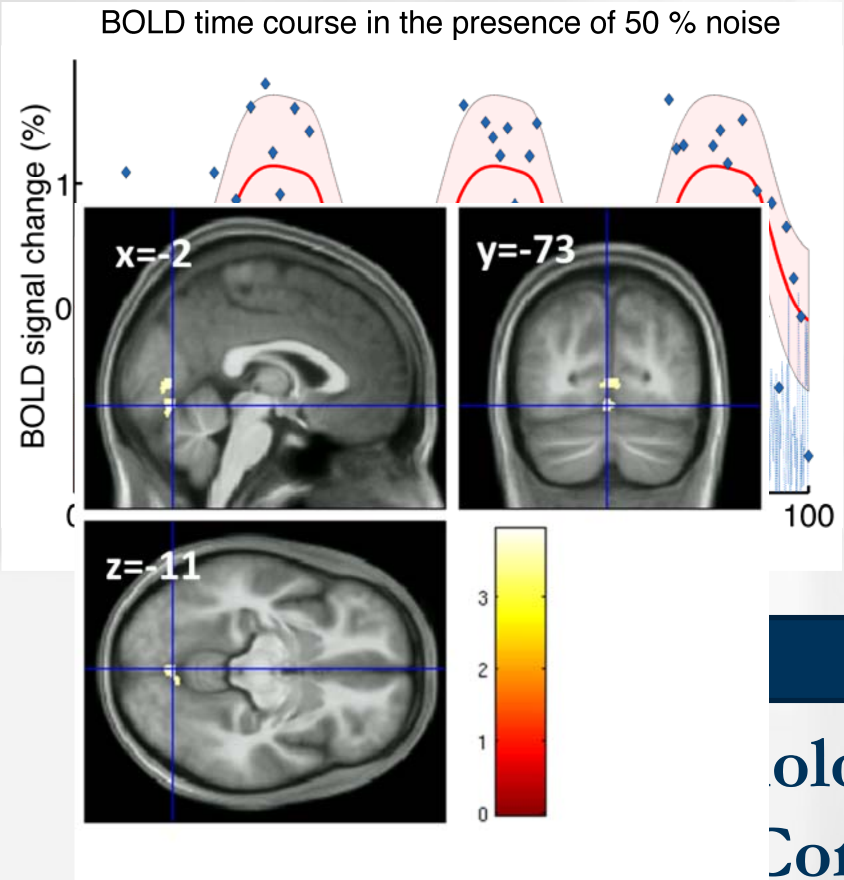
Nov 8th, 2016

MR-Technology Group & Translational Neuromodeling Unit

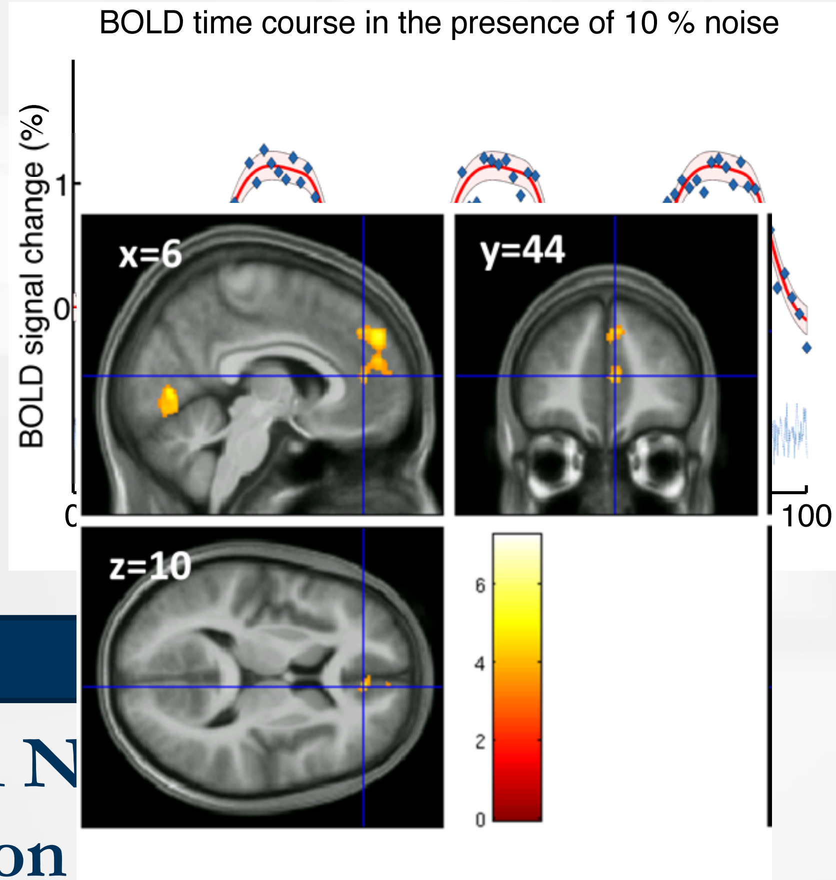
Institute for Biomedical Engineering
University of Zurich and ETH Zurich

The Goal of Noise Correction

Before

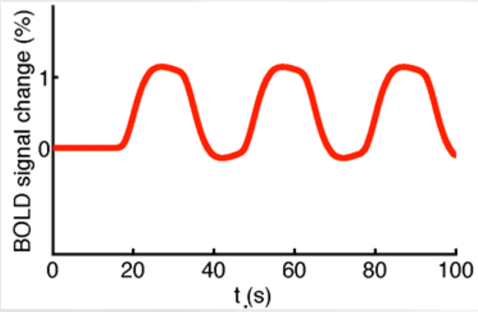


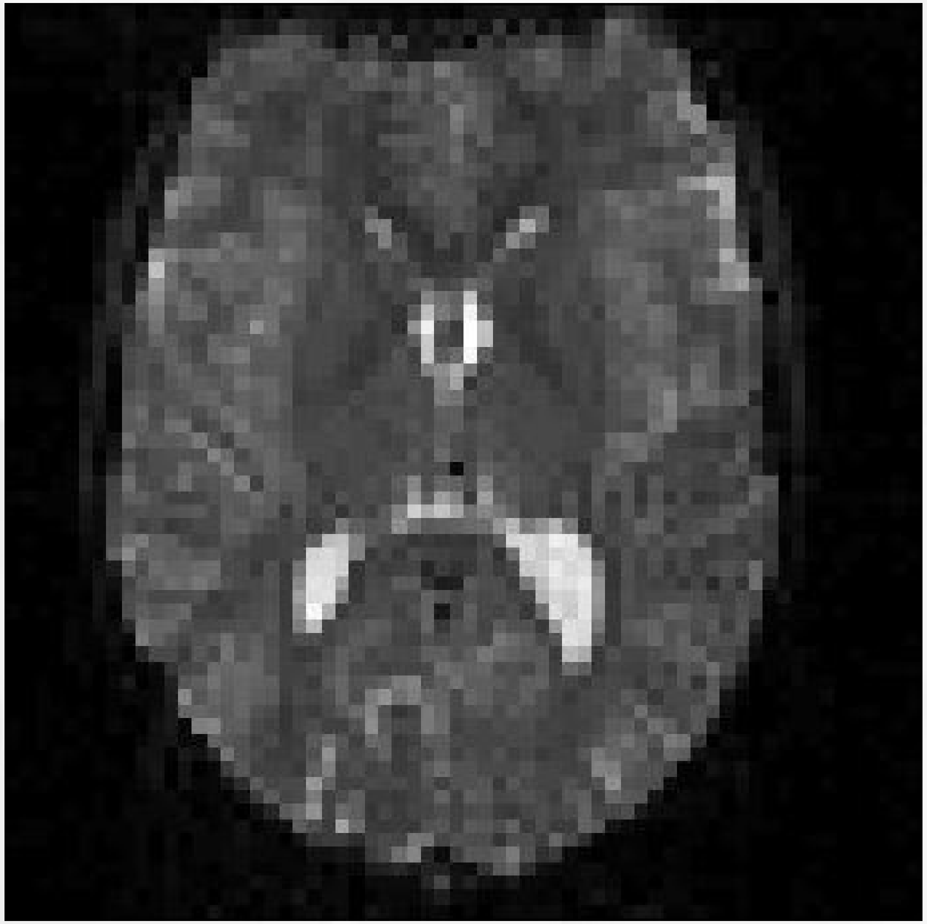
After



ological N
orrection

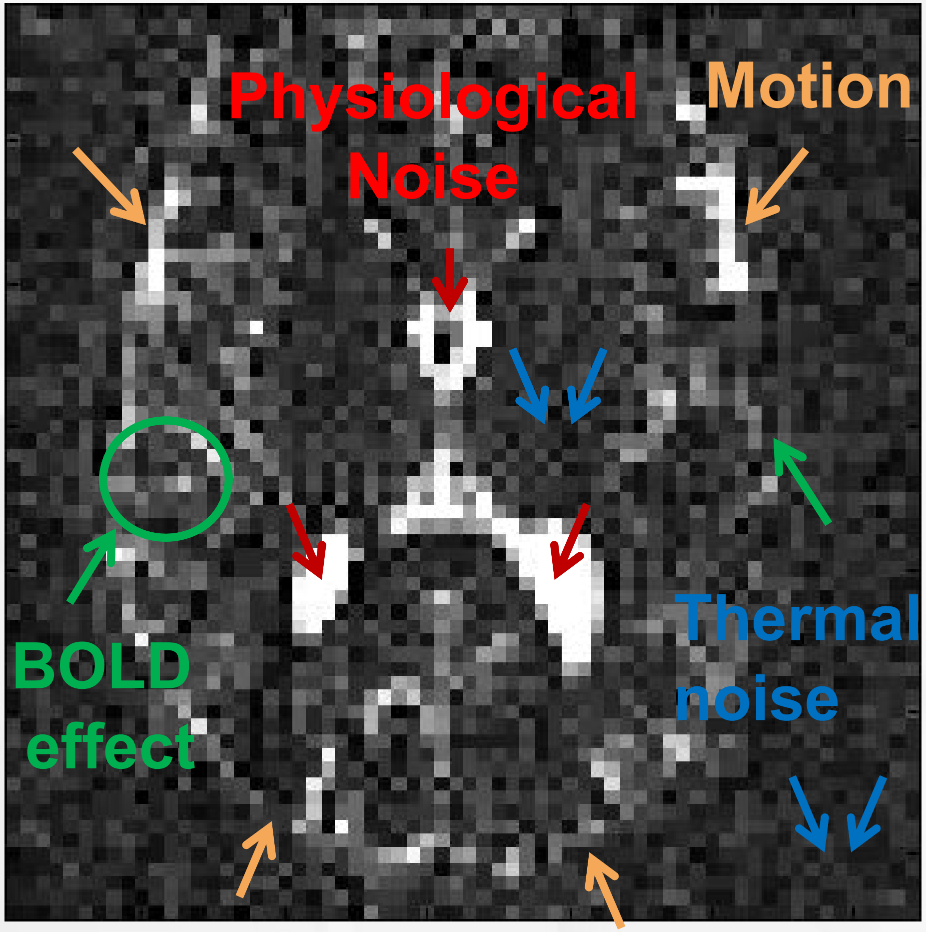
Reminder: fMRI Data is noisy…





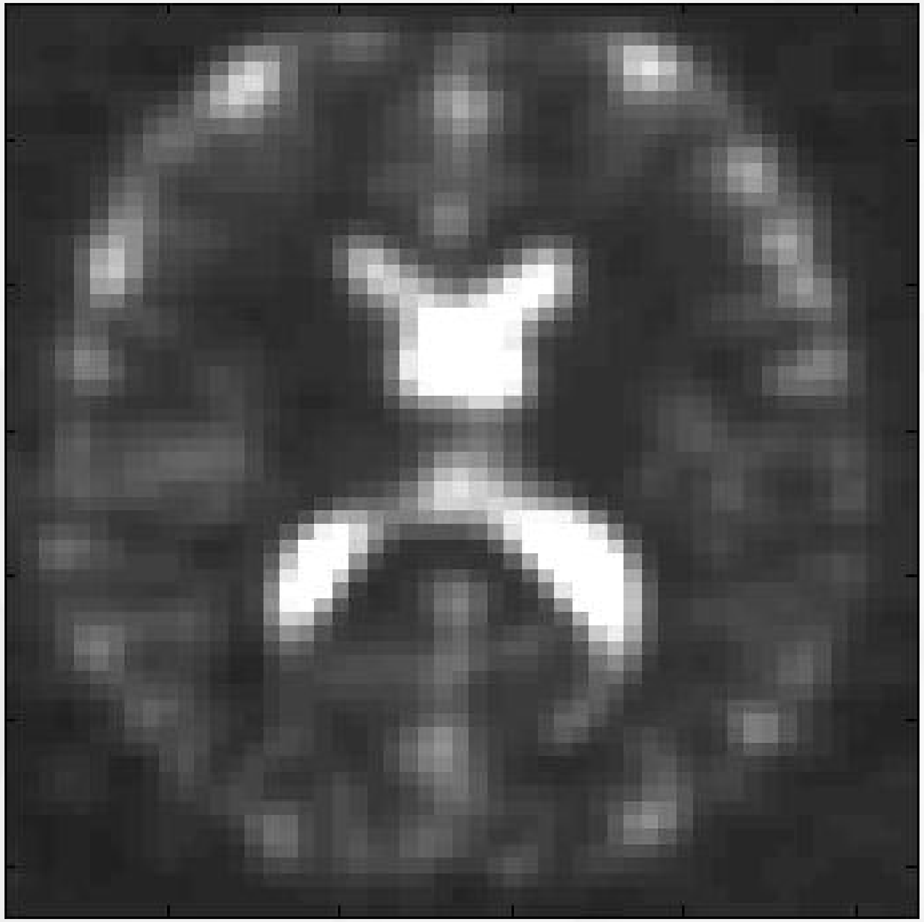
fMRI Data is noisy…

- Interest in fluctuations only: Subtract the mean



Previously…

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

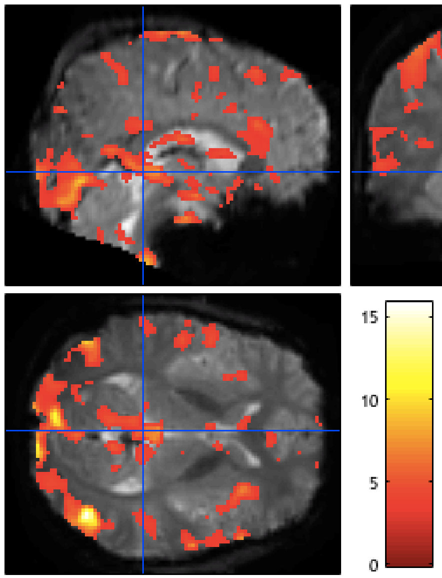


Sources of Noise in fMRI

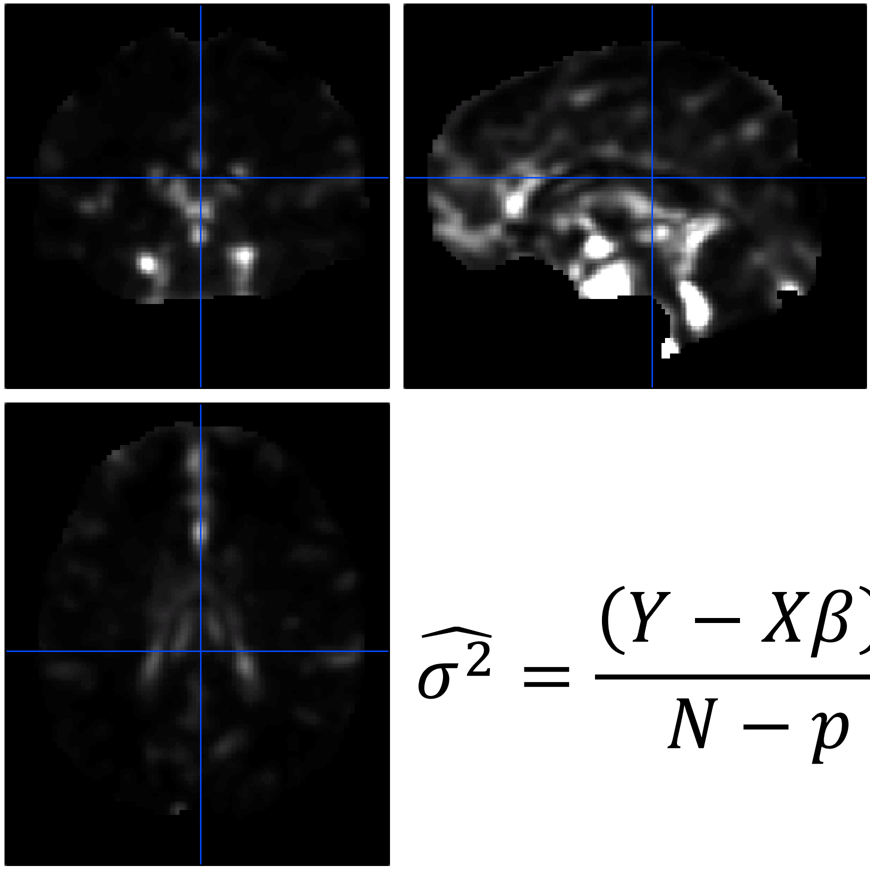
Acquisition Timing	Temporal Preproc	Slice-Timing
Subject Motion	Spatial Preproc	Realignment
Anatomical Identity	Spatial Preproc	Co-registration
Inter-subject variability	Spatial Preproc	Segmentation
Thermal Noise	Spatial Preproc	Smoothing
Physiological Noise	Noise Modeling	PhysIO Toolbox

Previously….(continued)

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



F contrast
All effects



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

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

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

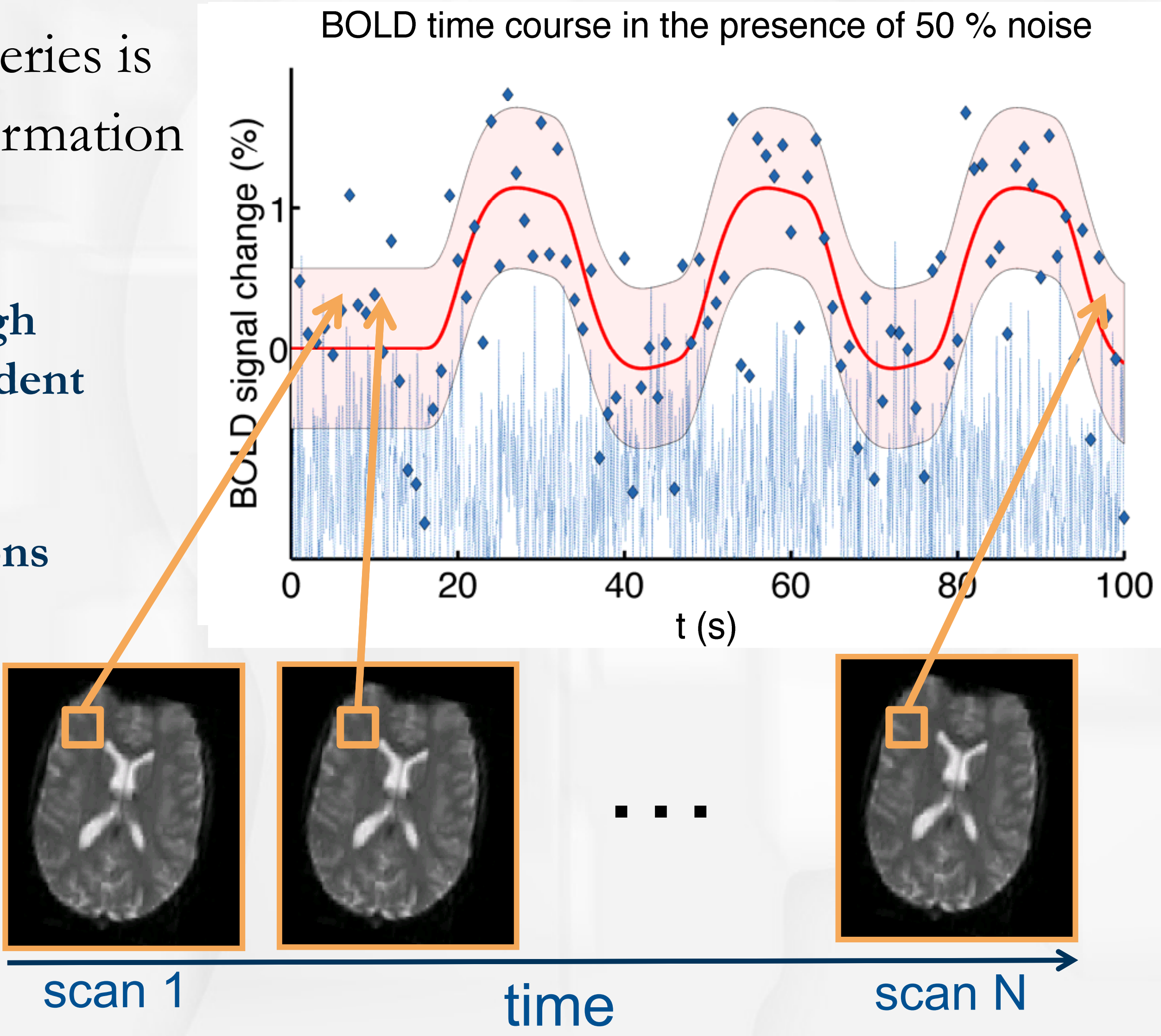
fMRI = Acquiring Movies

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

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

Noise: All other fluctuations

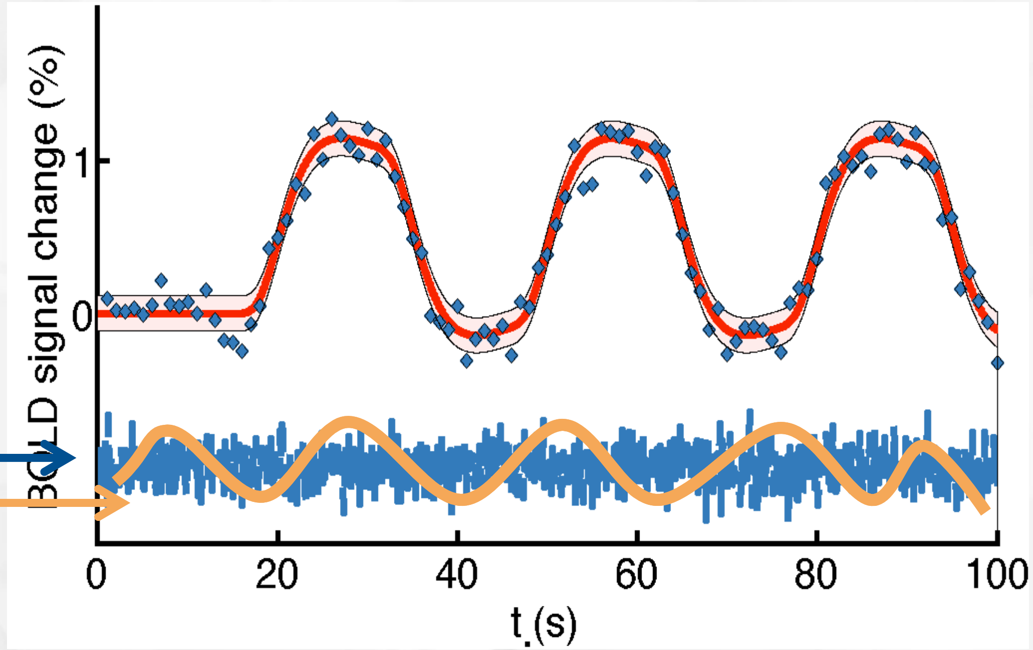
- Run/Session: Time Series of Images



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

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

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

Recap: MR Image Encoding

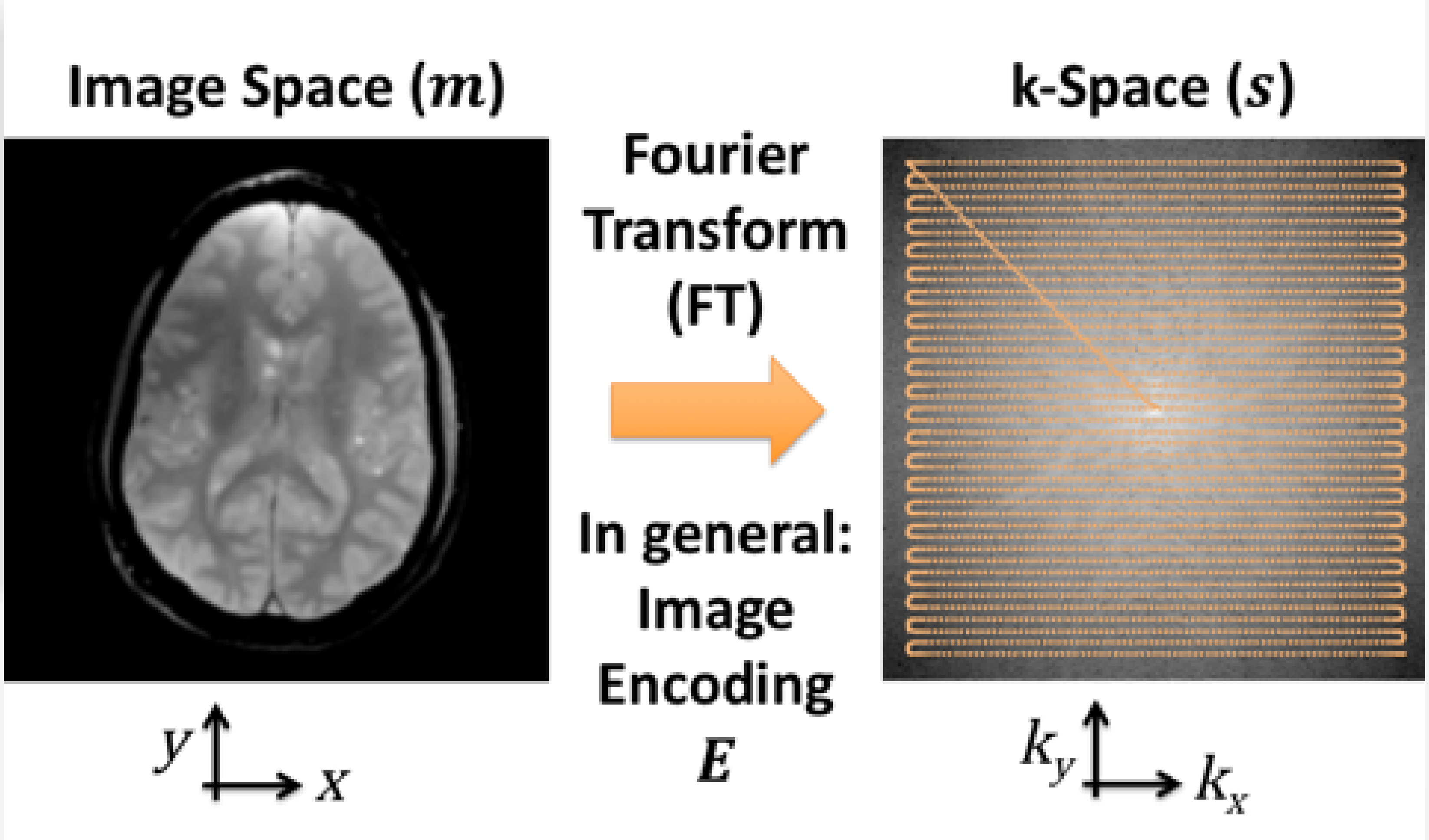
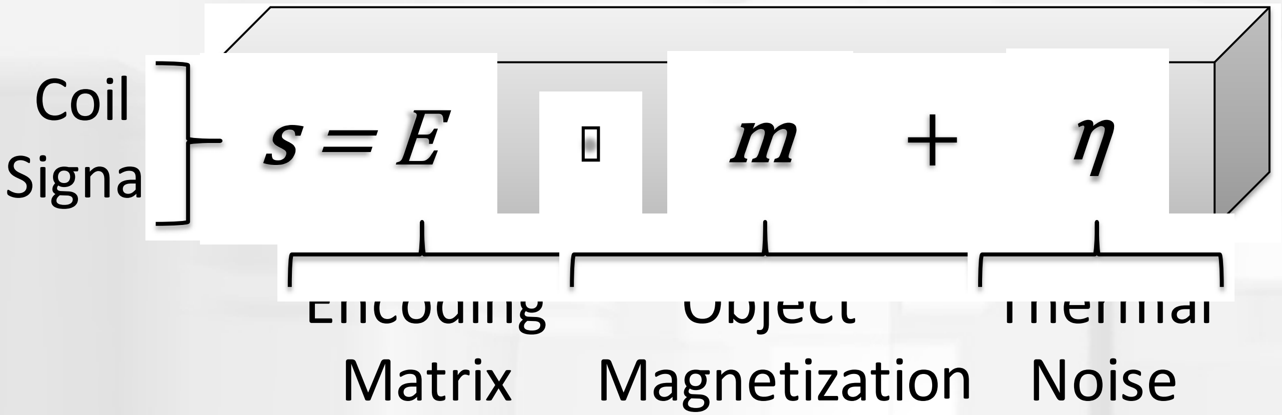
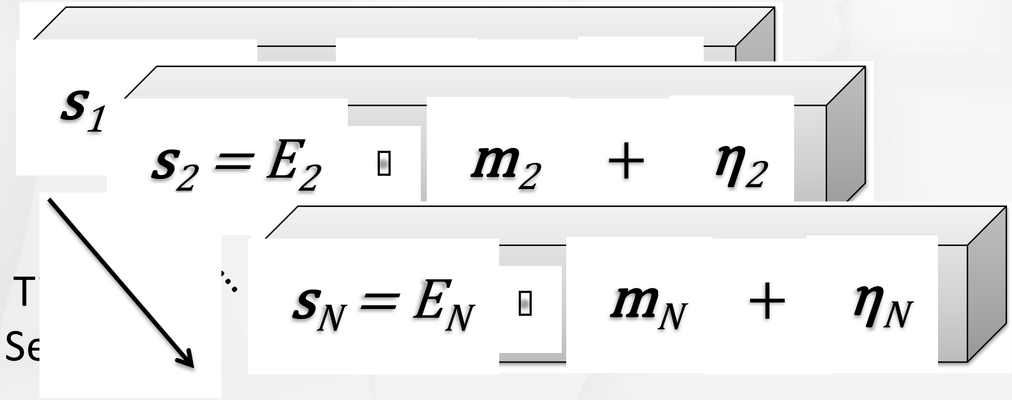


Image Reconstruction & Noise

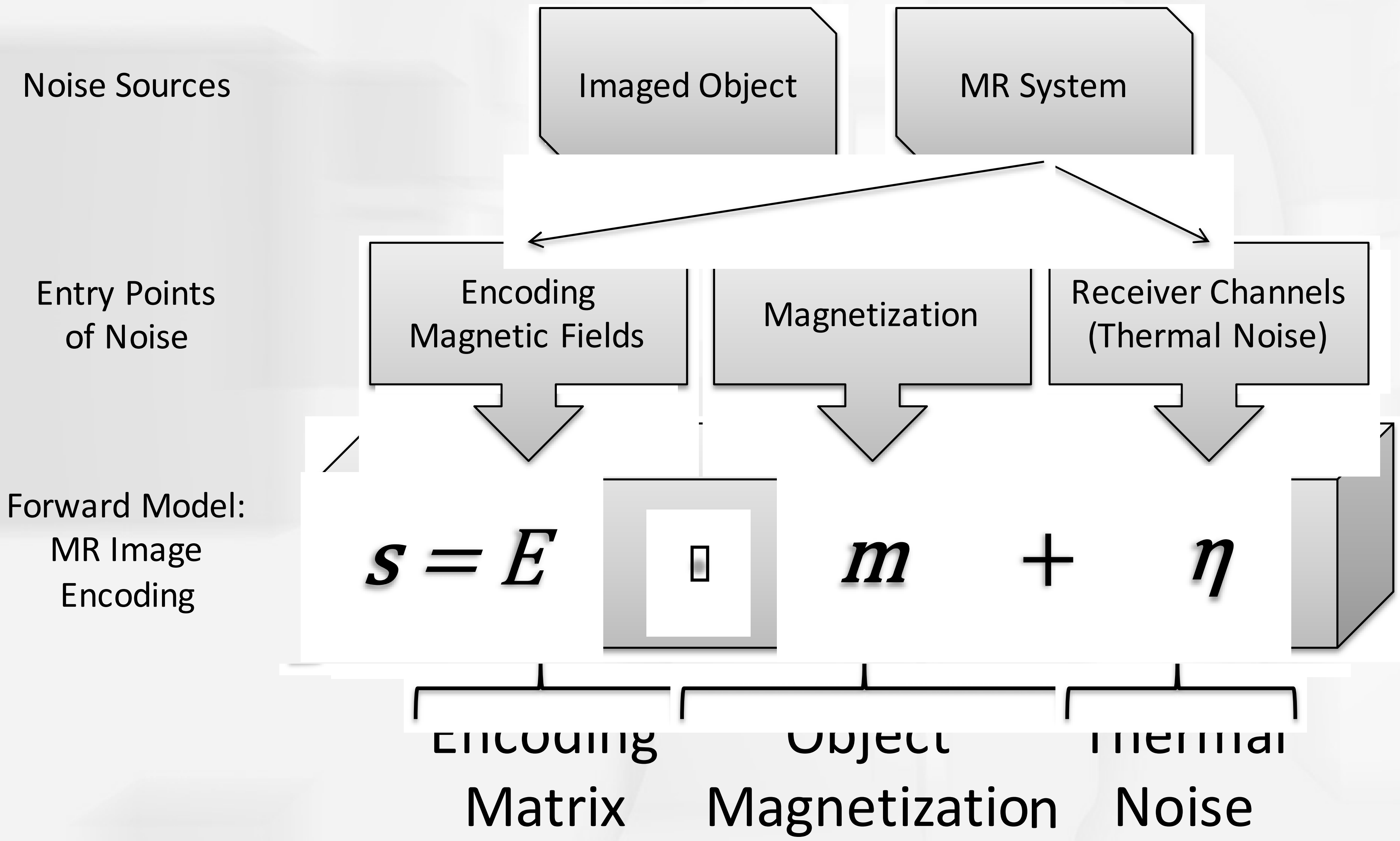


- Image reconstruction is also (often) a GLM, though a huge one, ~100.000 rows
- Any changes between encodings (images) in encoding matrix (field), object magnetization and thermally induces image noise

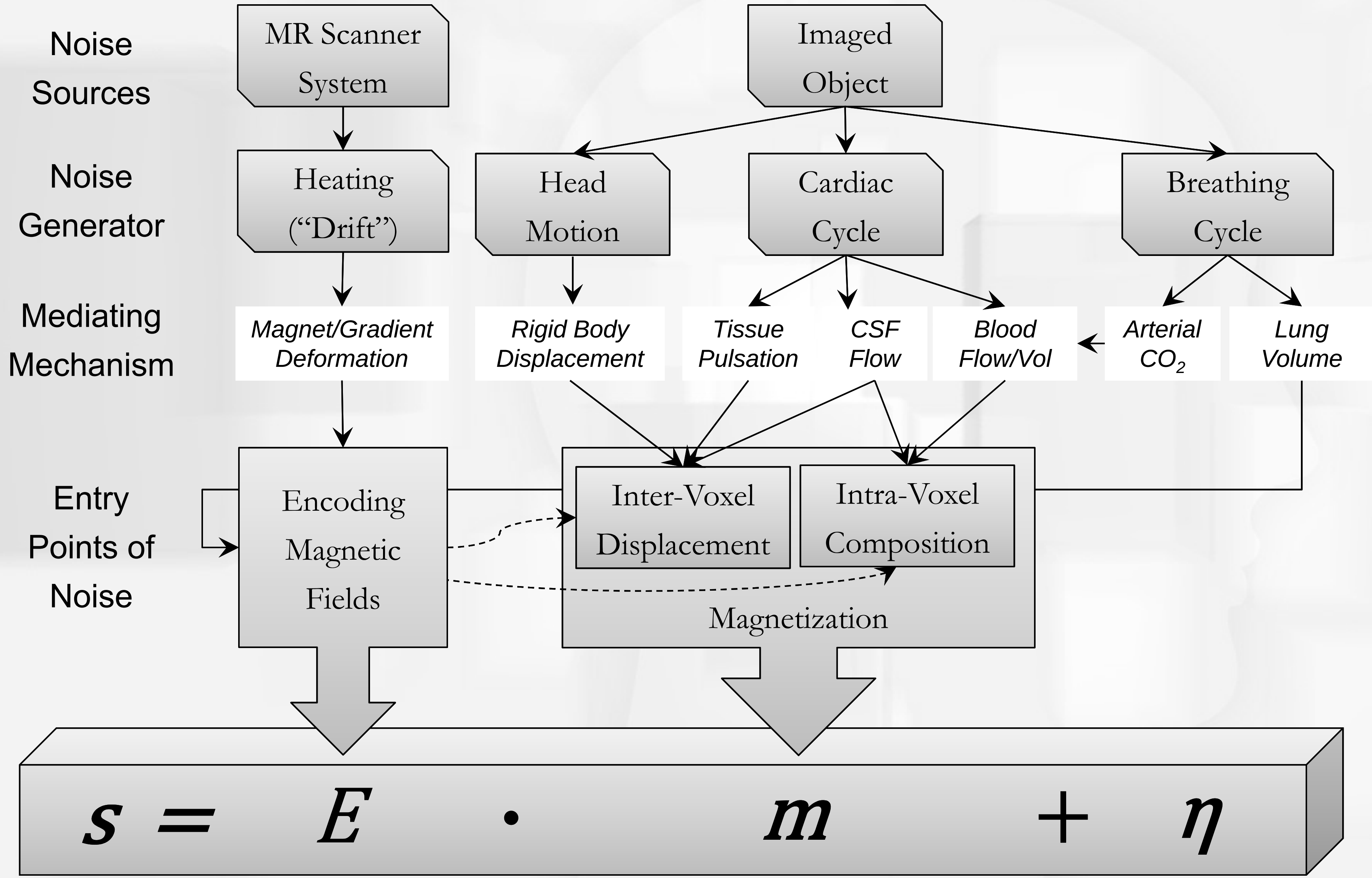
$$\hat{m} = \left(E^H E\right)^{-1} E^H s$$



What fluctuates?



Structured Noise in MRI



The Problem: Physiological Noise

- Cardiac effects
- Respiratory effects

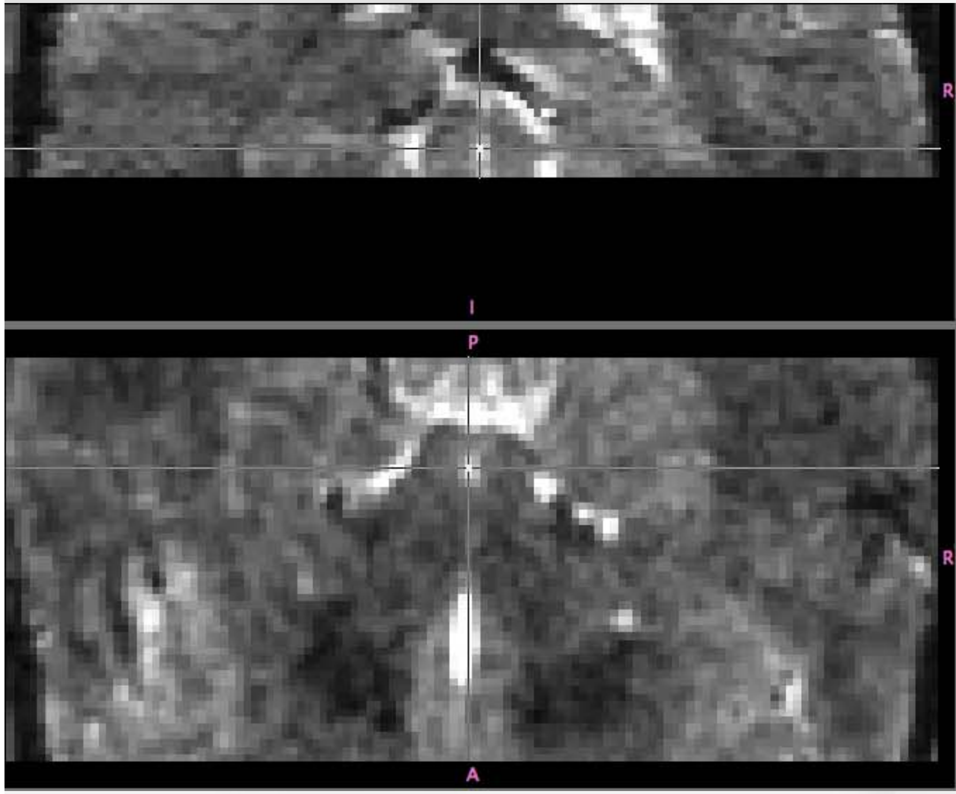
The Problem: Physiological Noise

- 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

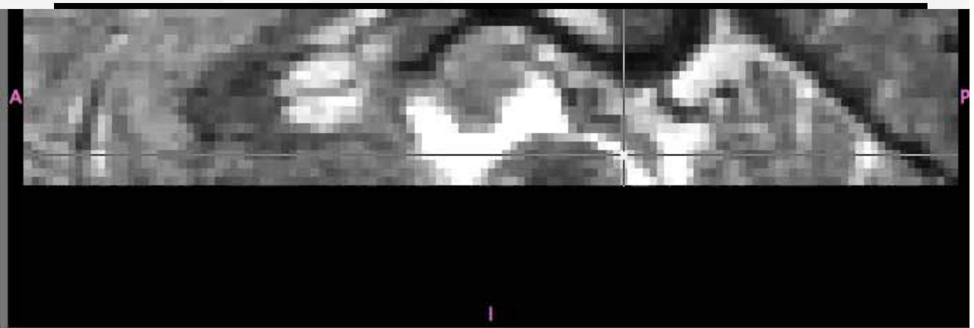
A Cardiac Cycle in the Brain

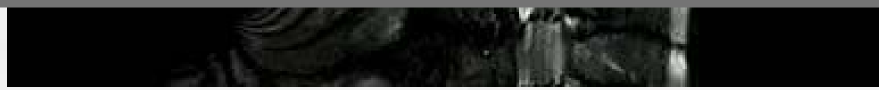
The Problem: Physiological Noise

Triggered High-Resolution fMRI



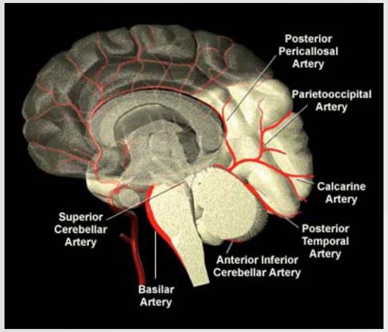
A Cardiac Cycle in the Brain

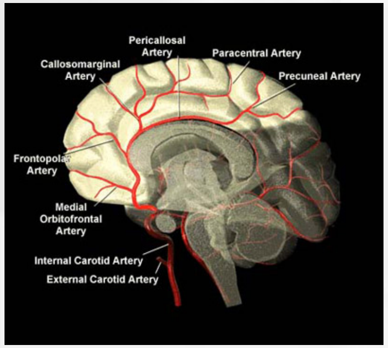


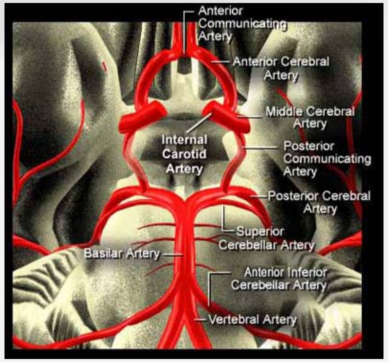


The Problem: Physiological Noise

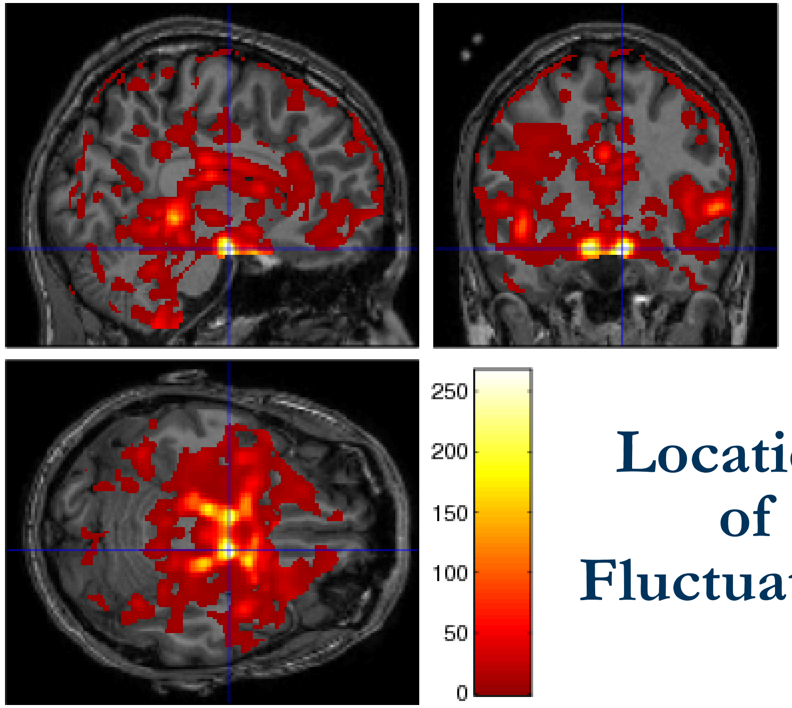
- Cardiac effects





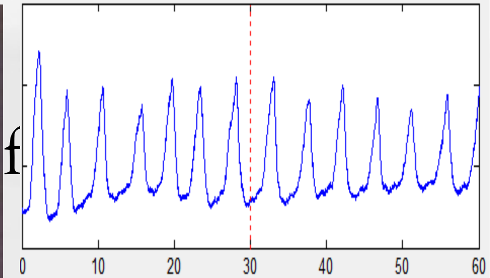


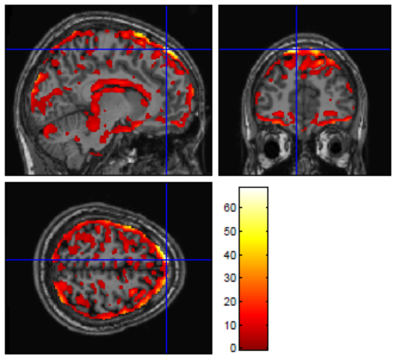
Vessel Anatomy

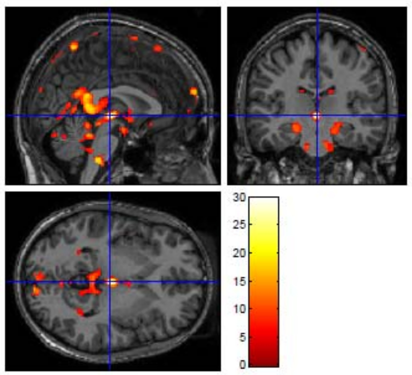


Locations of Fluctuations

The Problem: Physiological Noise





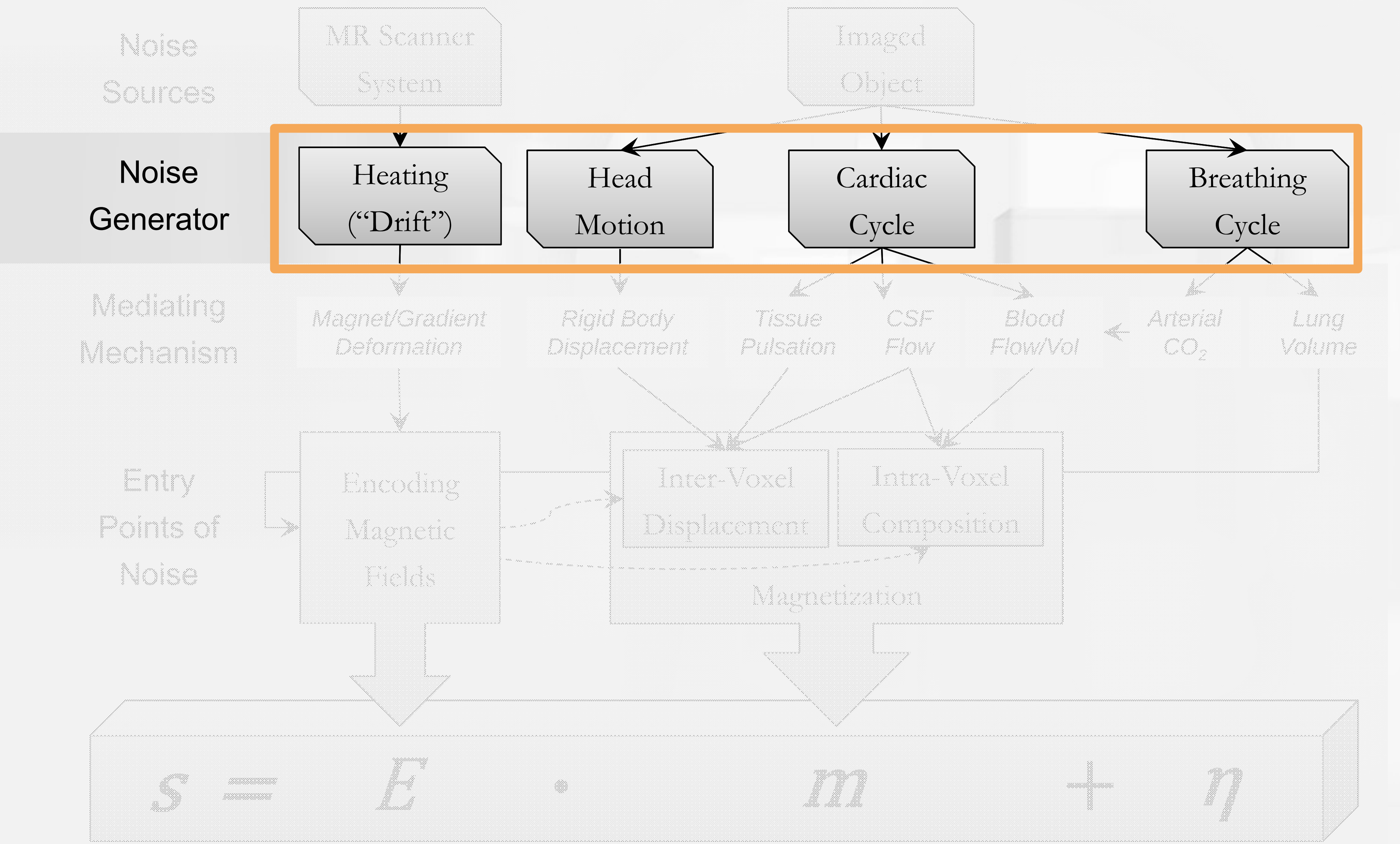


- Respiratory effects
  - Chest (&head) moves with respiratory cycle
  - Changes in lung volume change encoding magnetic field for MR
    - Geometric distortion/scaling
  - Respiratory-sinus arrythmia
    - Heart beats faster during inhalation

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

Noise Correction Targets



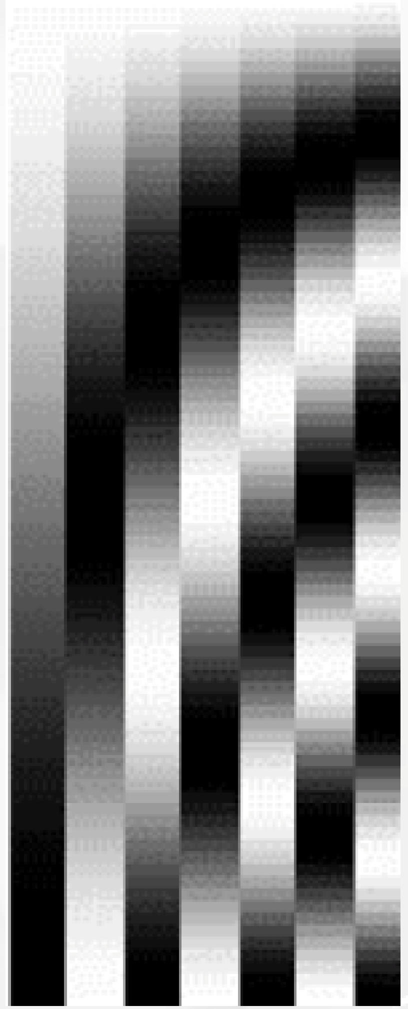
Drifts: High-Pass Filtering

- 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

$$K = 1 - X_0\left(X_0^T X_0\right)^{-1} X_0^T$$

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

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



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 it 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

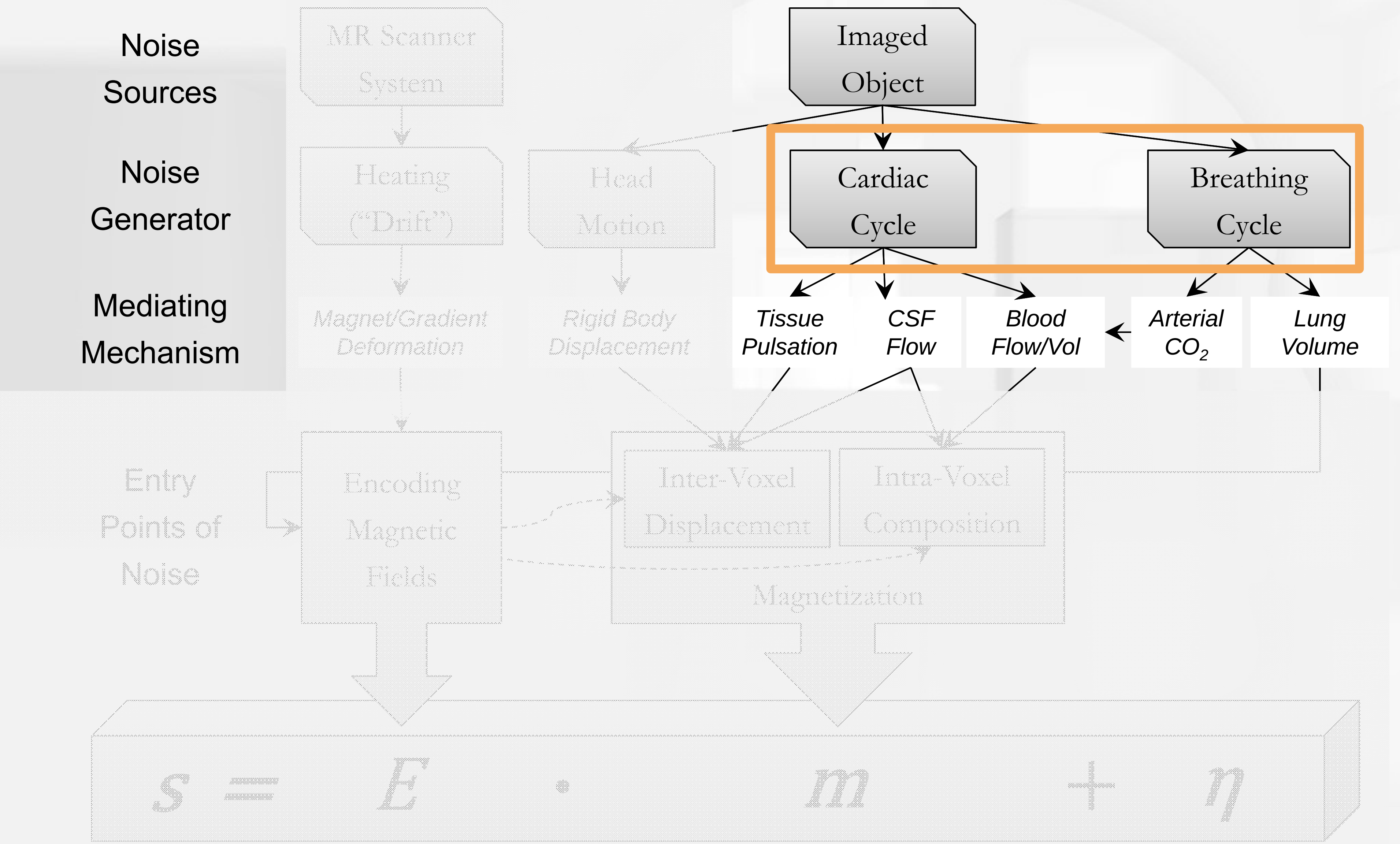
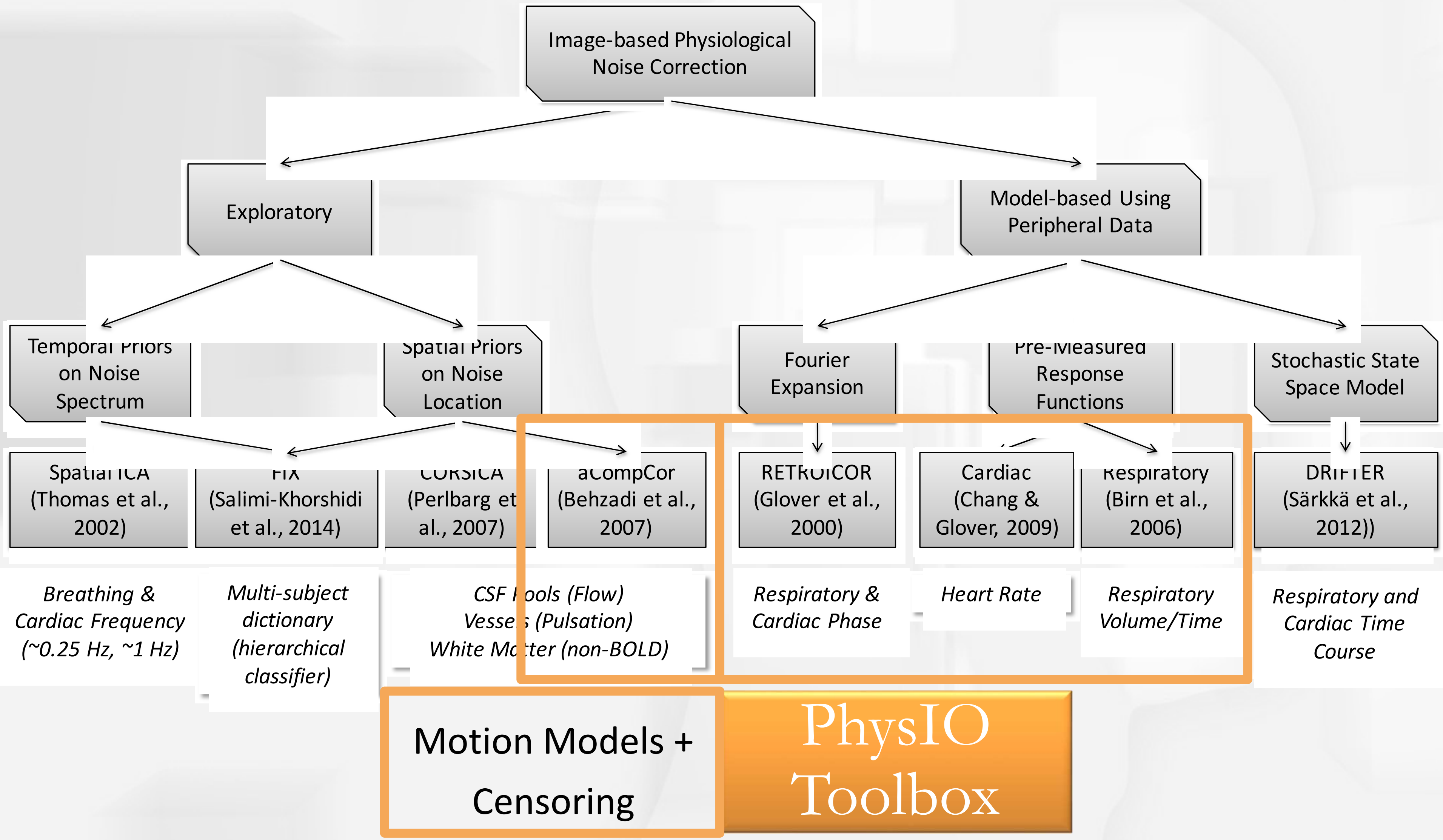
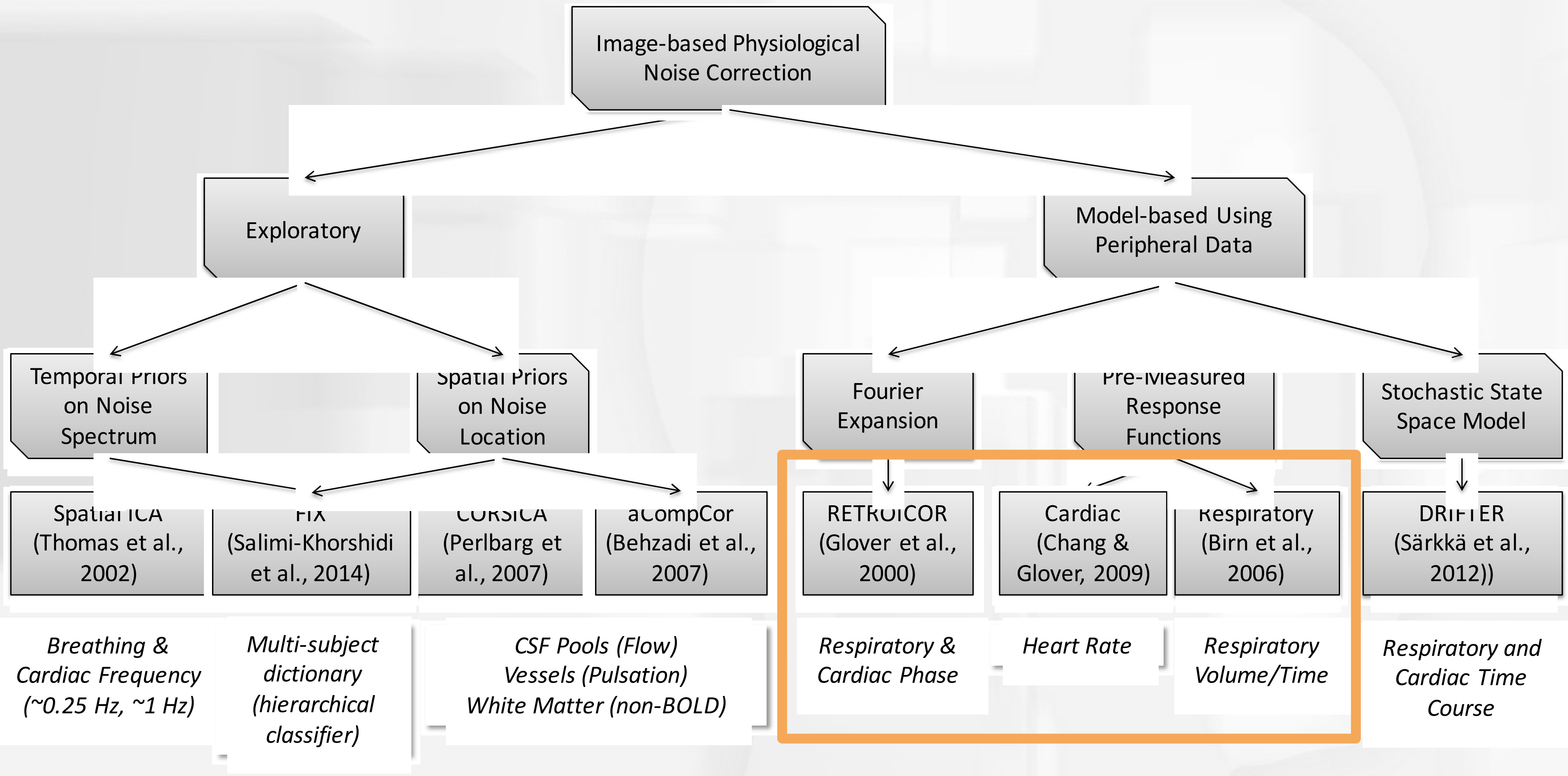


Image-based Noise Correction



Model-based Phys Noise Correction



Noise Modeling

RETROspective Image CORrection	Cardiac Response Function	Respiratory Response Function
▪ Cardiac/respiratory phase φ_c φ_r	▪ Heart Rate	▪ Resp. Volume per Time
▪ Fourier expansion (cosine/sine)	▪ convolved with CRF	▪ convolved with RRF

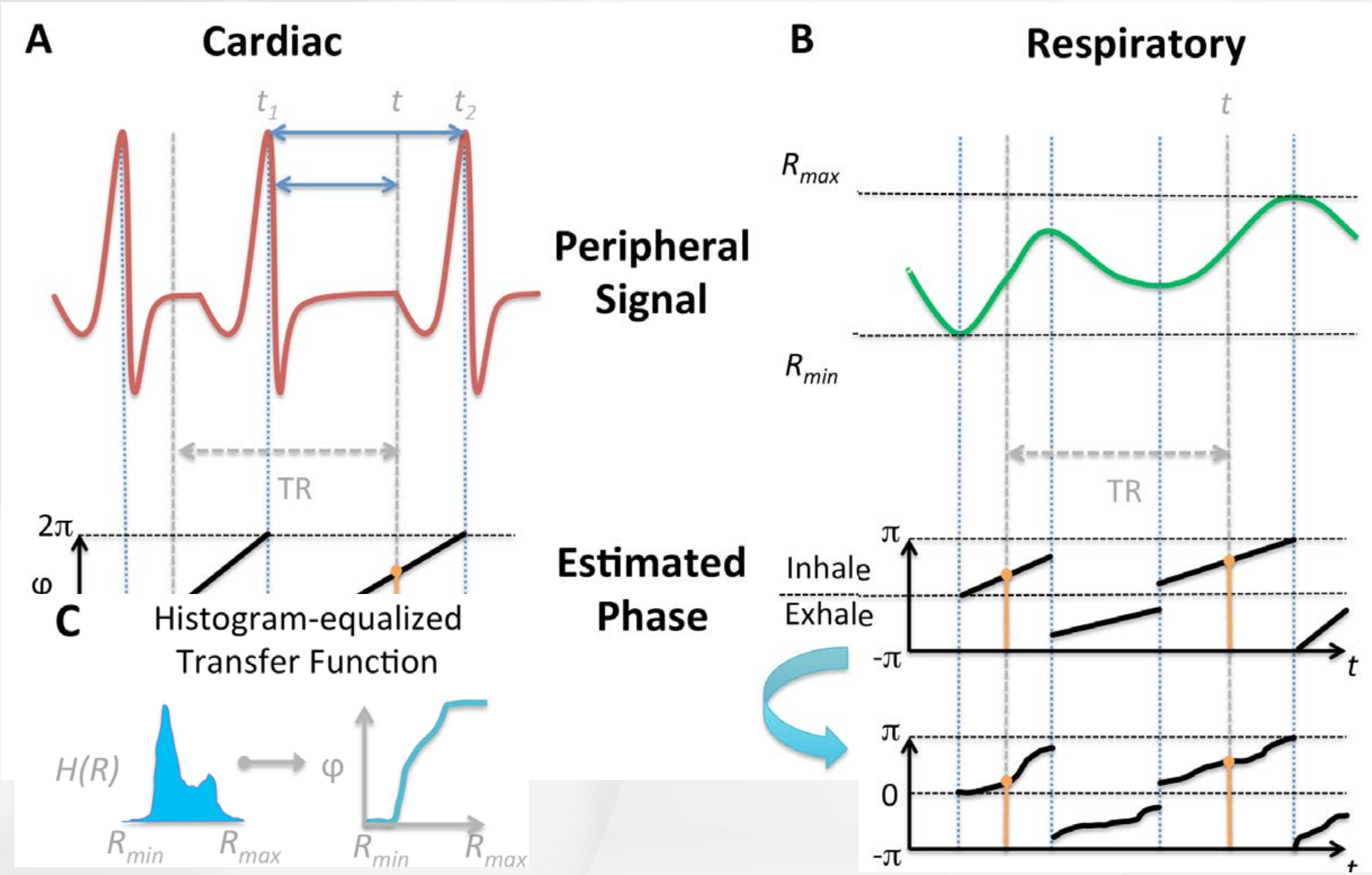
- evaluated at 1 time point (slice) per volume = regressor

Noise Modeling

RETROspective Image CORrection

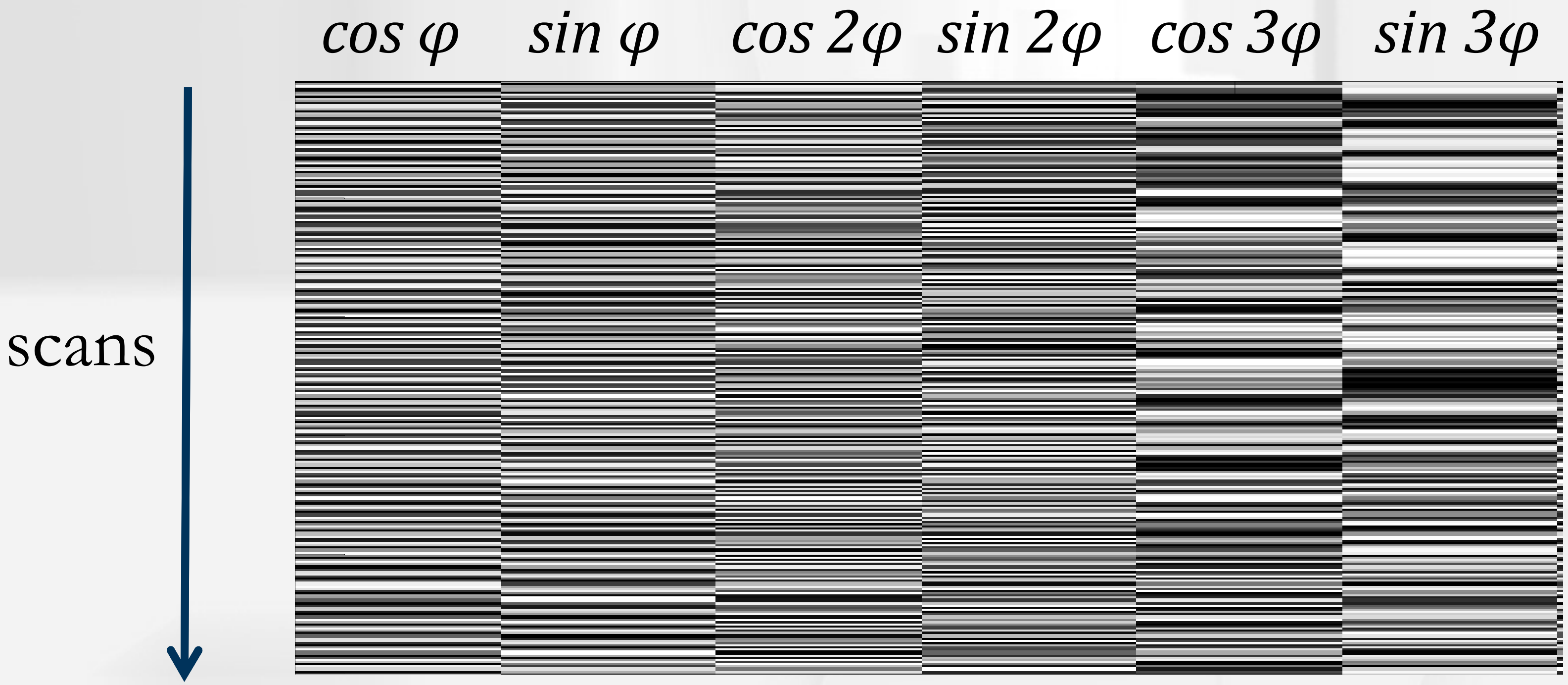
- Cardiac/respiratory phase

φ_c φ_r

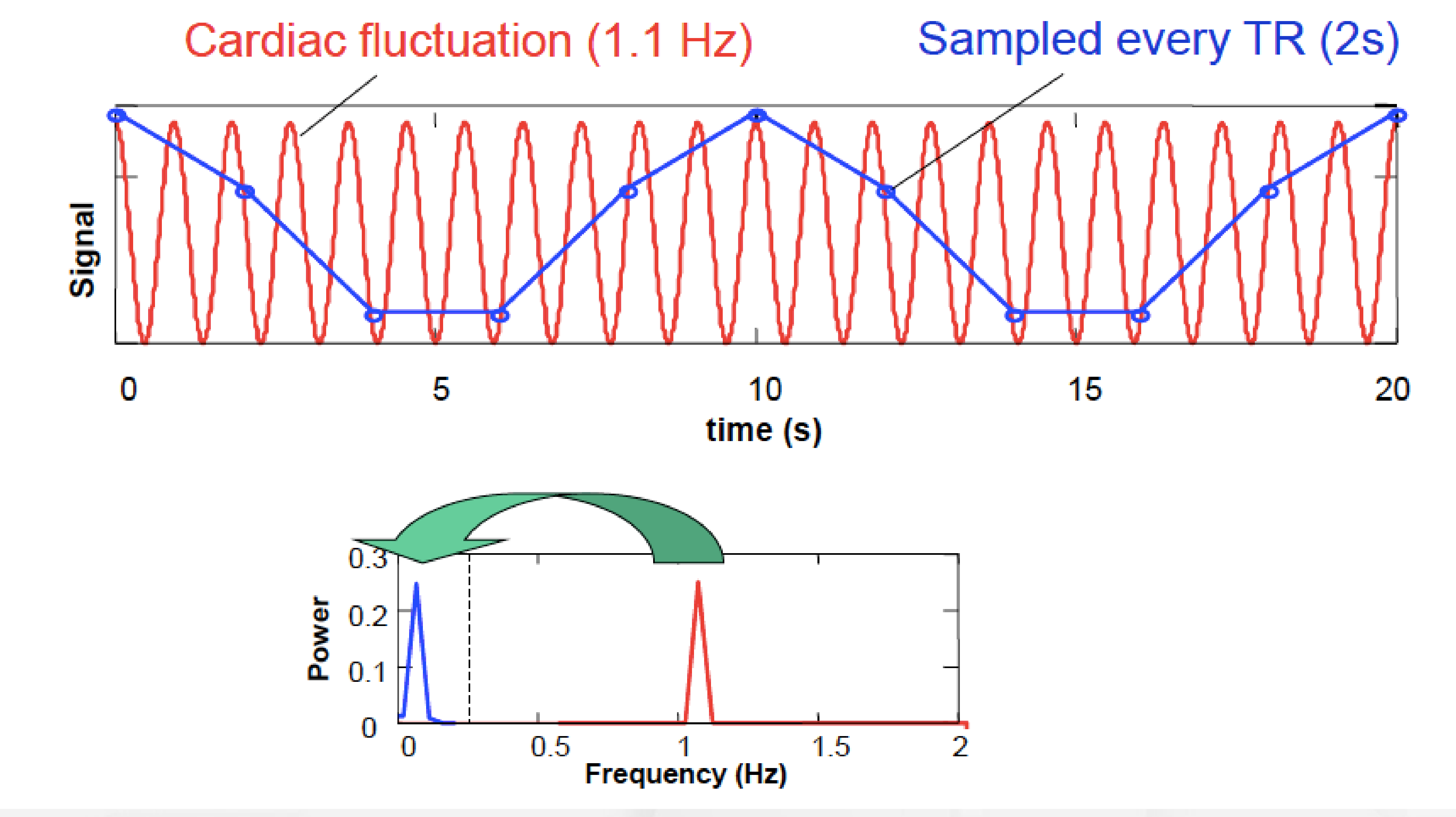


Model: Fourier Phase Expansion

- 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

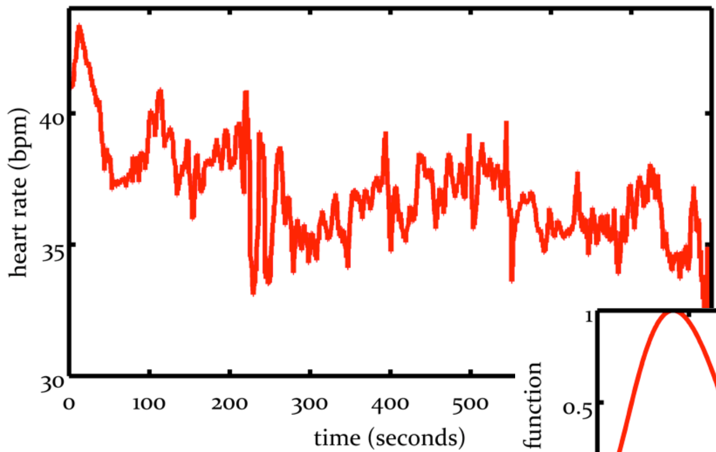


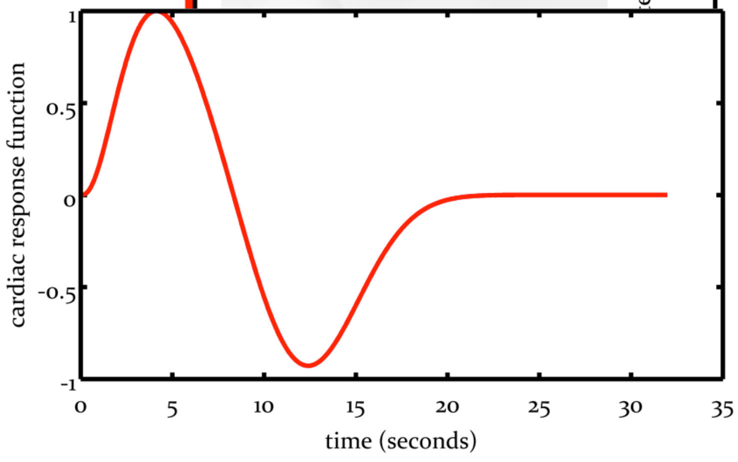
Courtesy: R. Birn, HBM 2015

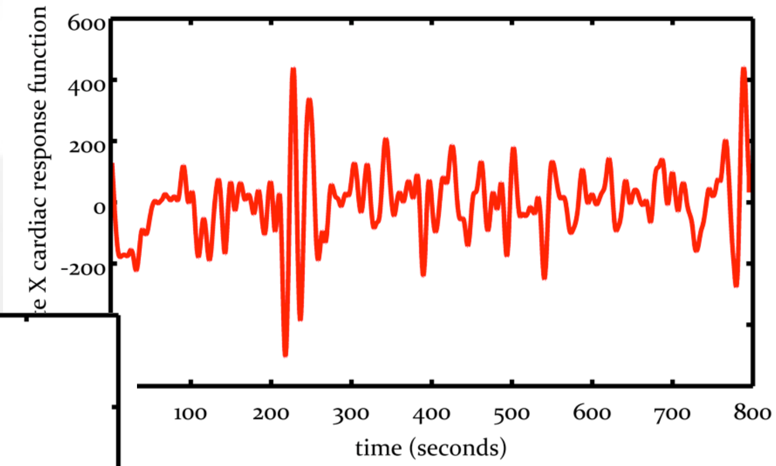
Noise Modeling

RETROspective Image CORrection | **Cardiac Response Function** | Respiratory Response Function

- Heart Rate
- convolved with CRF
- Heart Rate Variability Response Regressor



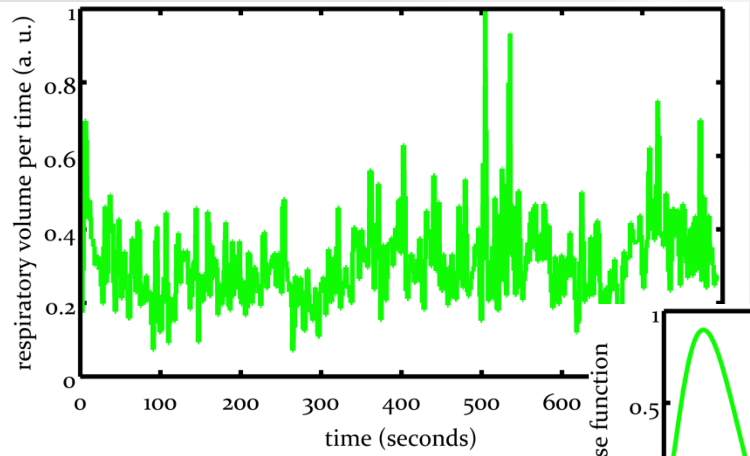


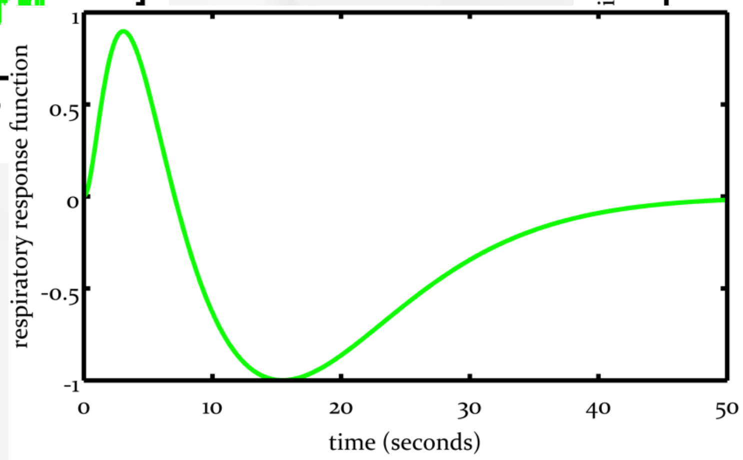


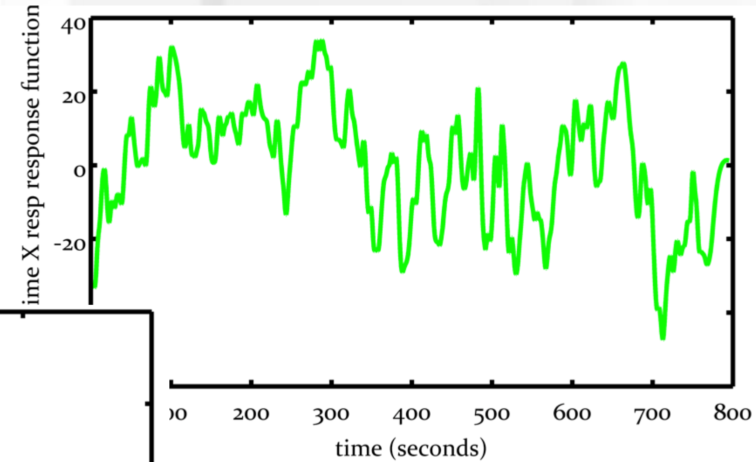
Noise Modeling

RETROspective Image CORrection | Cardiac Response Function | **Respiratory Response Function**

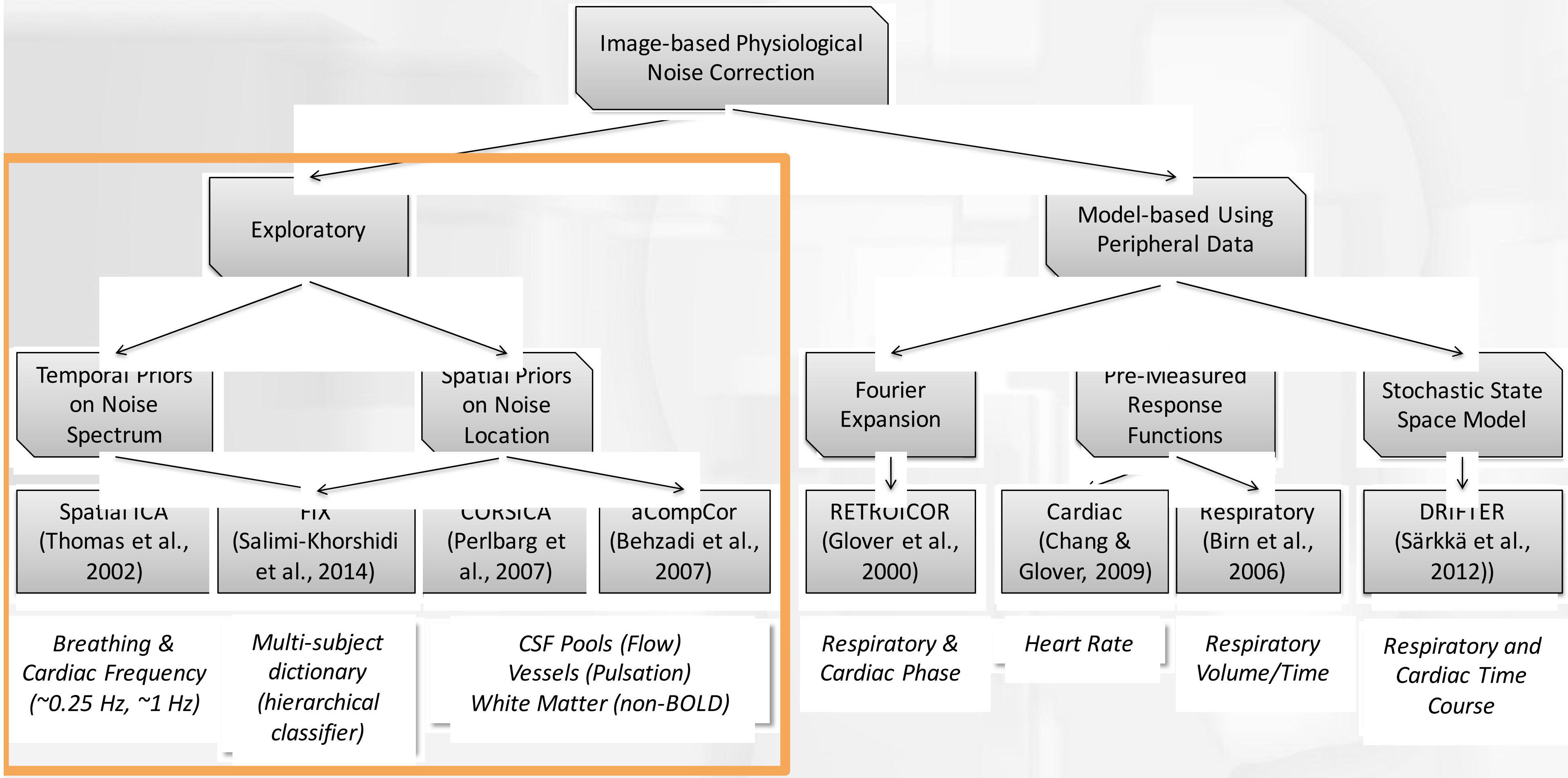
- Respiratory Volume per Time
- convolved with RRF
- Respiratory Volume per Time Regressor







Exploratory Phys Noise Correction



Noise Component Modeling

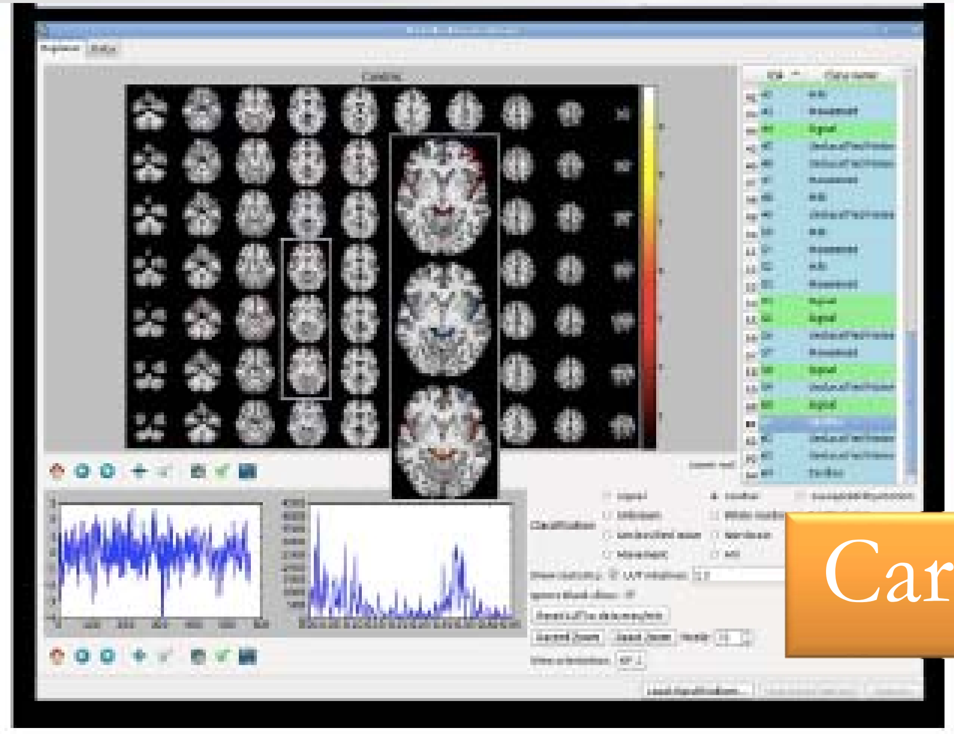
- Use priors about physiological noise to identify noise components (time series)
  - Spatial Priors: Mechanisms of physiological noise implicate physiological noise in CSF, blood vessels
  - Temporal Priors: Knowledge about typical physiological frequency contents (heart ~ 1Hz, breathing 0.2-0.4 Hz)
    - Note that simple filtering is impossible (cf. aliasing)
  - Population Priors: Use dictionary learning from manually labellled 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

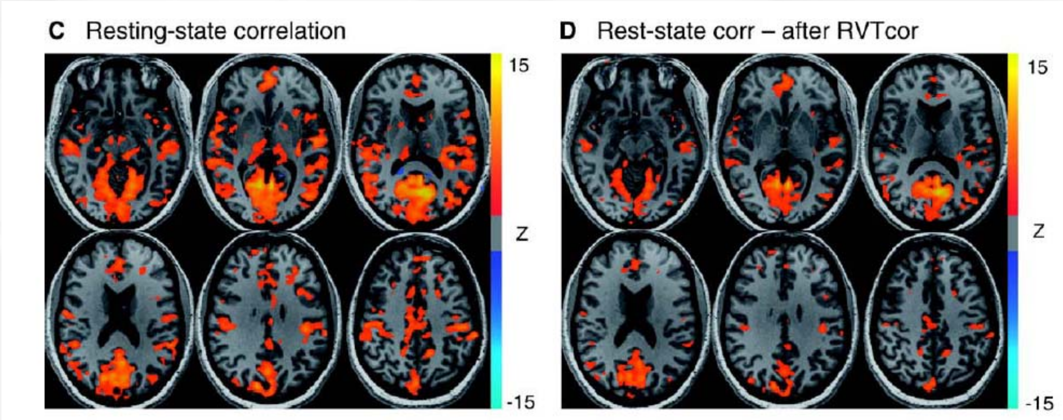
Olafsson, NeuroImage, 2015

Outline – Noise Correction

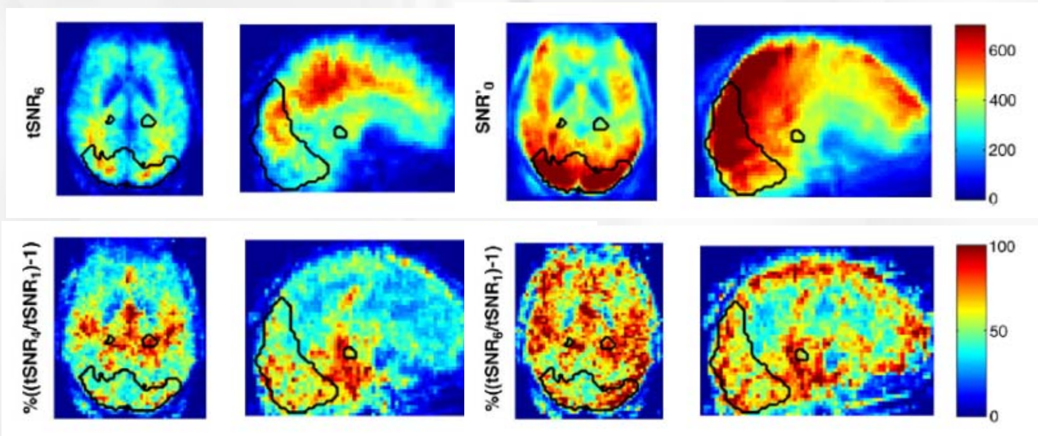
- MRI Time Series Recap and Noise Sources
  - Why de-noising? Structured Noise; Noise Pathways
- Noise Correction Approaches
  - Target: Scanner Drift, Motion, Cardiac/Breathing Cycle
  - Method: Modeling VS Preprocessing
  - Input: fMRI Data VS Peripheral Measures
- **Prospects for Improving Group Statistics**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

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:

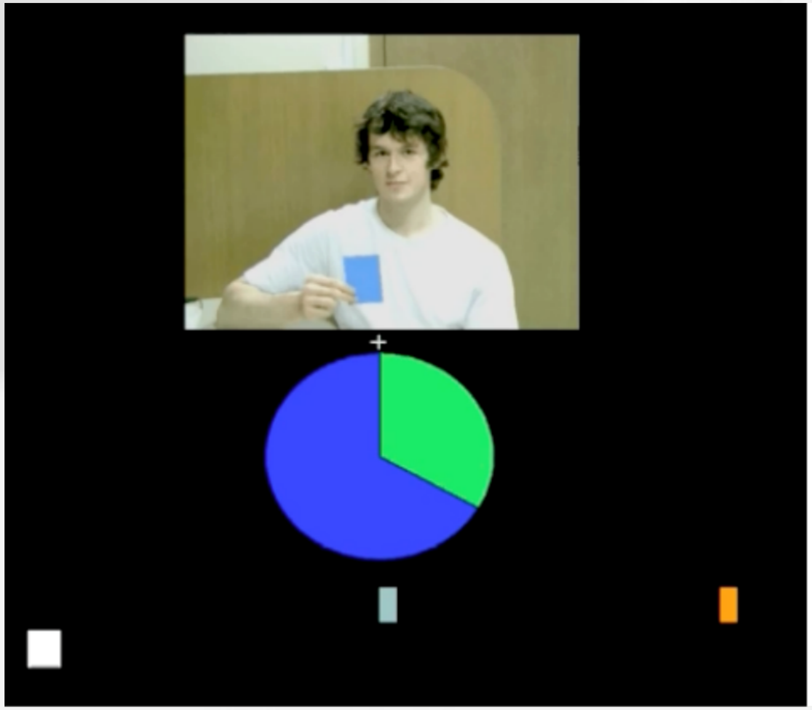


All these methods, but…

- 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 trustworthyness 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)

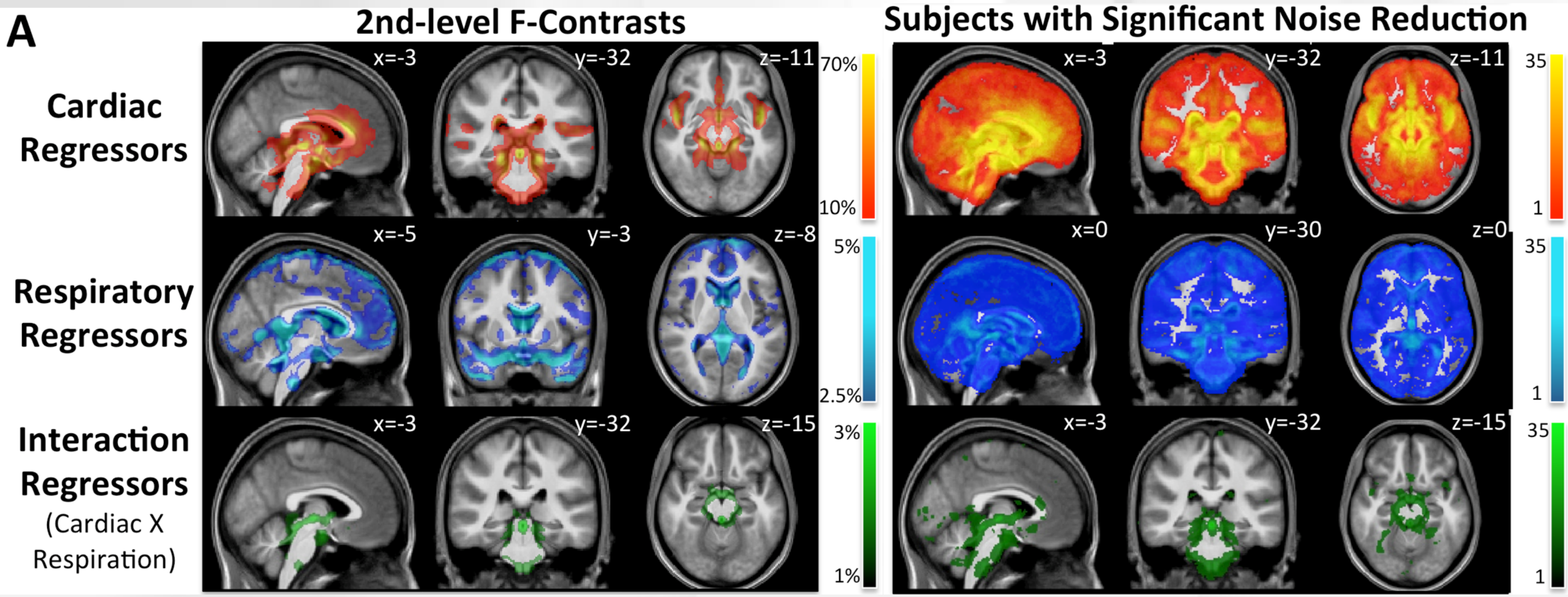
interactive, gender-matched (**40** male subjects)

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

Diaconescu et al, 2014, PLoS Comp. Biol.

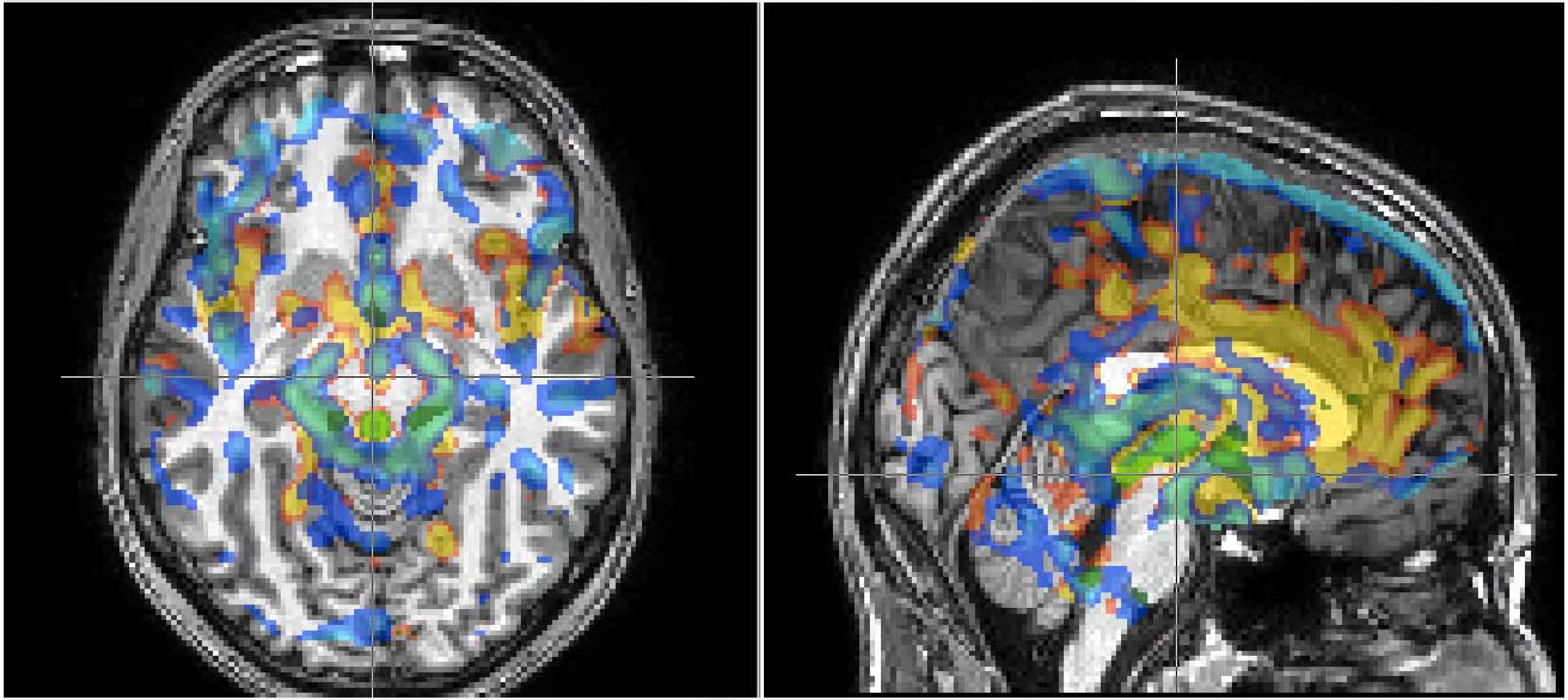
Group Level Impact PhysIO

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



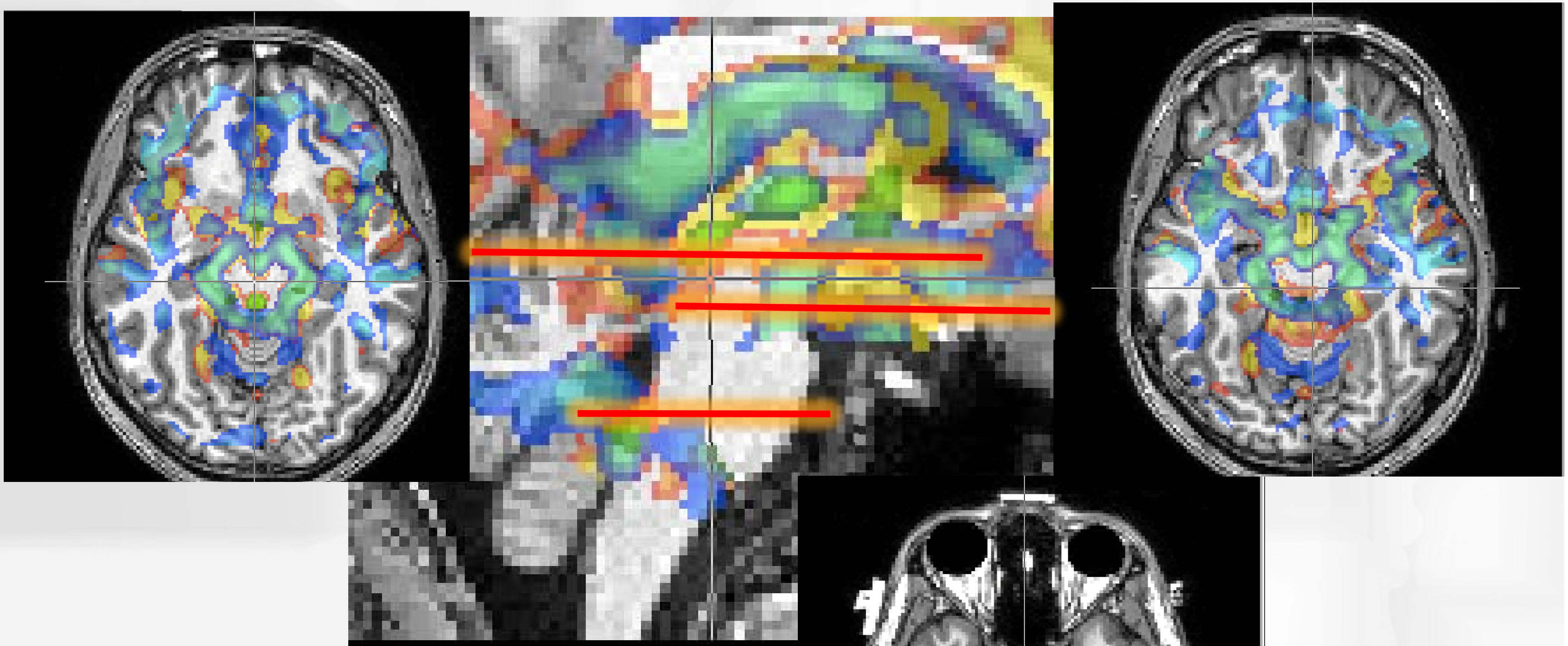
Relevance for Neuromodulation

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

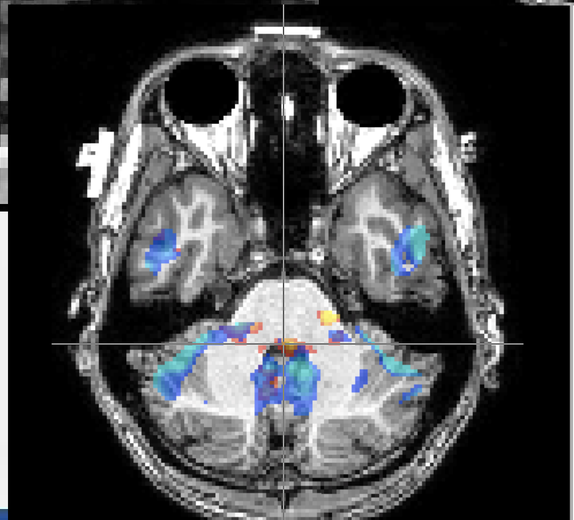


Relevance for Neuromodulation

- VTA (DA)
- Raphe Nuclei (5-HT)

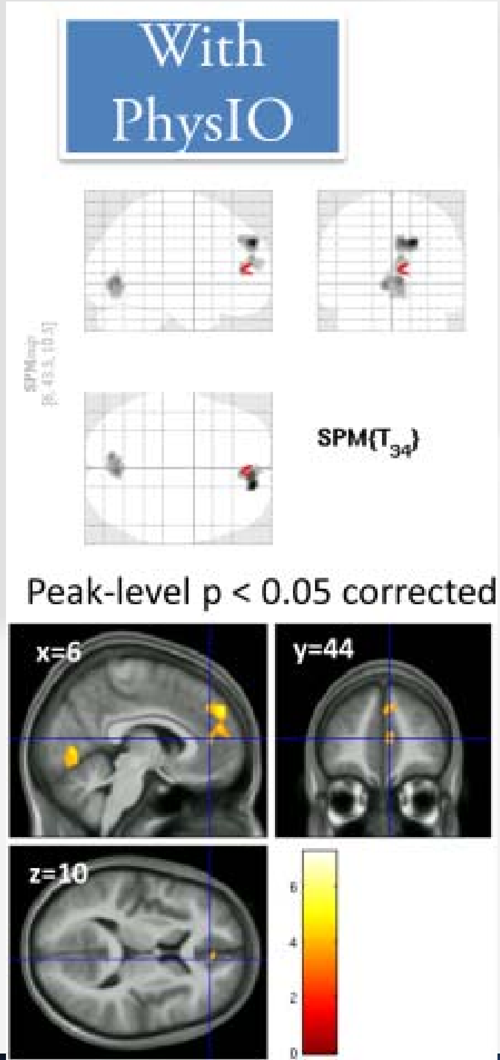


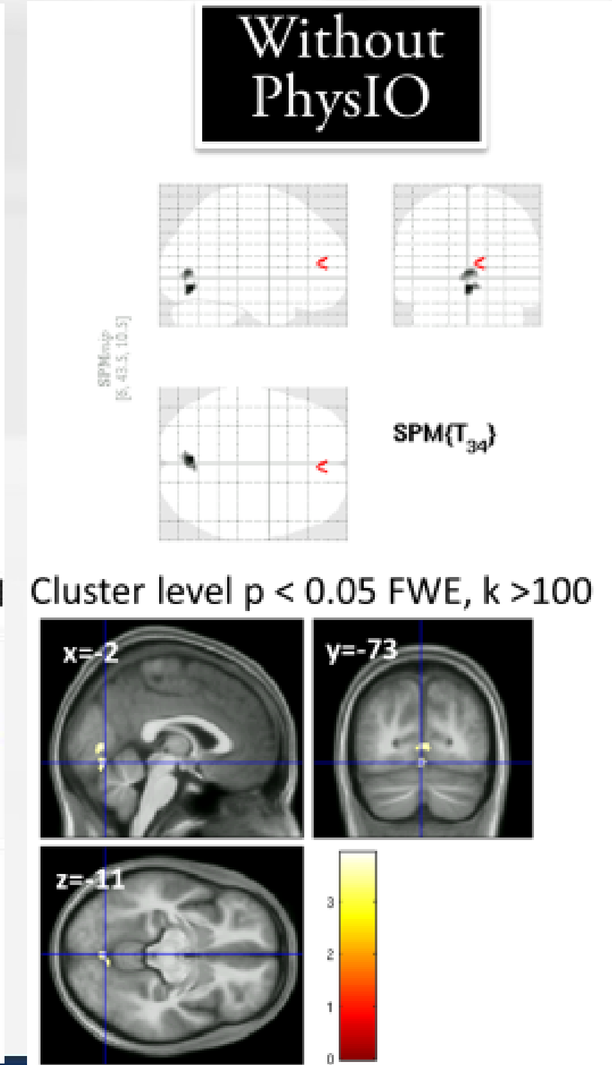
- Locus coeruleus (NA)



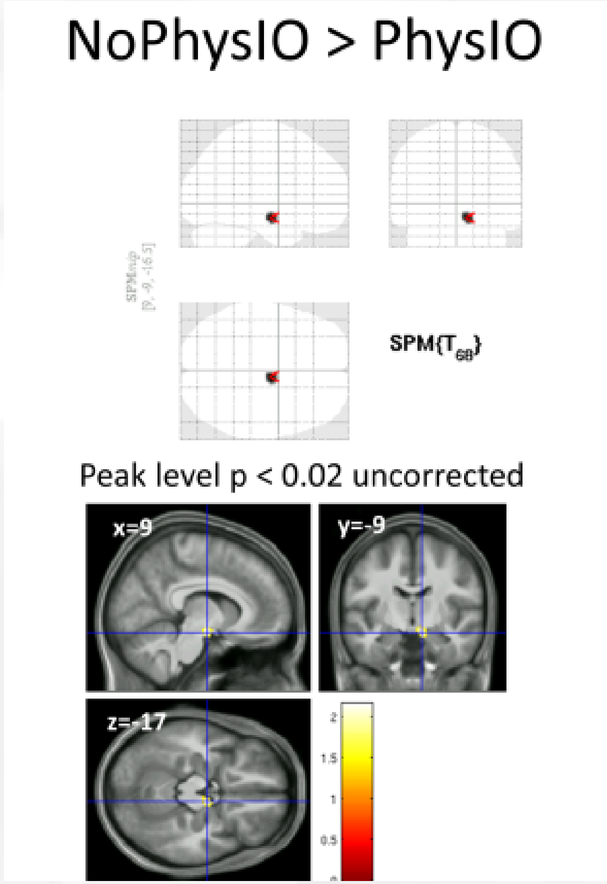
Effects on Group Contrasts

Higher Sensitivity





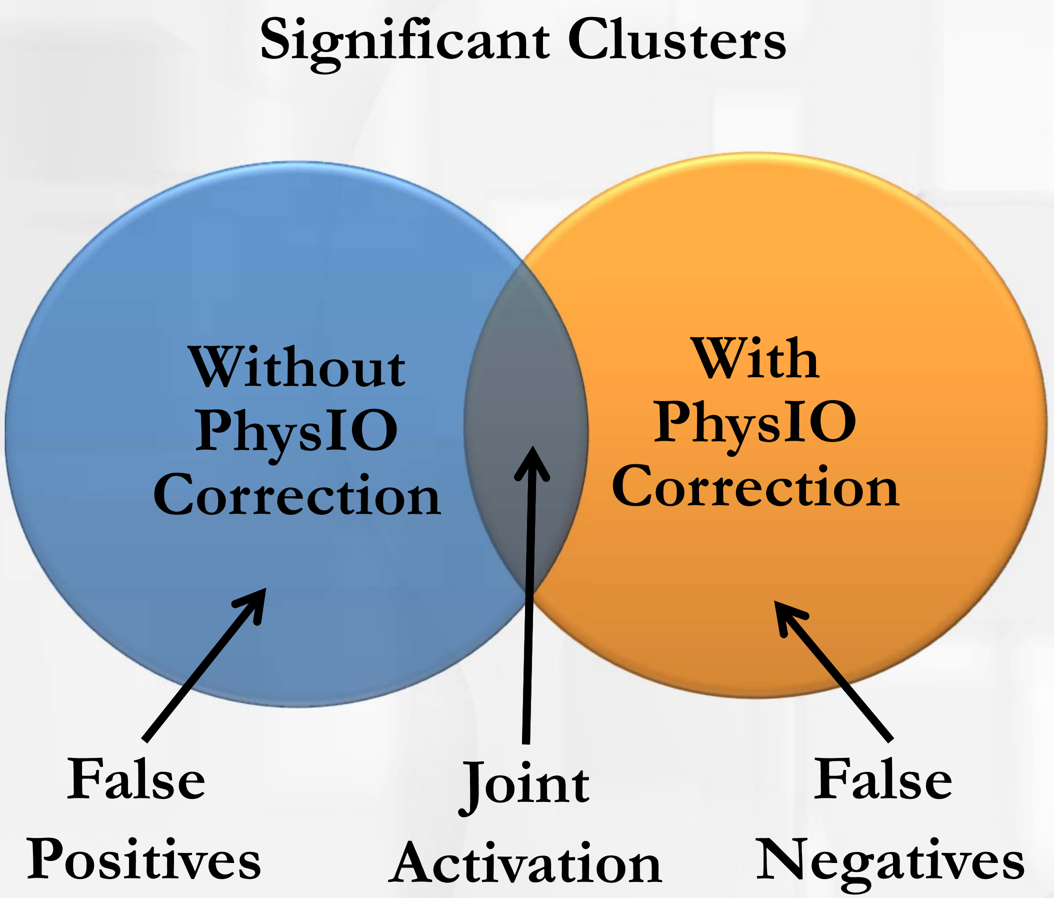
False Positives



2nd level t-contrast

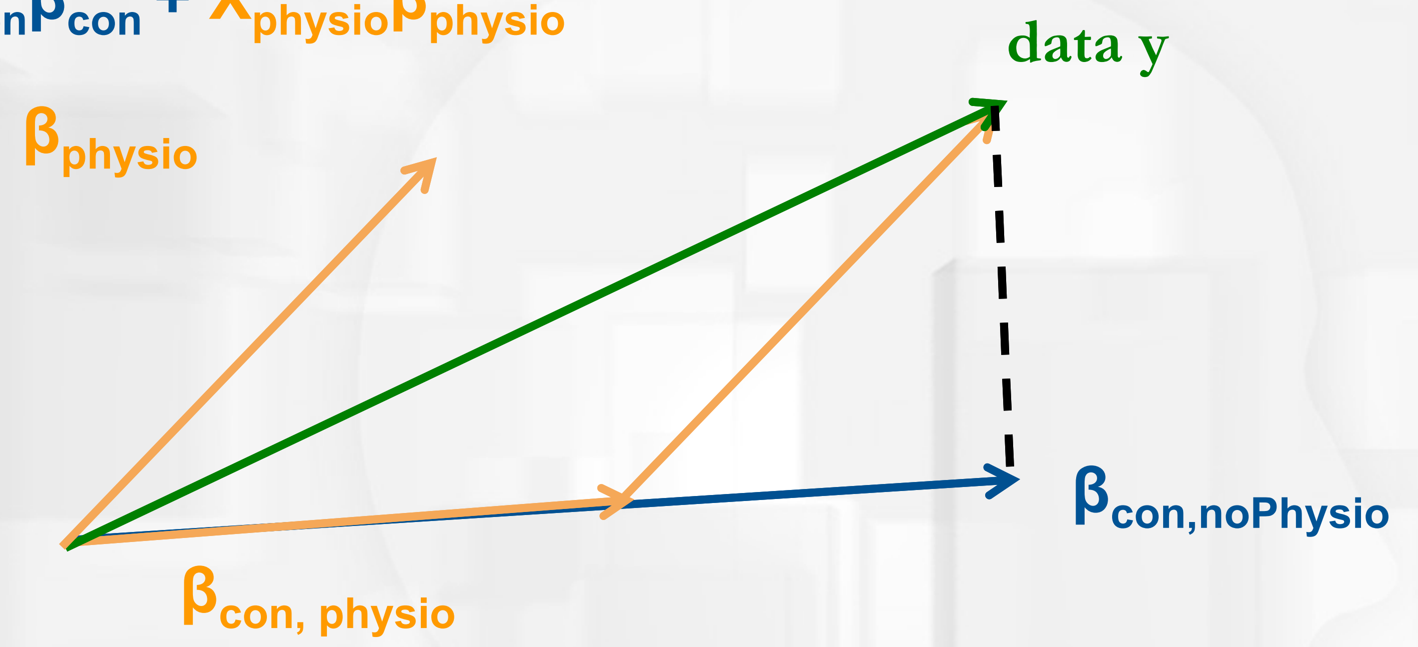
Social Prediction Error

Venn-Diagramme Cluster Analysis



Noise modeling impact on task?

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



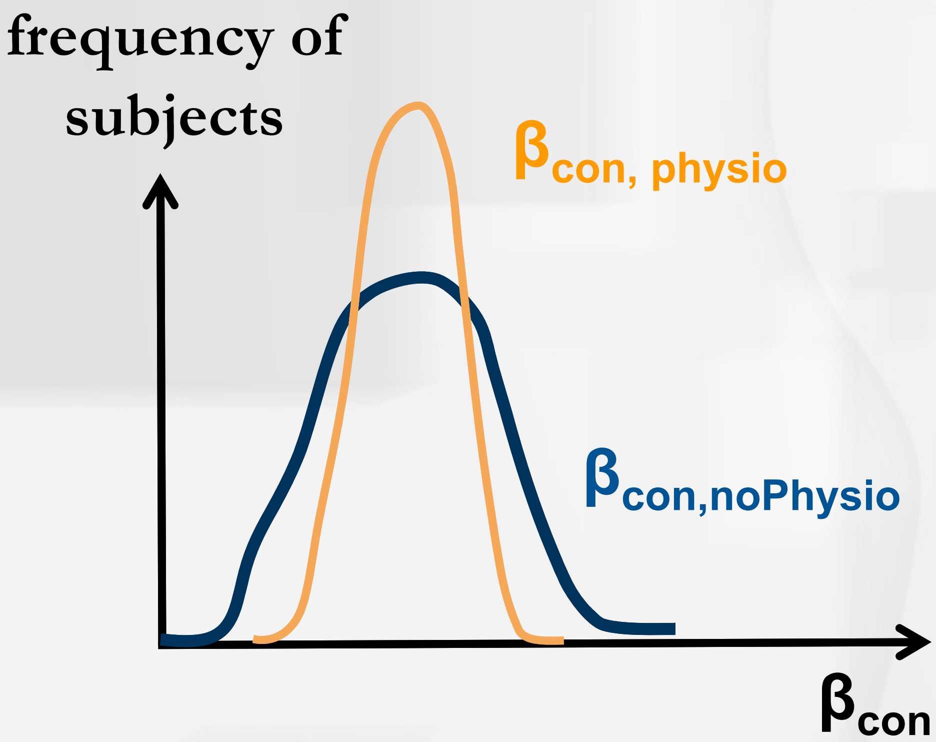
⇒ $\beta_{con, physio} < \beta_{con,noPhysio}$

- Phys noise correction can change parameter estimates for regressors of interest (correlation!)
- Thereby change distribution of β ⇒ Mean? Variance?

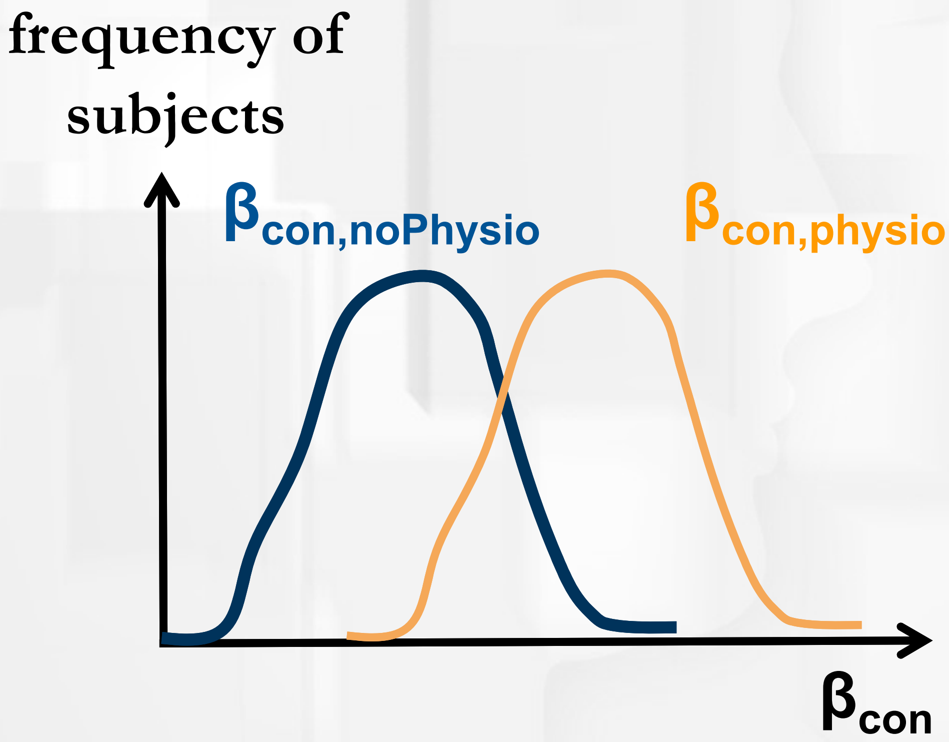
Group Effect: Correlated Regressors

- Two mechanisms imaginable

Reduced inter-subject variance

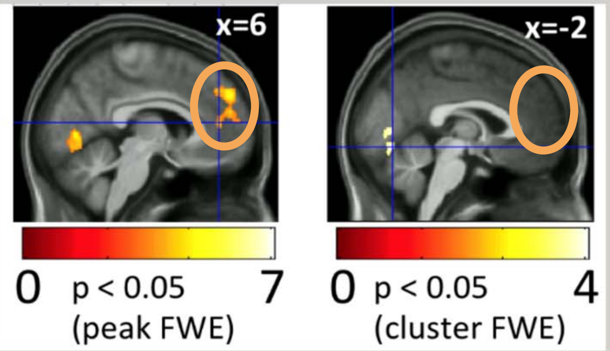


Increased inter-subject mean estimates

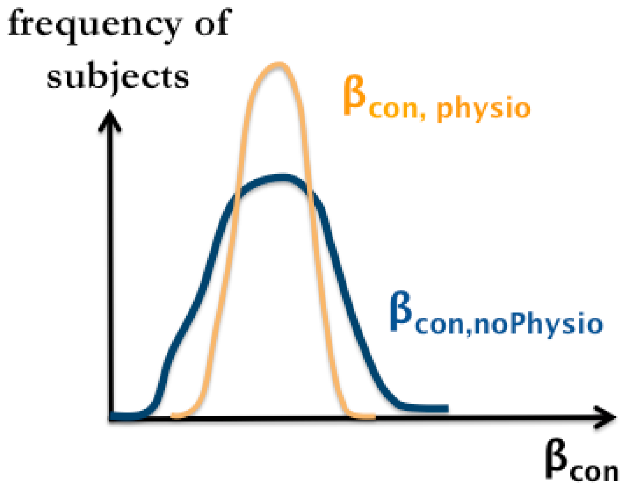


The Corrective Mechanism

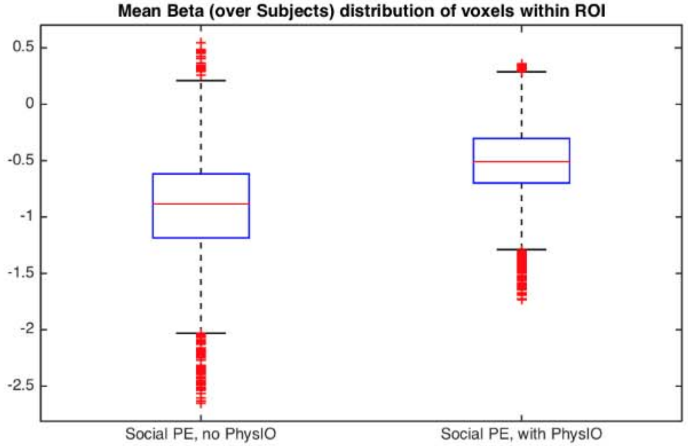
Social Pred. Error

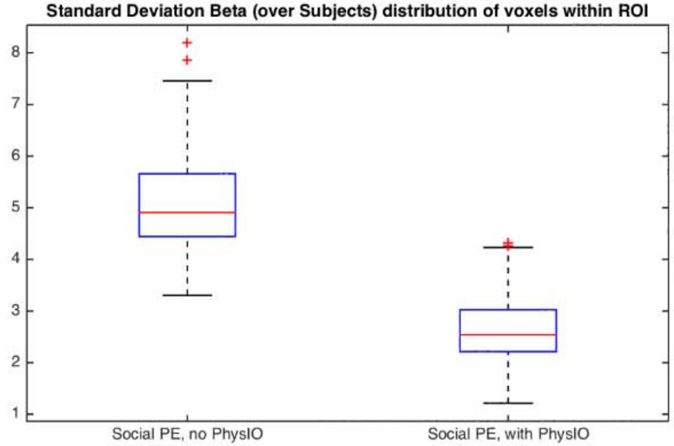


Reduced inter-subject variance



Mean





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)

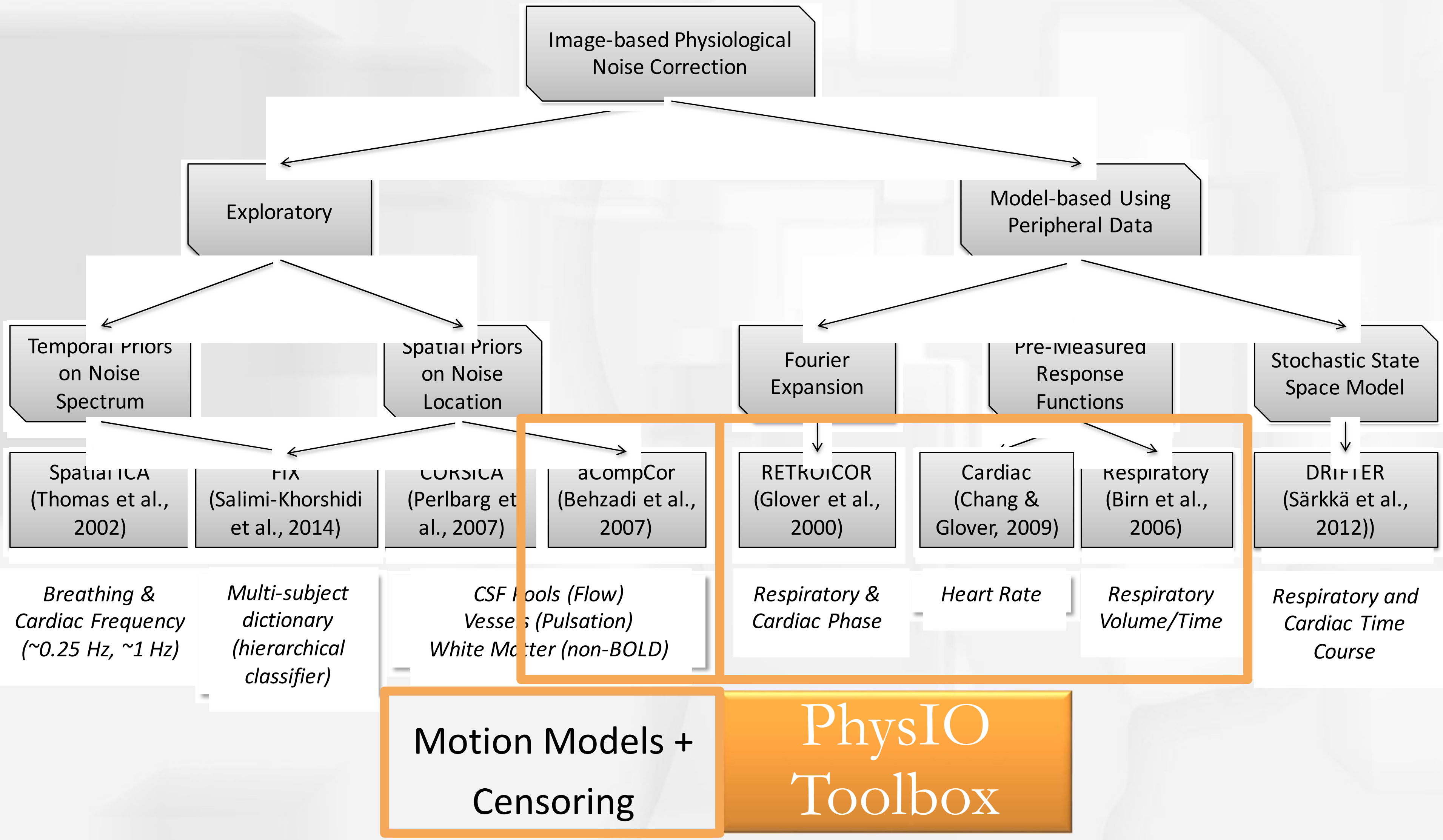
Conclusion

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

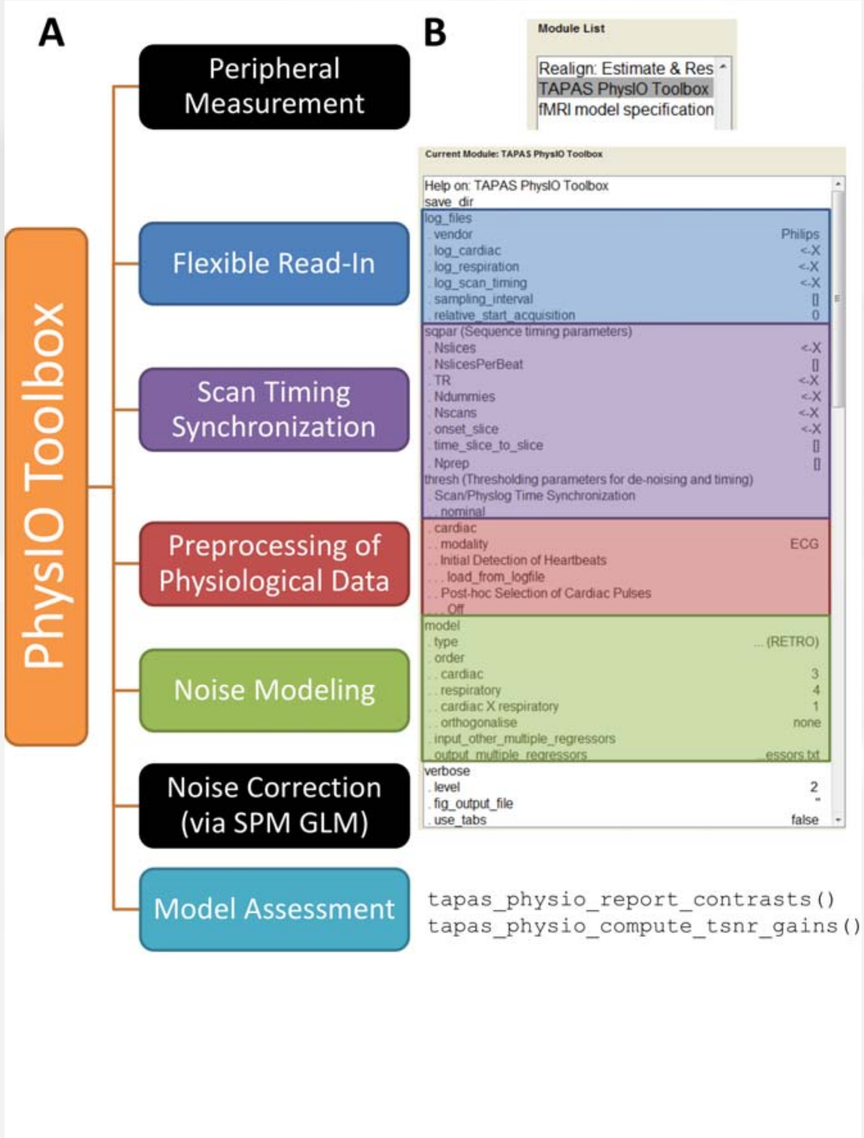
Image-based Noise Correction



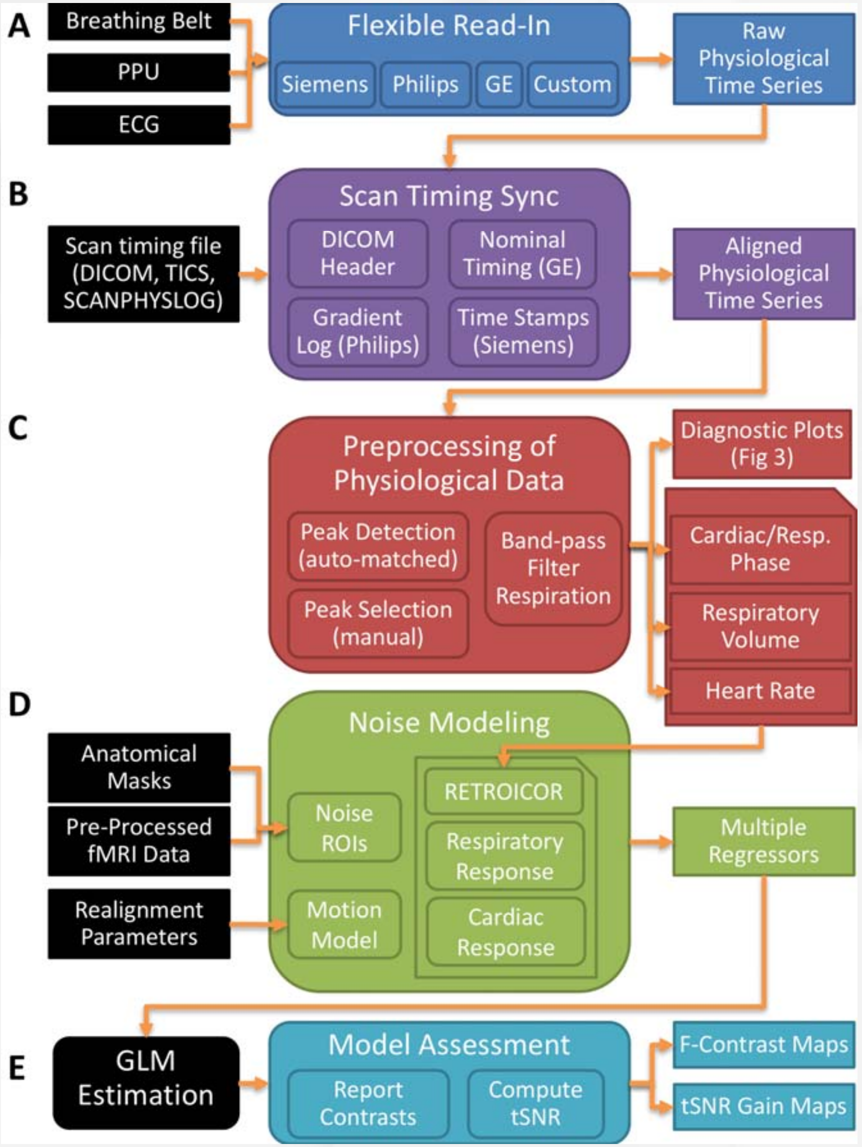
The PhysIO Toolbox

- Developed at the Translational Neuromodeling Unit (TNU) since 2008
  - Lead programmer: Lars Kasper (TNU)
  - Contributors: Jakob Heinzle (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, PhDThesis; 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

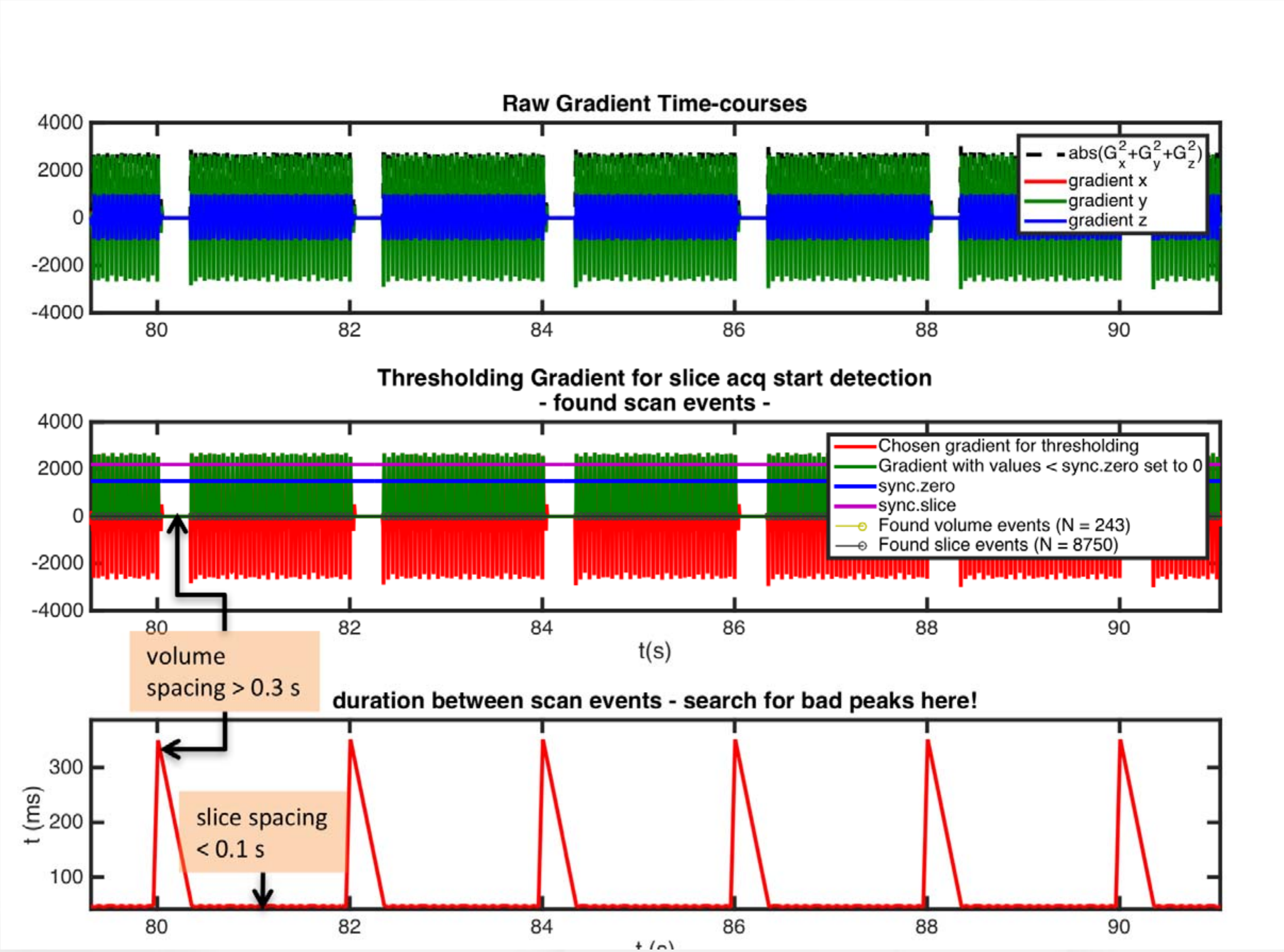
Workflow of the PhysIO Toolbox



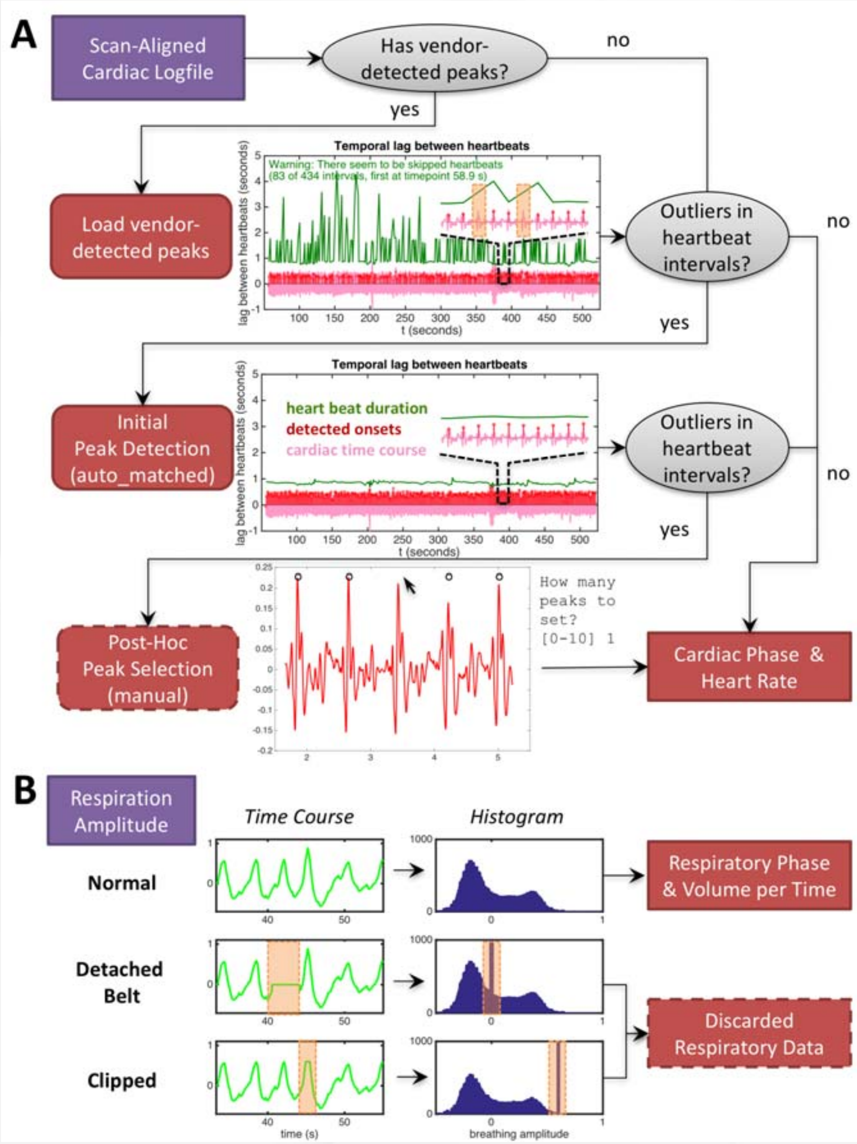
Flowchart of Noise Correction



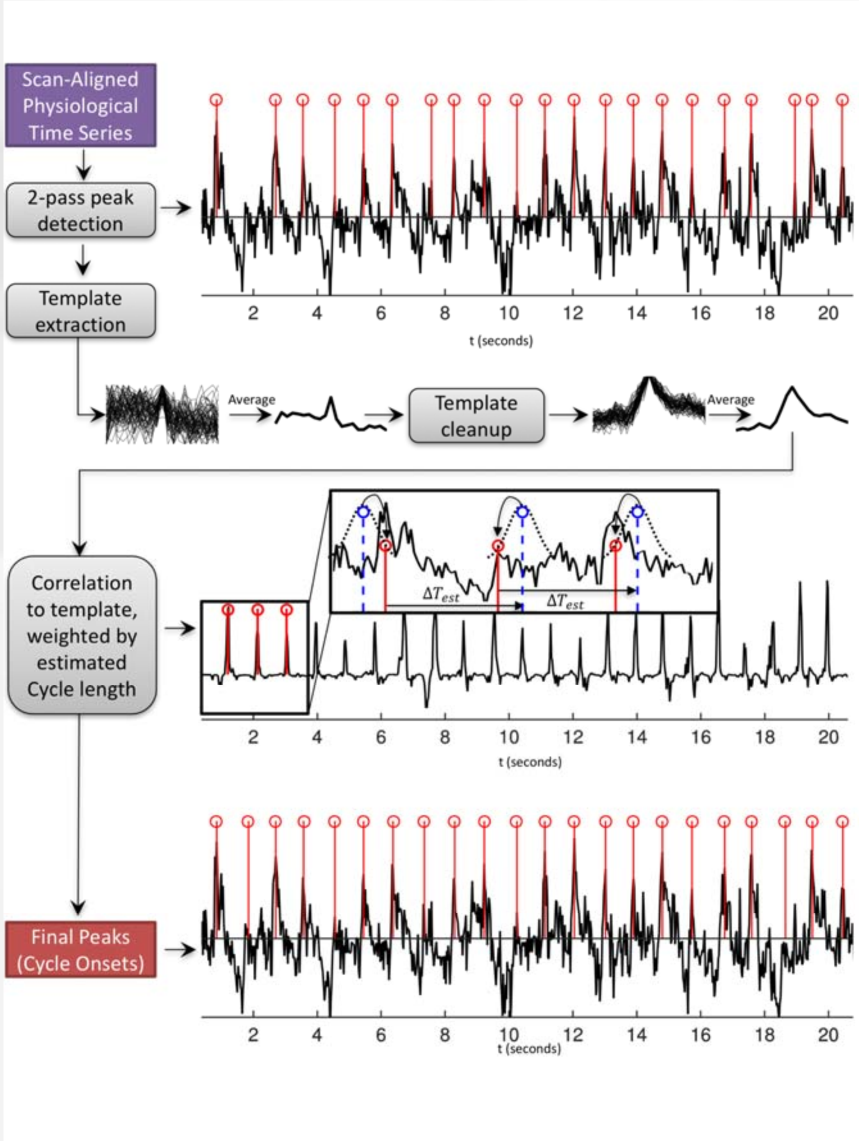
Scan Sync with Philips Gradients



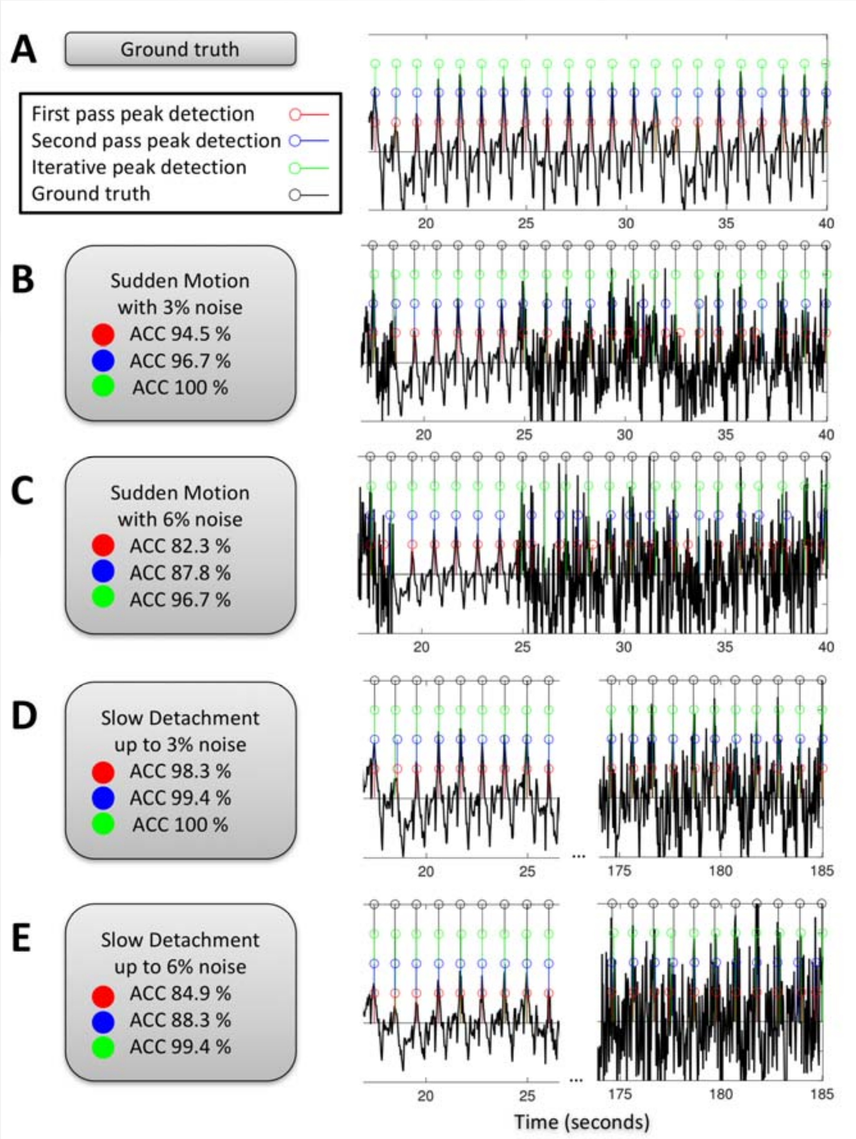
Data Preprocessing Overview



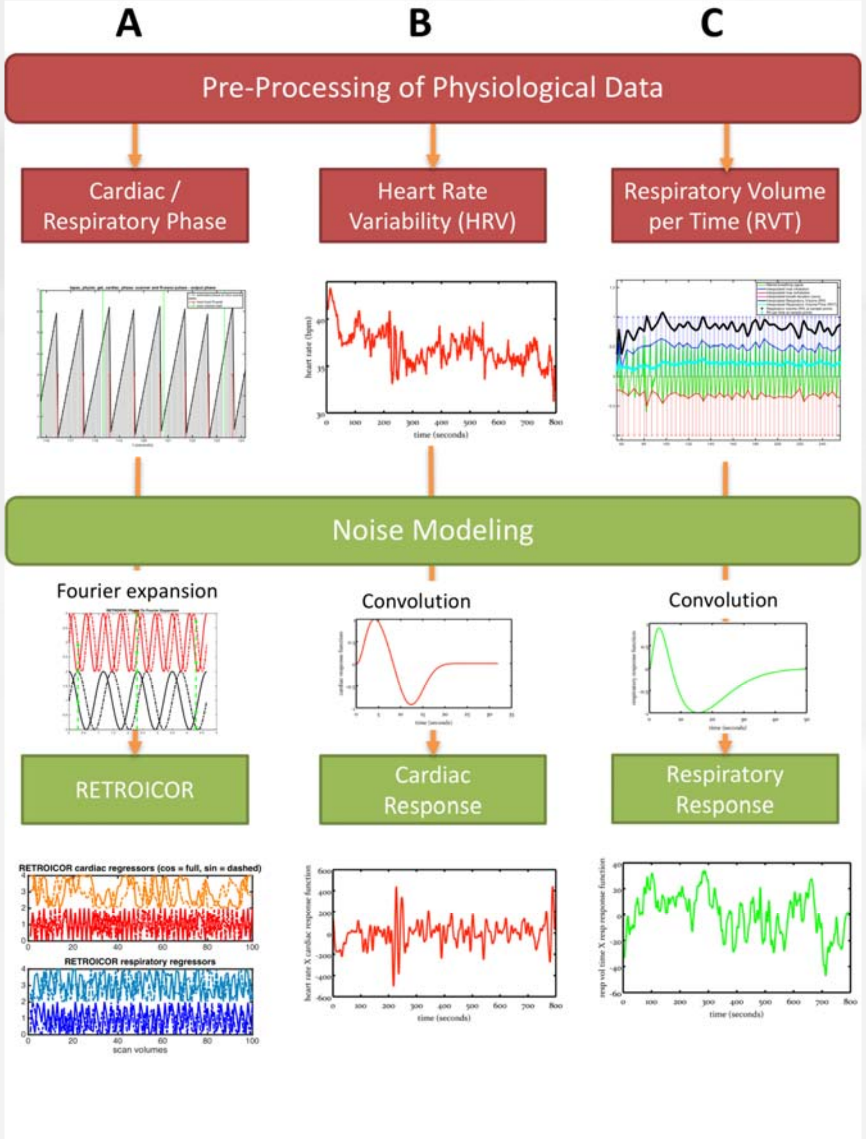
Preprocessing: Peak Detection



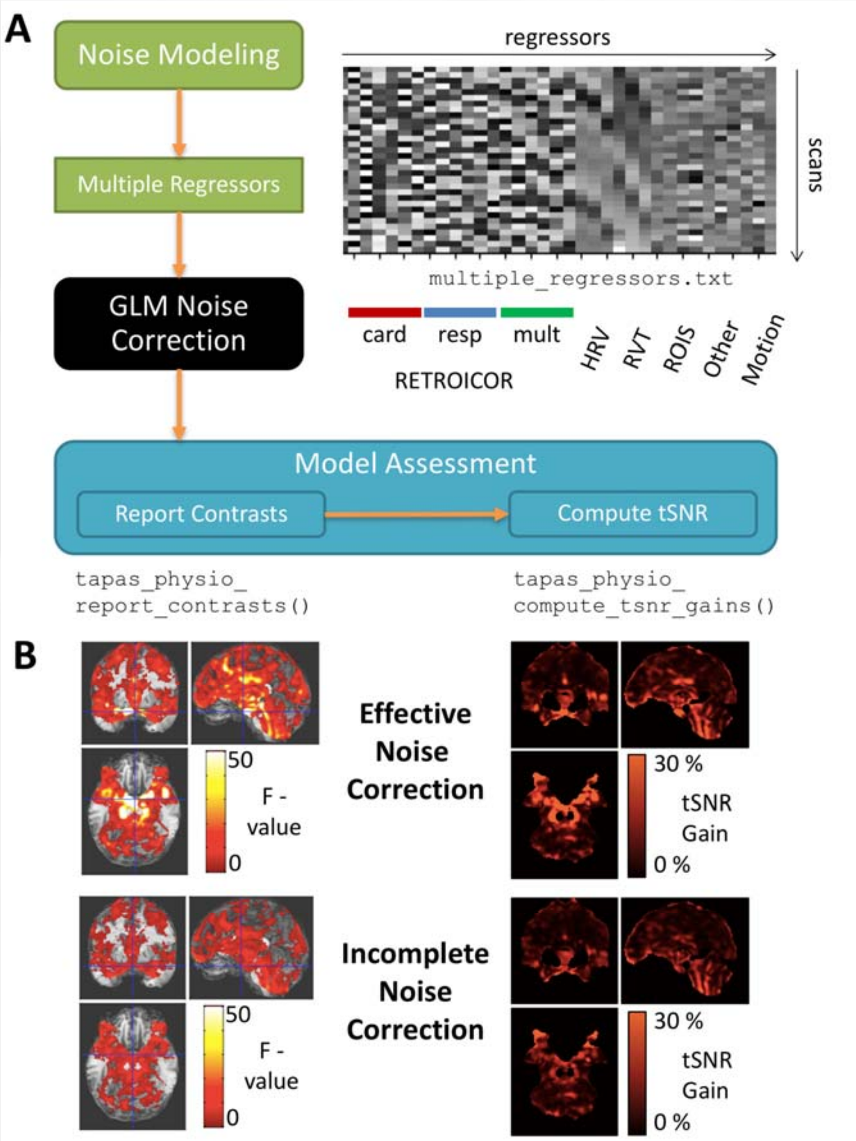
Peak Detection: Robustness



Noise Modeling

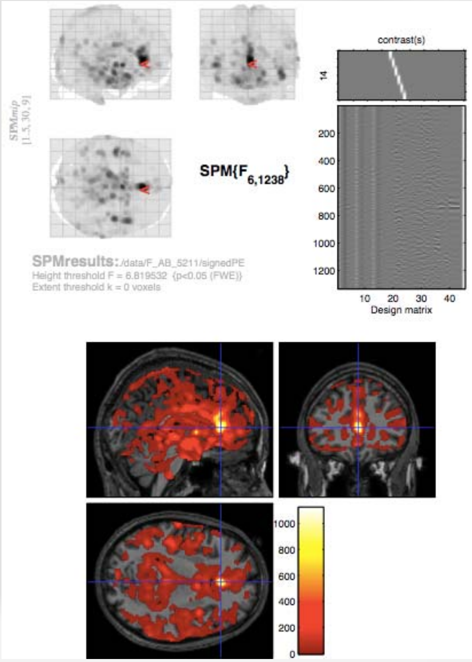


Diagnostics: Model Assessment

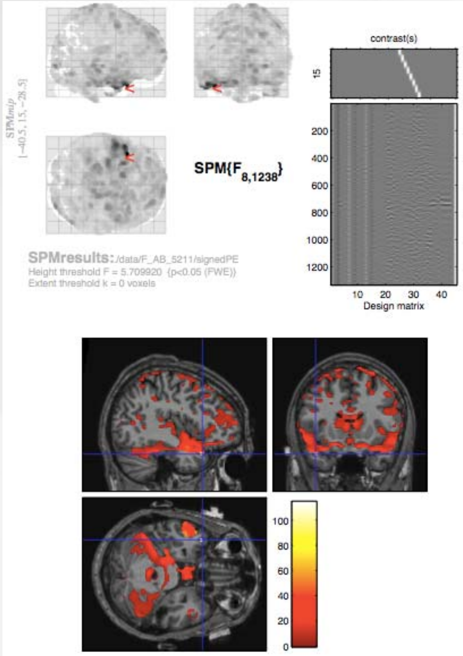


Model Check: SPM F-contrasts

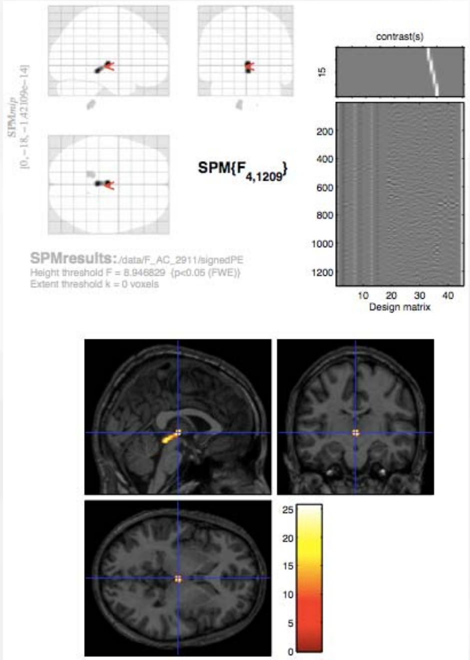
Cardiac regressors



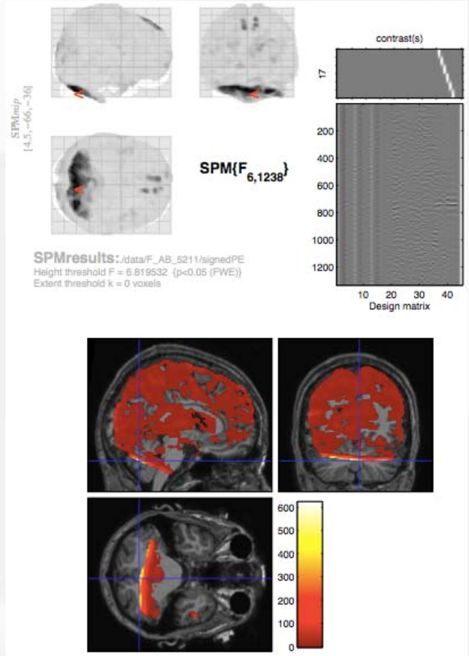
Respiratory regressors



Cardiac x Respiratory



Movement regressors

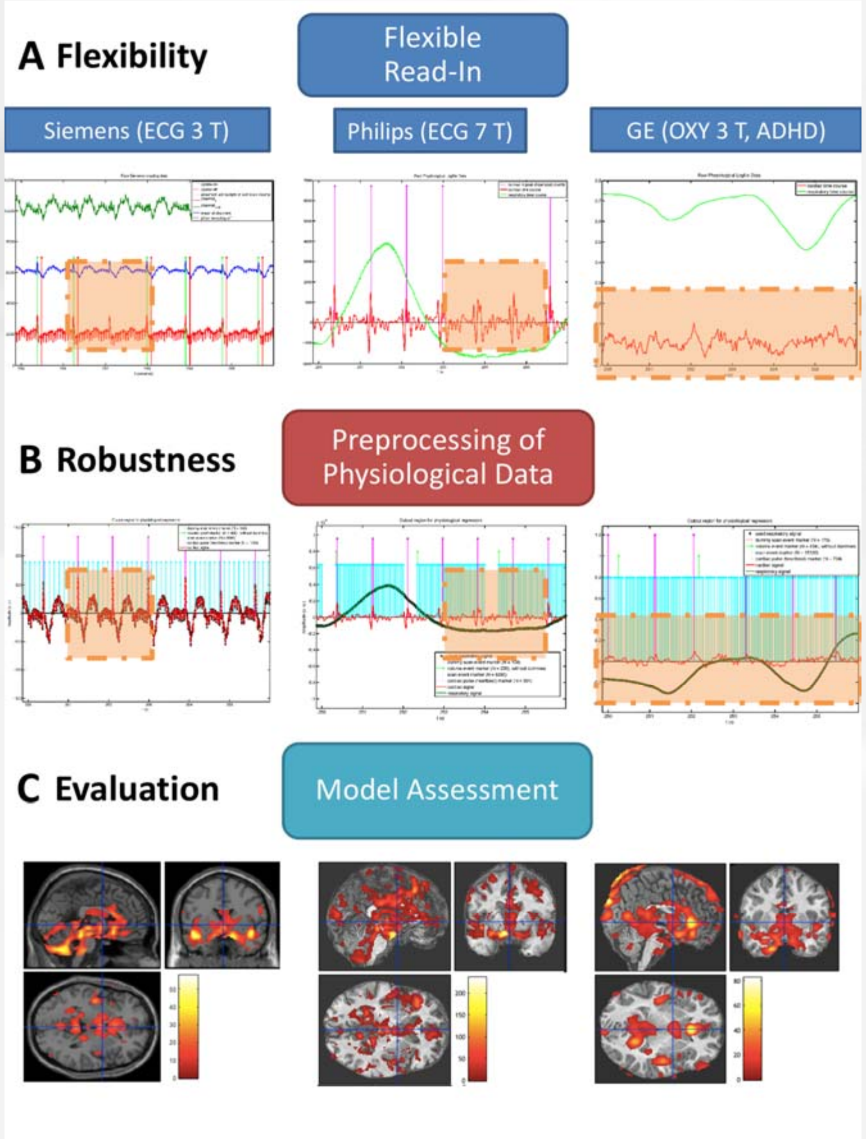


Finally:

Check Influence of Physiological Noise (Correction) on Data

- SPM
- F-contrast on 1st and second level

Flexibility: Scanner vendors

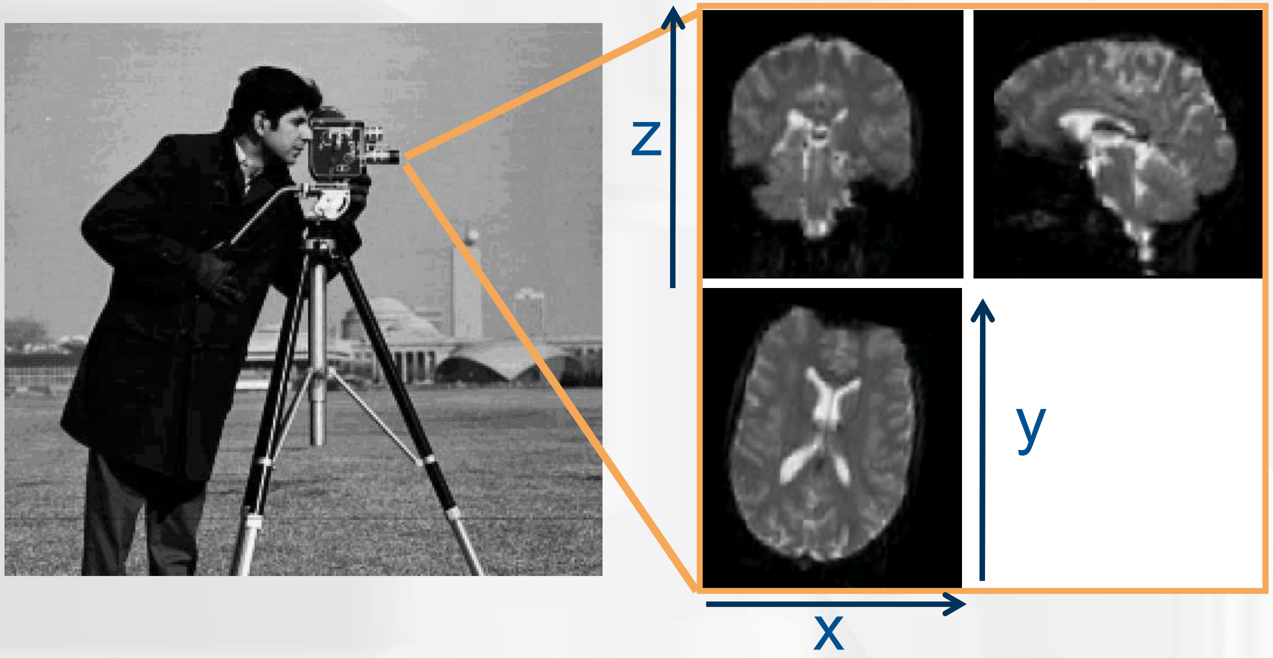


References

- **Birn**, Rasmus M., Jason B. Diamond, Monica A. Smith, and Peter A. Bandettini. 2006. "Separating Respiratory-variation-related Fluctuations from Neuronal-activity-related Fluctuations in fMRI." NeuroImage 31 (4) (July 15): 1536–1548. doi:10.1016/j.neuroimage.2006.02.048.
- **Glover**, G H, T Q Li, and D Ress. 2000. "Image-based Method for Retrospective Correction of Physiological Motion Effects in fMRI: RETROICOR." Magnetic Resonance in Medicine: Official Journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 44 (1) (July): 162–7.
- **Harvey**, Ann K., Kyle T.S. Pattinson, Jonathan C.W. Brooks, Stephen D. Mayhew, Mark Jenkinson, and Richard G. Wise. 2008. "Brainstem Functional Magnetic Resonance Imaging: Disentangling Signal from Physiological Noise." Journal of Magnetic Resonance Imaging 28 (6): 1337–1344. doi:10.1002/jmri.21623.
- **Hutton**, C., O. Josephs, J. Stadler, E. Featherstone, A. Reid, O. Speck, J. Bernarding, and N. Weiskopf. 2011. "The Impact of Physiological Noise Correction on fMRI at 7 T." NeuroImage 57 (1) (July 1): 101–112. doi:10.1016/j.neuroimage.2011.04.018.
- **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., Heinzle, 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