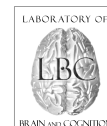


Multi-echo EPI for resting state and activation based fMRI

Javier González-Castillo

Section on Functional Imaging Methods, NIMH, NIH

August 2015, National Institutes of Health, Bethesda, MD



❖ WHAT IS MULTI-ECHO (ME) FMRI

❖ WHAT CAN YOU DO WITH ME TIMESERIES

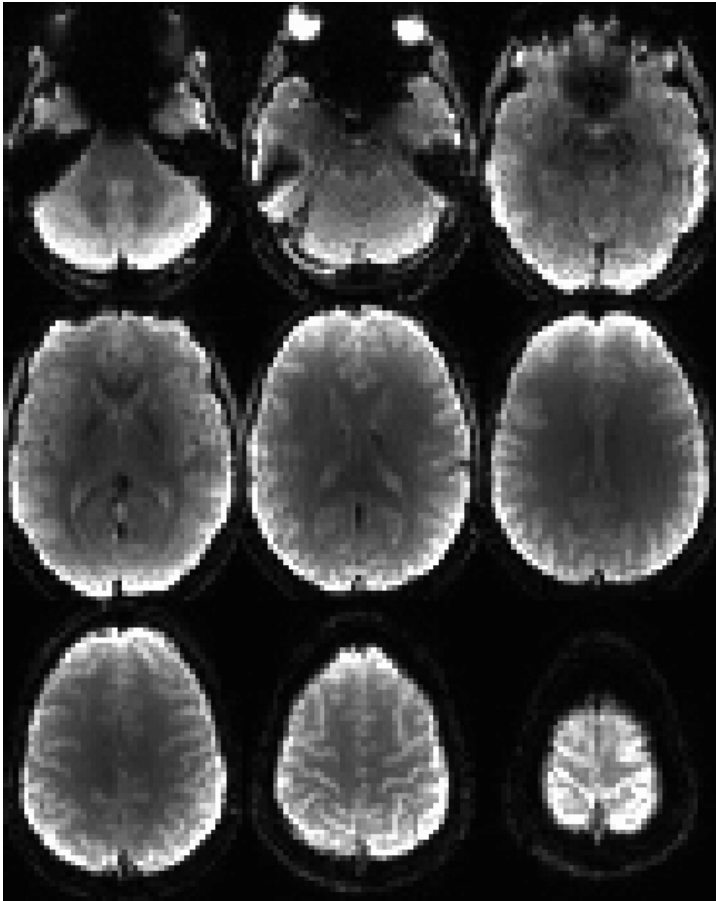
- Compute static S_0 and T_2^* Maps
- Compute voxel-wise time-series of S_0 (Non-BOLD) and T_2^* (BOLD)
- Combine echoes to improve SNR/spatially equalize functional contrast
- Echo Time Dependence Analysis

❖ ME-ICA Denoising

- ME-ICA Pipeline
- ME-ICA Outputs
- ME-ICA Web Reporting Tool

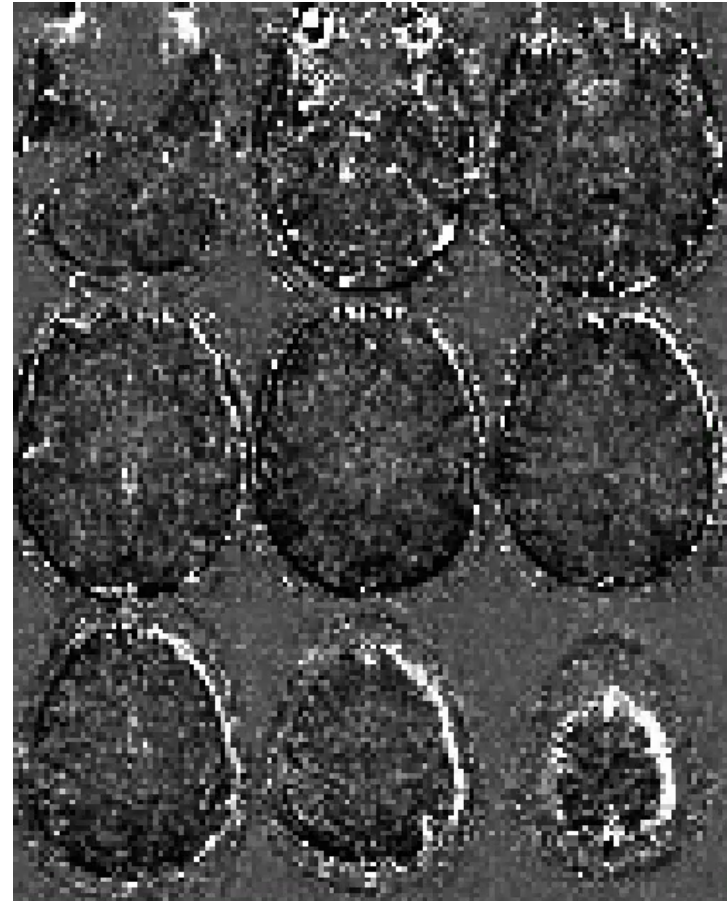
❖ ME-ICA Applications

RAW DATA

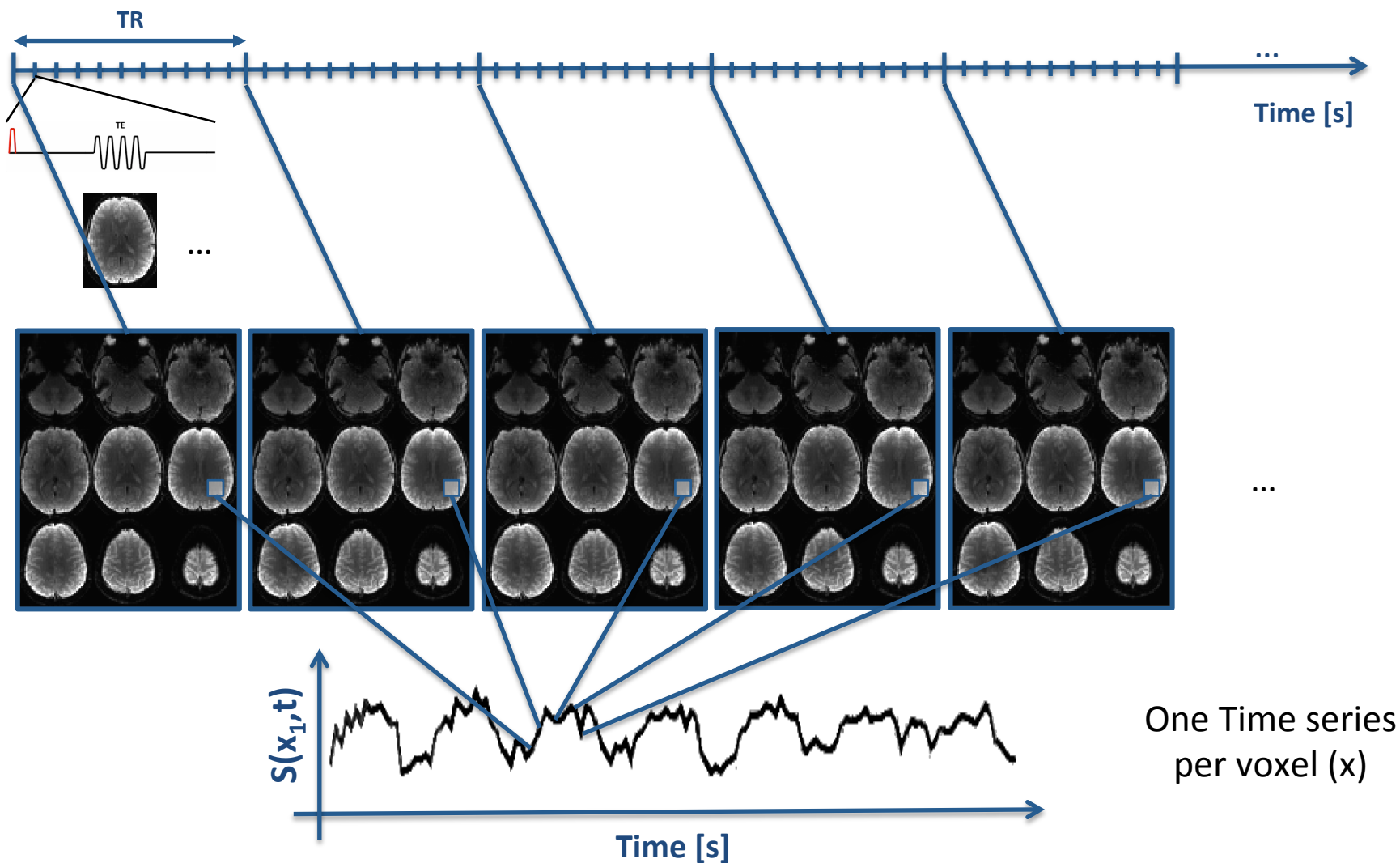


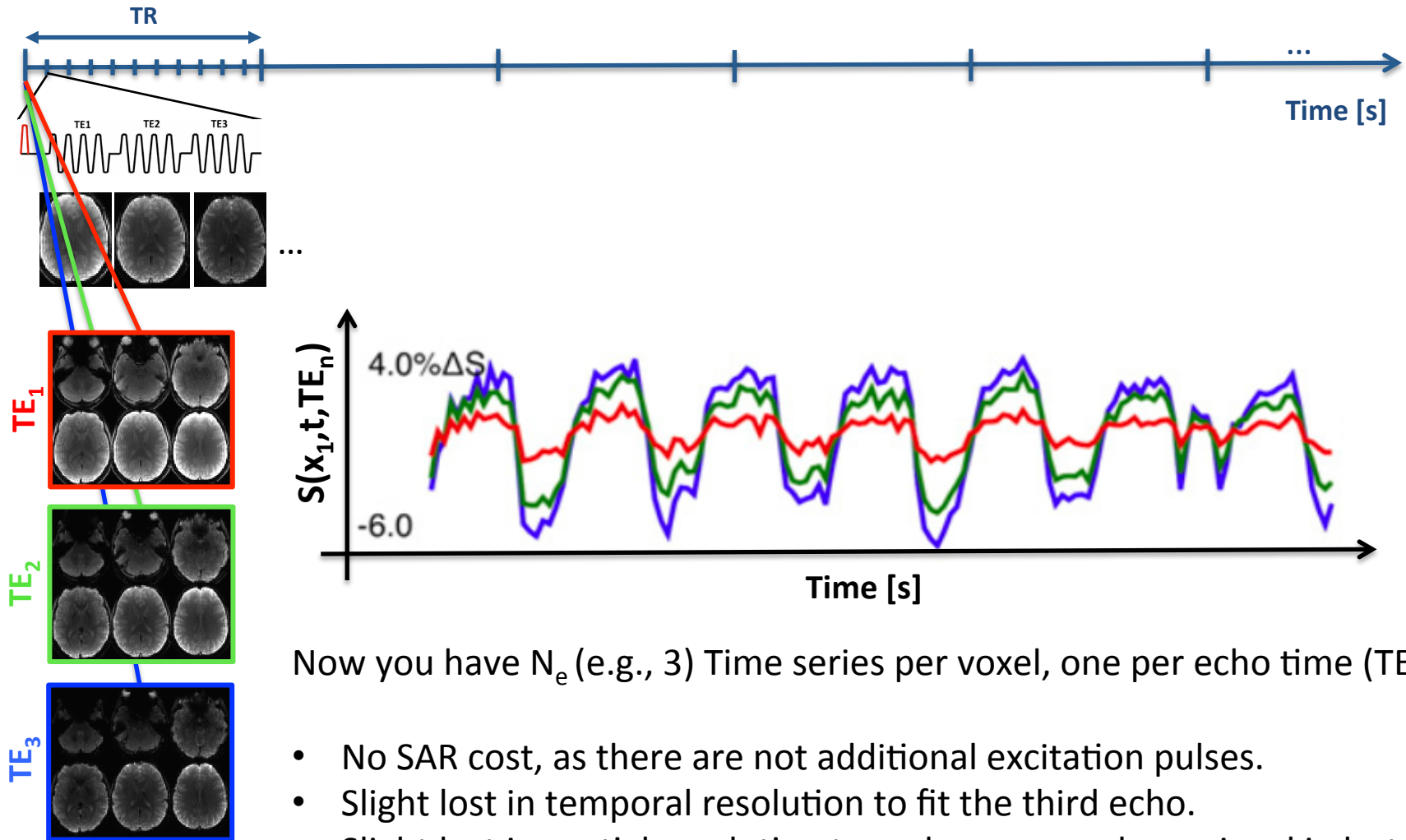
$$S(x, t)$$

SIGNAL CHANGE



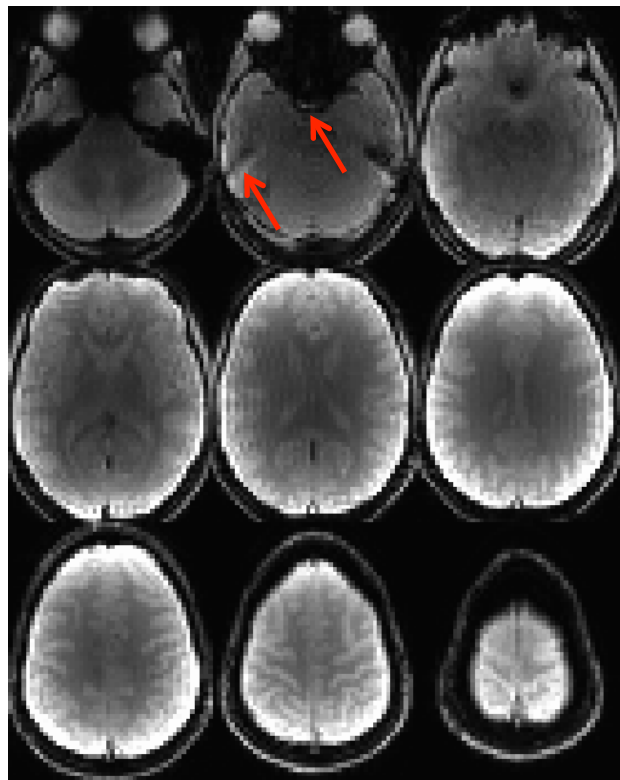
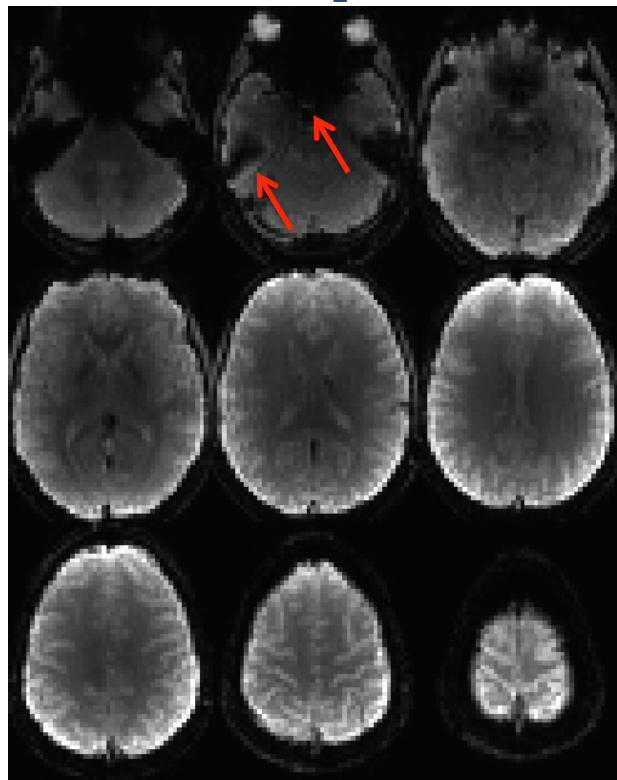
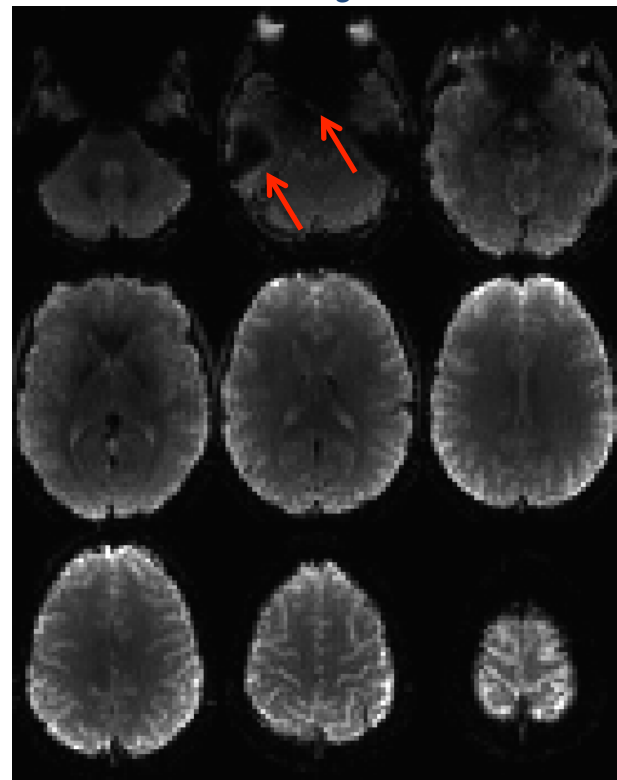
$$\Delta S(x, t) = \left[S(x, t) - \overline{S(x)} \right] / \overline{S(x)}$$





Now you have N_e (e.g., 3) Time series per voxel, one per echo time (TE_n):

- No SAR cost, as there are not additional excitation pulses.
- Slight lost in temporal resolution to fit the third echo.
- Slight lost in spatial resolution to make sure you have signal in last echo.

TE_1  TE_2  TE_3 

16

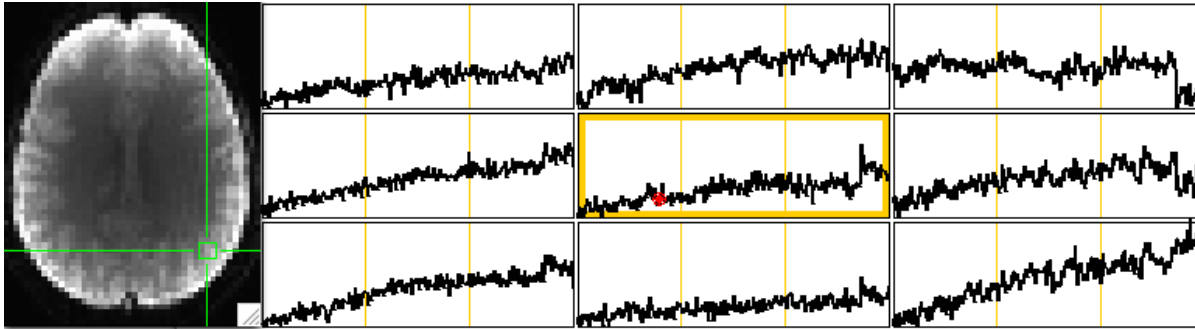
907

16

907

16

907



Signal in voxel x , at time point t , measured at echo time TE

$$S(x, t, TE) = \underbrace{S_o(x, t)}_{\text{Captures local fluctuations due to T1 changes (e.g., inflow) and HW instabilities}} e^{-\underbrace{R_2^*(x, t) \cdot TE}_{\text{Captures local fluctuations in field inhomogeneity (including BOLD)}}} + \text{Noise}$$

Captures local fluctuations due to T1 changes (e.g., inflow) and HW instabilities

Captures local fluctuations in field inhomogeneity (including BOLD)

$$S_o(x, t) = \overline{S_o(x)} + \Delta S_o(x, t)$$

$$\Delta S_o(x, t) \ll \overline{S_o(x)}, \forall x$$

$$R_2^*(x, t) = \overline{R_2^*(x)} + \Delta R_2^*(x, t)$$

$$\Delta R_2^*(x, t) \ll \overline{R_2^*(x)}, \forall x$$

❖ WHAT IS MULTI-ECHO (ME) FMRI

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- Compute static S_0 and T_2^* Maps
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❖ ME-ICA Denoising

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- ME-ICA Web Reporting Tool

❖ ME-ICA Applications

$$S(x, t, TE) = S_o(x, t) e^{-R_2^*(x, t) TE}$$

$$S_o(x, t) = \overline{S_o(x)} + \Delta S_o(x, t)$$

$$R_2^*(x, t) = \overline{R_2^*(x)} + \Delta R_2^*(x, t)$$

By definition, the average across time of $\Delta S_o(x, t)$ and $\Delta R_2^*(x, t)$ are zero, and then it follows that the average signal across time for a given voxel (x) and echo time (TE) is:

$$\overline{S(x, TE)} = \overline{S_o(x)} \cdot e^{-\overline{R_2^*(x)} \cdot TE}$$

↓

$$\log(\overline{S(x, TE)}) = \log(\overline{S_o(x)} \cdot e^{-\overline{R_2^*(x)} \cdot TE})$$

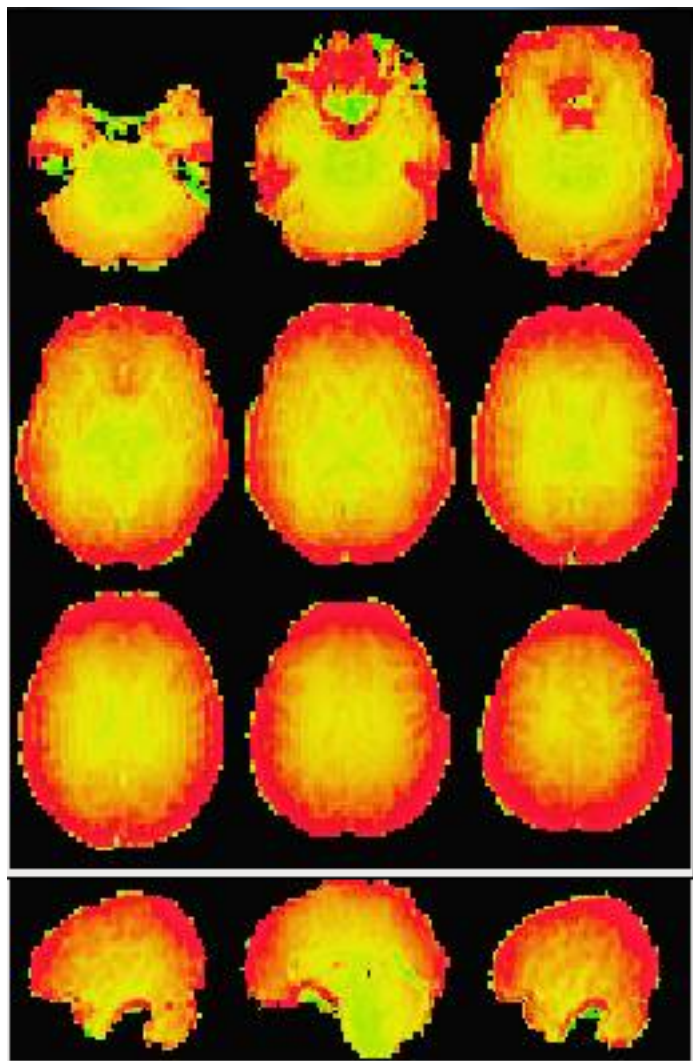
↓

$$\log(\overline{S(x, TE)}) = -\overline{R_2^*(x)} \cdot TE + \log(\overline{S_o(x)})$$

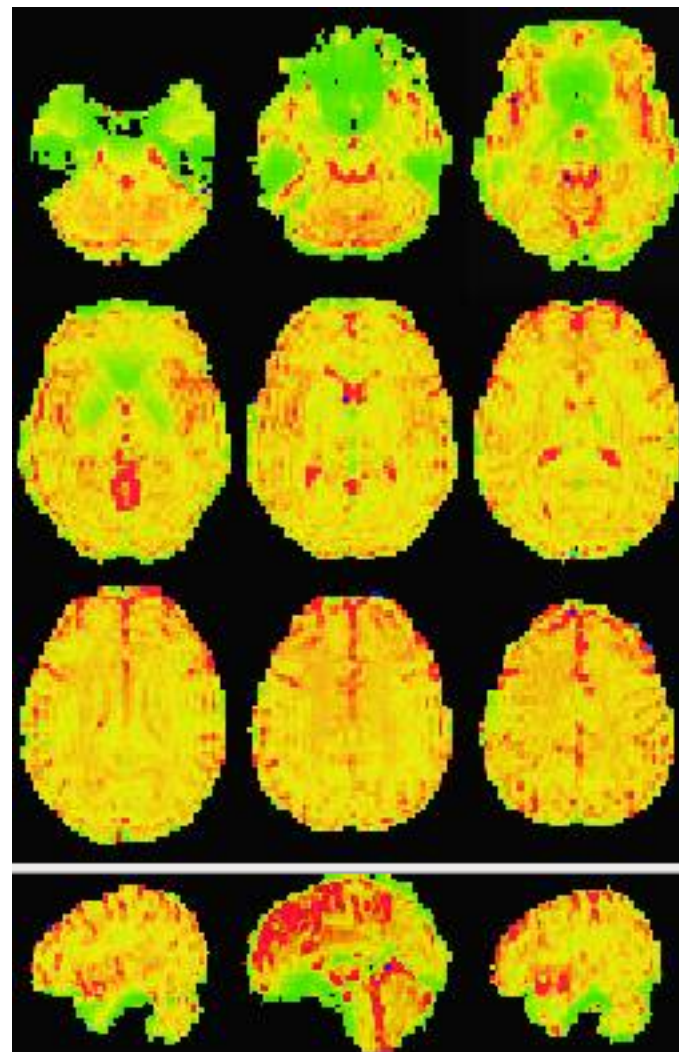
$$y(x, TE) = a(x) * TE + b(x)$$

Linear
system of
equations for
3 echoes

$$\begin{cases} \log(\overline{S(x, TE_1)}) = -\overline{R_2^*(x)} \cdot TE_1 + \log(\overline{S_o(x)}) \\ \log(\overline{S(x, TE_2)}) = -\overline{R_2^*(x)} \cdot TE_2 + \log(\overline{S_o(x)}) \\ \log(\overline{S(x, TE_3)}) = -\overline{R_2^*(x)} \cdot TE_3 + \log(\overline{S_o(x)}) \end{cases}$$



Static S_0 Map (s0v.nii)



Static T_2^* Map (t2sv.nii)

$$S(x, t, TE) = S_o(x, t) e^{-R_2^*(x, t) TE}$$

$$S_o(x, t) = \overline{S_o(x)} + \Delta S_o(x, t)$$

$$R_2^*(x, t) = \overline{R_2^*(x)} + \Delta R_2^*(x, t)$$

$$\overline{S(x, TE)} = \overline{S_o(x)} \cdot e^{-\overline{R_2^*(x)} TE}$$

$$S(x, t, TE) = \left[\overline{S_o(x)} + \Delta S_o(x, t) \right] \cdot e^{\left[-\overline{R_2^*(x)} + \Delta R_2^*(x, t) \right] TE} \quad (1)$$

$$S(x, t, TE) = \overline{S(x, TE)} \left[1 + \frac{\Delta S_o(x, t)}{\overline{S_o(x)}} \right] \cdot e^{-\Delta R_2^*(x, t) TE} \quad (2)$$

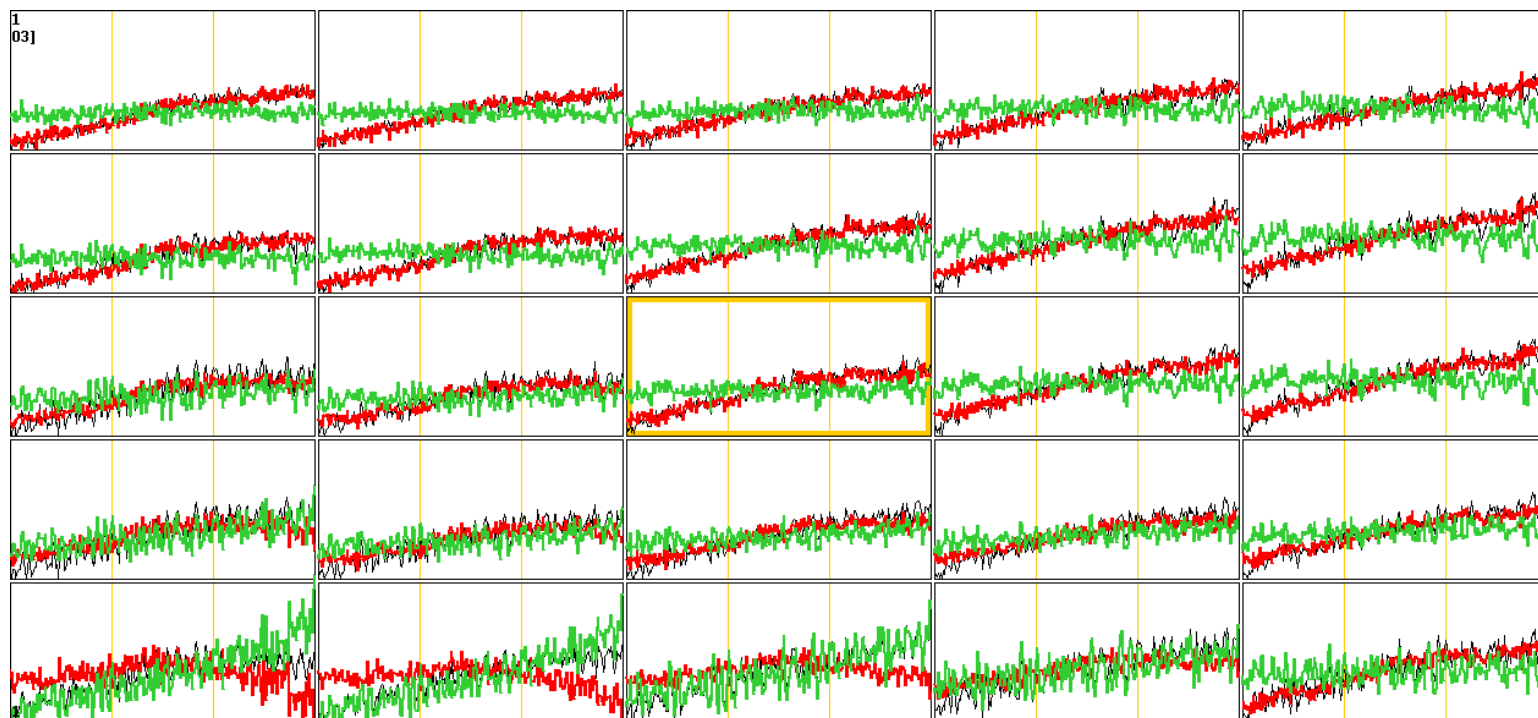
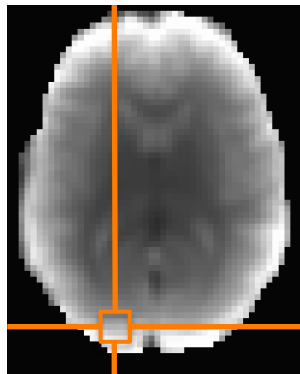
Using a first order Taylor expansion for the exponential term: $e^{-\Delta R_2^*(x, t) TE} \approx (1 - \Delta R_2^*(x, t) \cdot TE)$

$$S(x, t, TE) \approx \overline{S(x, TE)} \left[1 - \Delta R_2^*(x, t) \cdot TE + \frac{\Delta S_o(x, t)}{\overline{S_o(x)}} - \frac{\Delta R_2^*(x, t) \cdot TE \cdot \Delta S_o(x, t)}{\overline{S_o(x)}} \right] \quad (3)$$

$$S(x, t, TE) \approx \overline{S(x, TE)} \left[1 - \Delta R_2^*(x, t) \cdot TE + \frac{\Delta S_o(x, t)}{\overline{S_o(x)}} \right] \quad (4)$$

$$\left. \begin{array}{l} \Delta \rho(x, t) = \Delta S_o(x, t) / \overline{S_o(x)} \\ \Delta \kappa(x, t) = \Delta R_2^*(x, t) / TE \end{array} \right\} \rightarrow S(x, t, TE) \approx \overline{S(x, TE)} \cdot \left[1 + \Delta \rho(x, t) - \frac{TE}{TE} \Delta \kappa(x, t) \right] \quad (5)$$

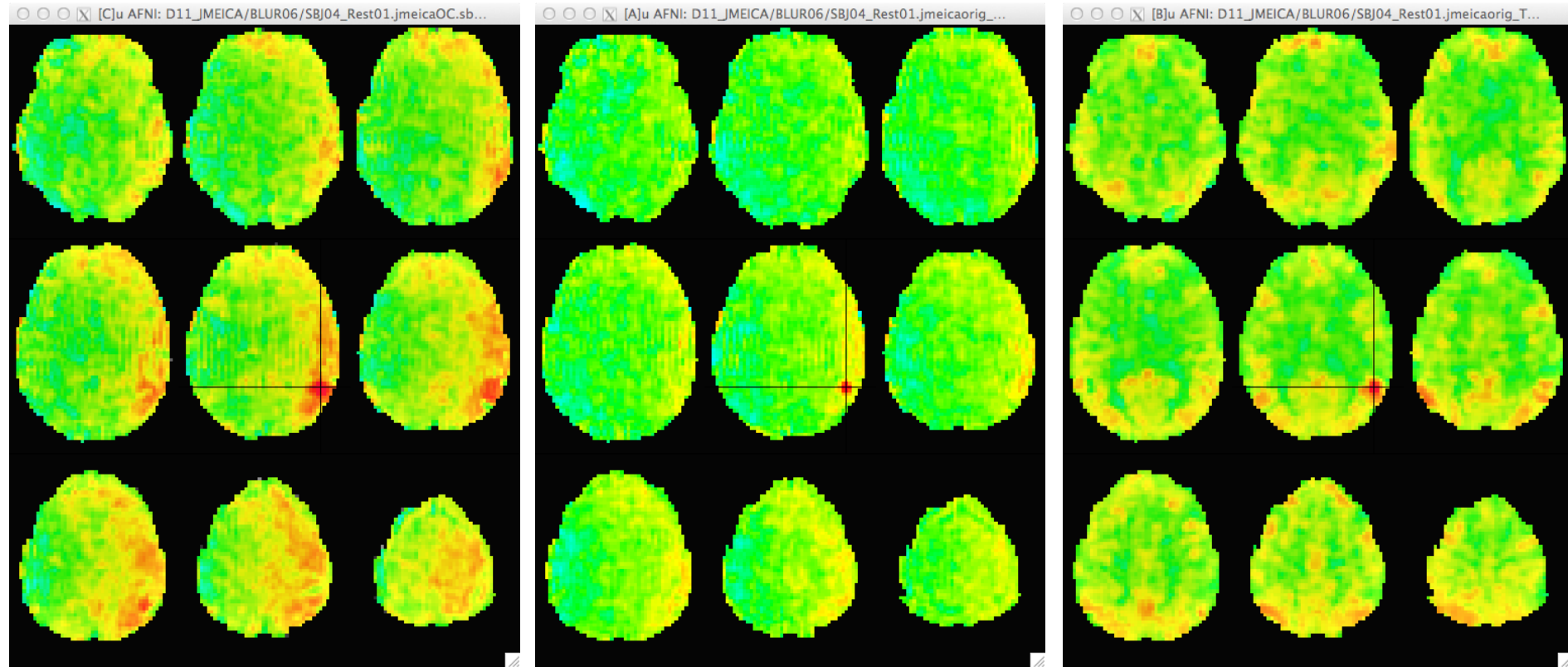
$$S(x, t, TE) - \overline{S(x, TE)} \approx \overline{S(x, TE)} \left[\Delta \rho(x, t) - \frac{TE}{TE} \Delta \kappa(x, t) \right] \quad (6)$$



— $S(x,t,TE_2)$

— $\Delta S_0(x,t)$

— $\Delta R_2^*(x,t)$



Raw Data

 ΔS_0 ΔR_2^*

Motion Correction & Smoothing (6mm)
No Filtering | No Detrending

We have N_e pseudo-concurrent measurements \rightarrow why not simply combine them to reduce uncorrelated white noise present in each individual measurement?

1. Simple Summation

$$\hat{S}(x,t) = \sum_{n=1}^N S(x,t,TE_n)$$

- Noisy data at longer echoes reduce the overall gain in sensitivity.

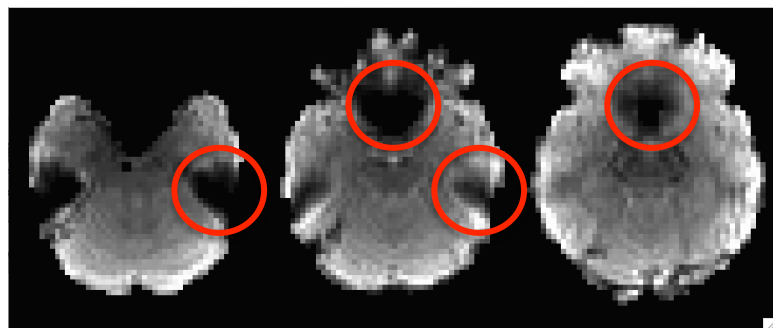
2. Weighted Summation

$$\hat{S}(x,t) = \sum_{n=1}^N S(x,t,TE_n) \cdot w_v(TE_n)$$

$$w_v(TE_n) = \frac{TE_n e^{-TE_n/T_{2,v}^*}}{\sum_n TE_n \cdot e^{-TE_n/T_{2,v}^*}}$$

- Helps to spatially maximize CNR and also to recover some signal level in regions affected by drop-out.

Posse et al., MRM 1999

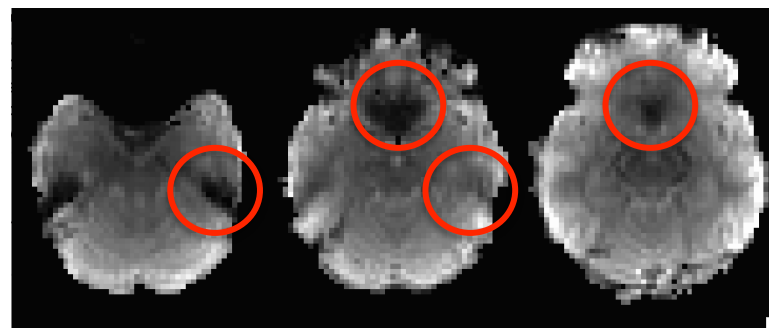


SINGLE ECHO

500



0



OPTIMALLY COMBINED

We have N_e pseudo-concurrent measurements, why not simply combine them to reduce uncorrelated white noise present in each individual measurement.

1. Simple Summation

$$\hat{S}(x,t) = \sum_{n=1}^N S(x,t,TE_n)$$

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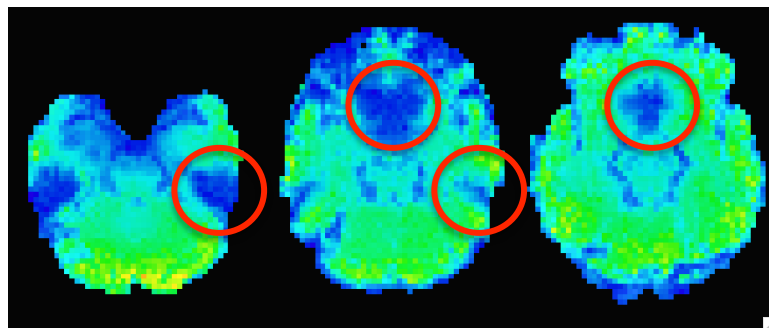
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- Optimizes CNR compared to Single Echo.
- Helps to spatially maximize CNR, by helping recover some signal in regions with large drop-outs at regular single echo acquisitions.

Posse et al., MRM 1999

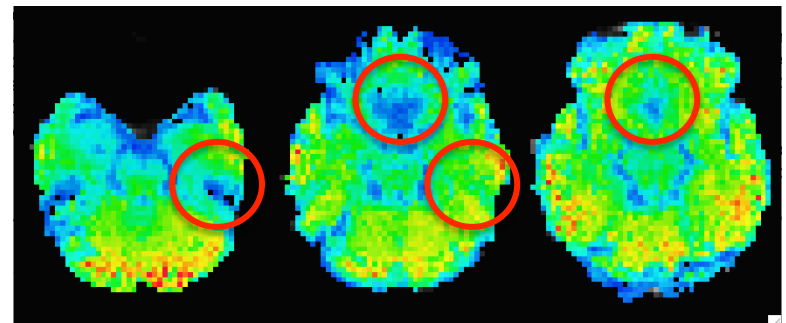


SINGLE ECHO

150



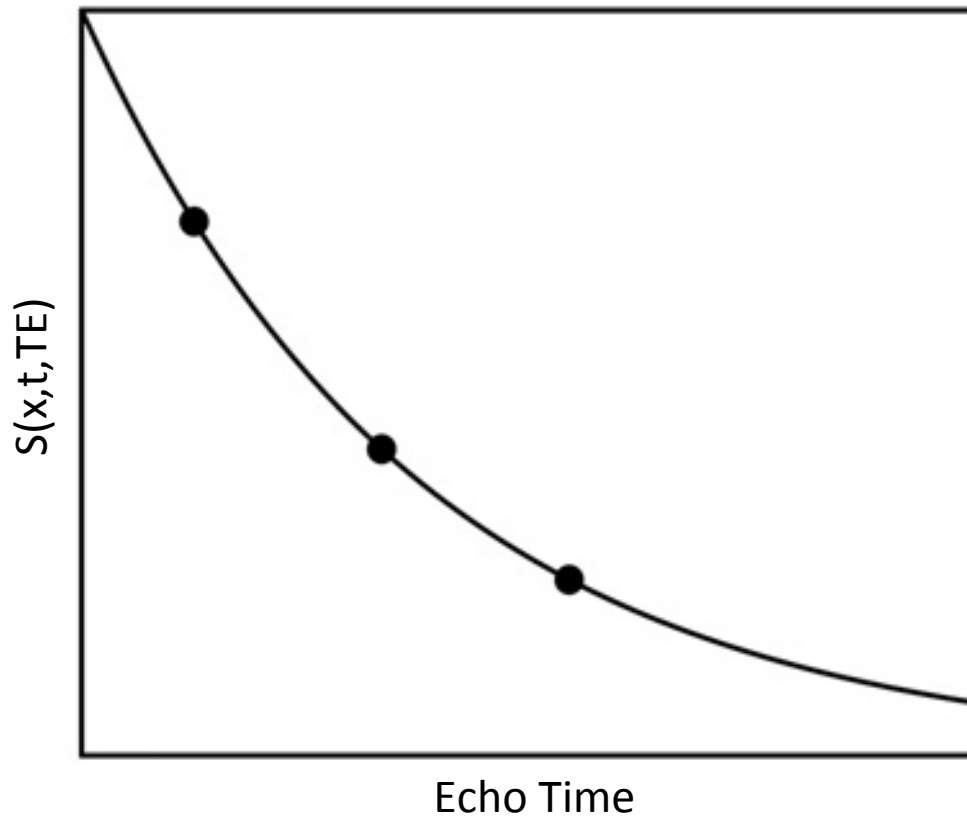
0



OPTIMALLY COMBINED

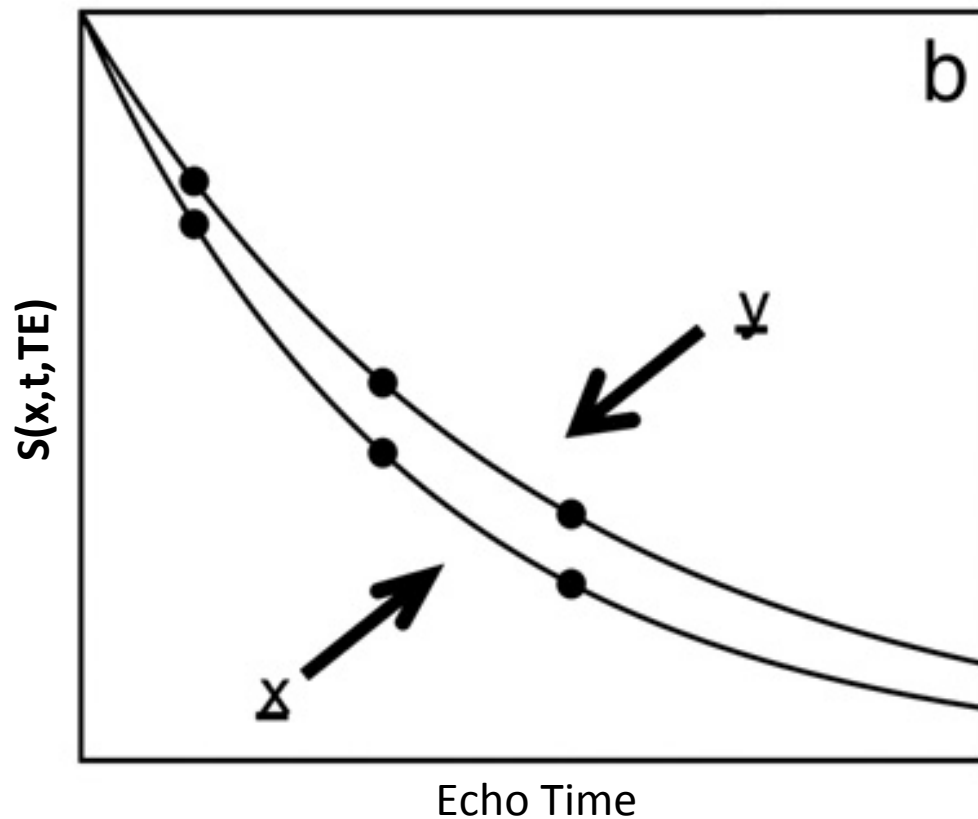
$$S(x,t,TE) = S_o(x,t) e^{-R_2^*(x,t) \cdot TE}$$

Let's assume that a given voxel (x) and time (t) ... $S_o(x,t)=5000$ and $T2^*(x,t)=30\text{ms}$



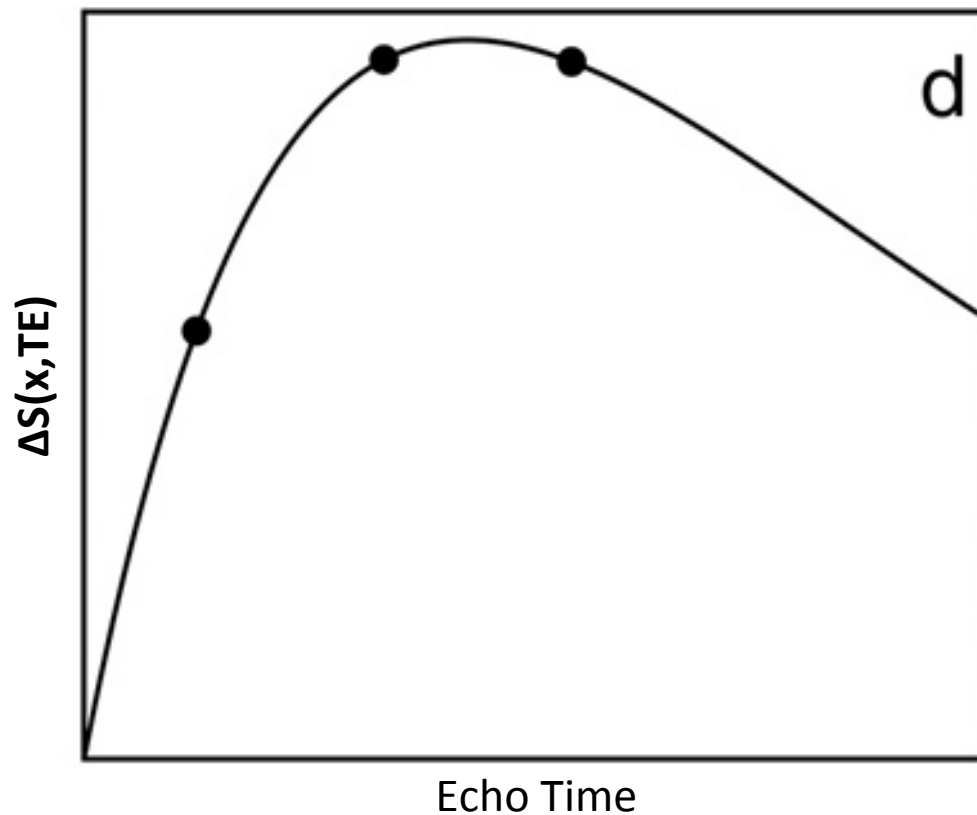
$$S(x,t,TE) = S_o(x,t) e^{-R_2^*(x,t) \cdot TE}$$

Let's assume now, that a local change in oxygenation happens (T_2^* effect)



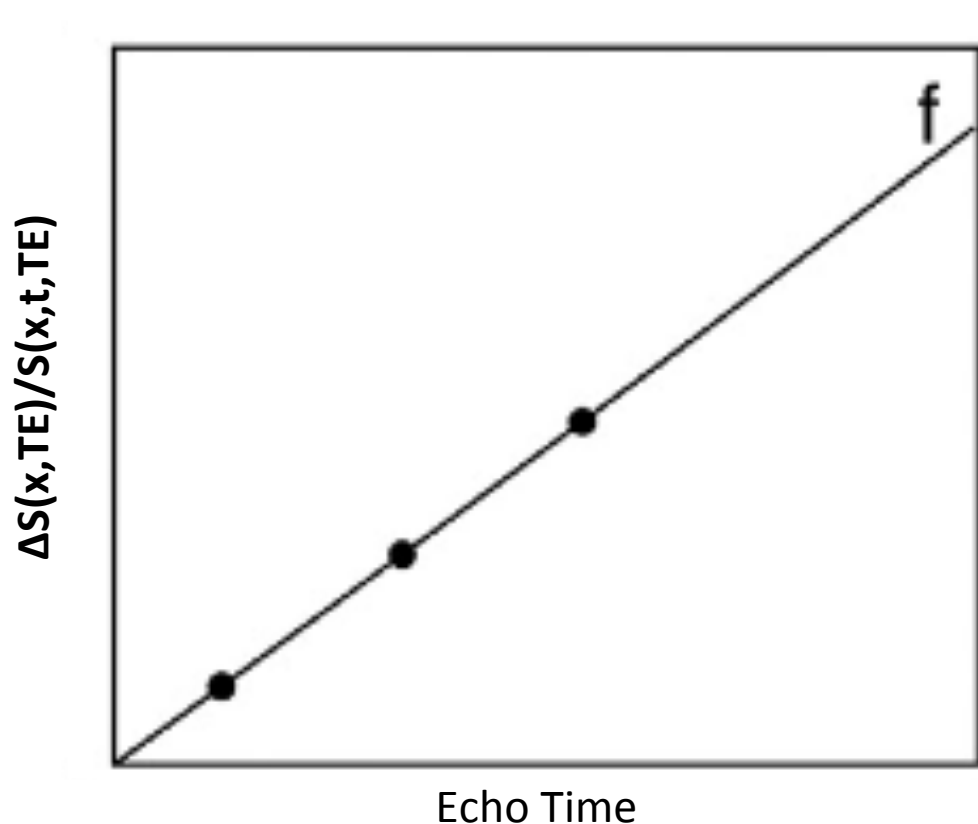
$$S(x, t, TE) = S_o(x, t) e^{-R_2^*(x, t) TE}$$

We could then use the difference between two curves to examine which is the optimal TE to maximize BOLD contrast



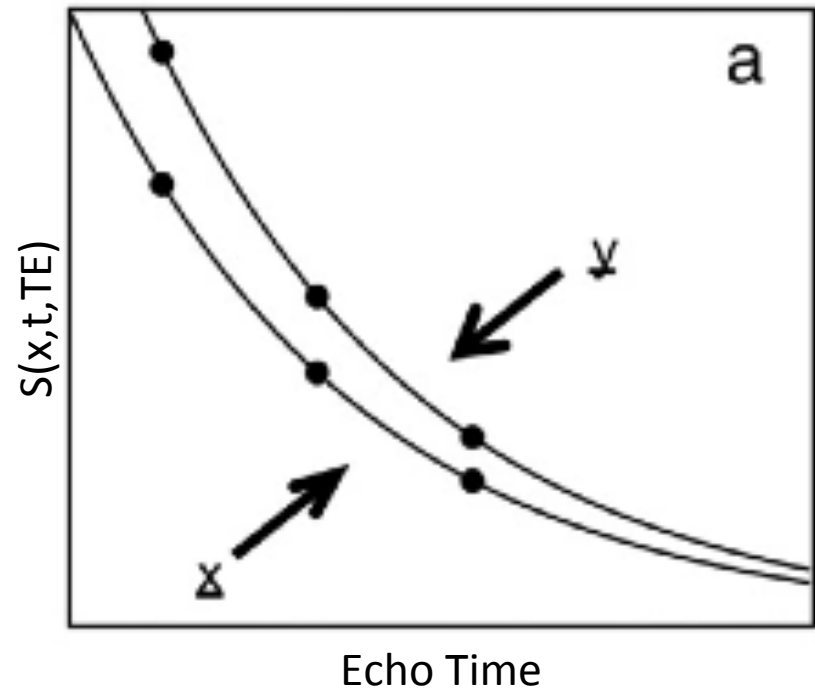
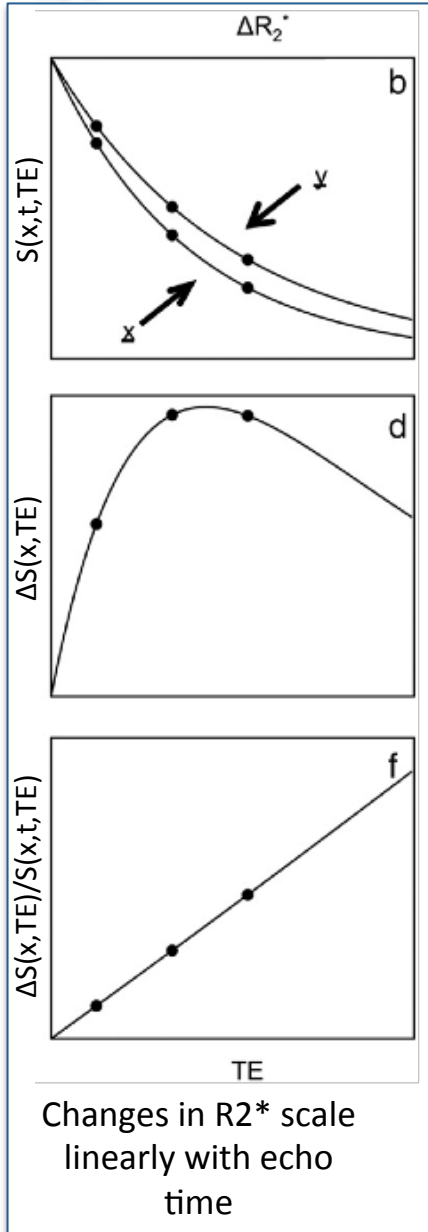
$$S(x, t, TE) = S_o(x, t) e^{-R_2^*(x, t) \cdot TE}$$

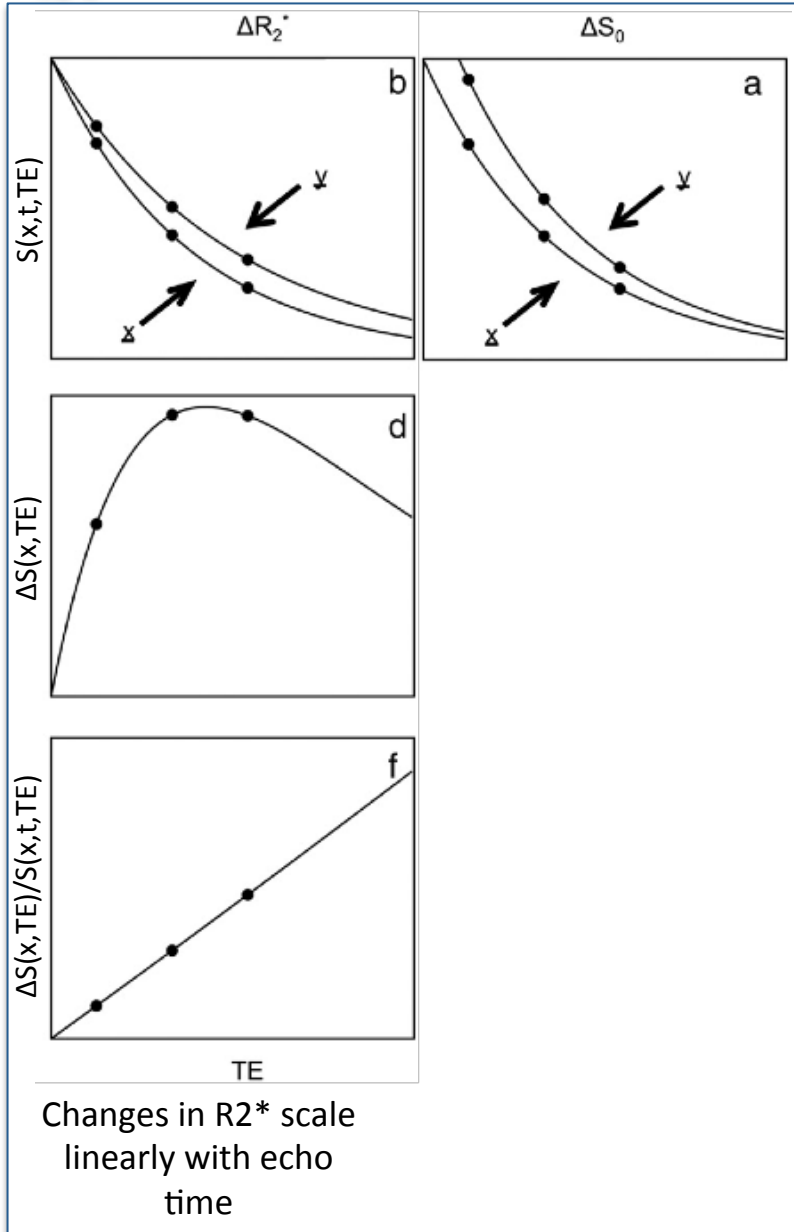
Most importantly for our discussion, for T_2^* signal changes, there is a linear relationship between echo time and measured signal (in terms of signal percent change)



$$S(x, t, TE) = S_o(x, t) e^{-R_2^*(x, t) \cdot TE}$$

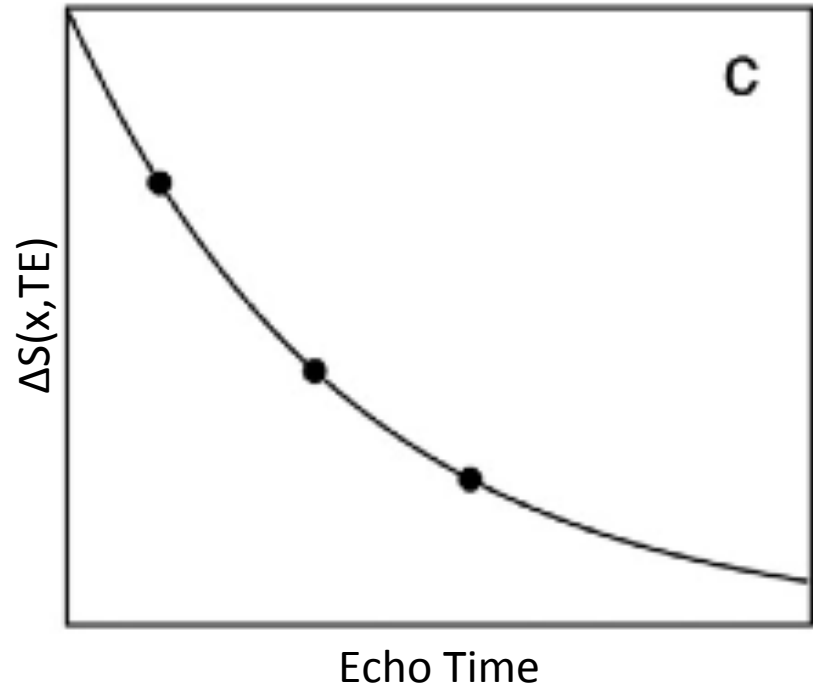
Let's now examine what happens when there is a change in S_o (T1 effect)

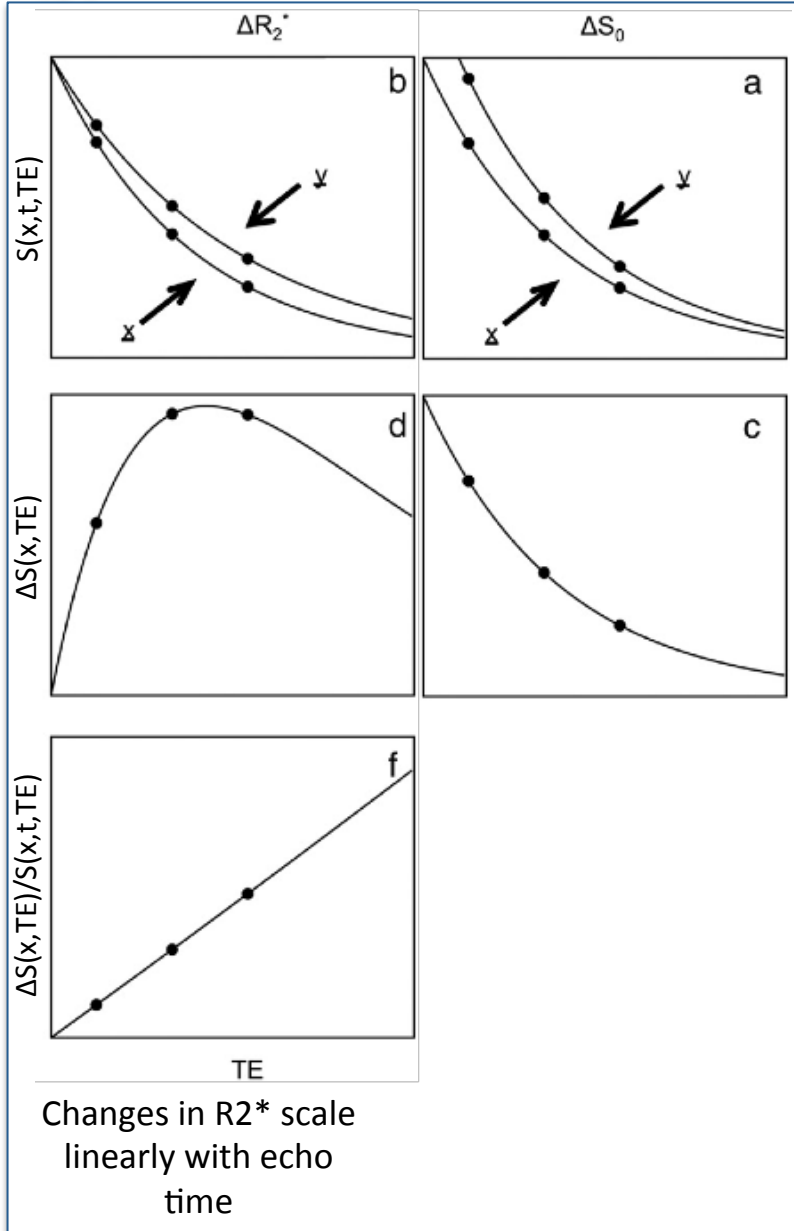




$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)TE}$$

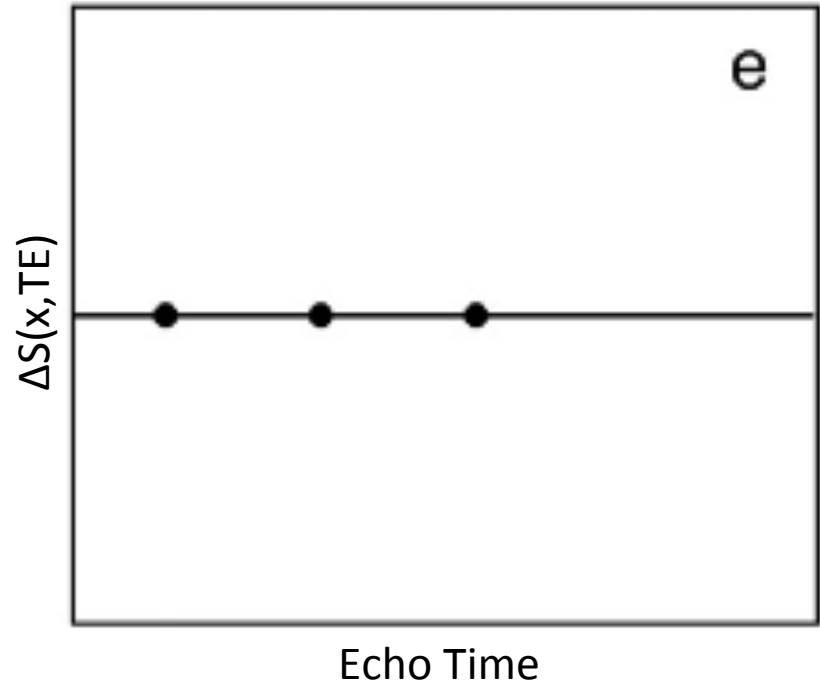
This time the difference between both curves looks very different

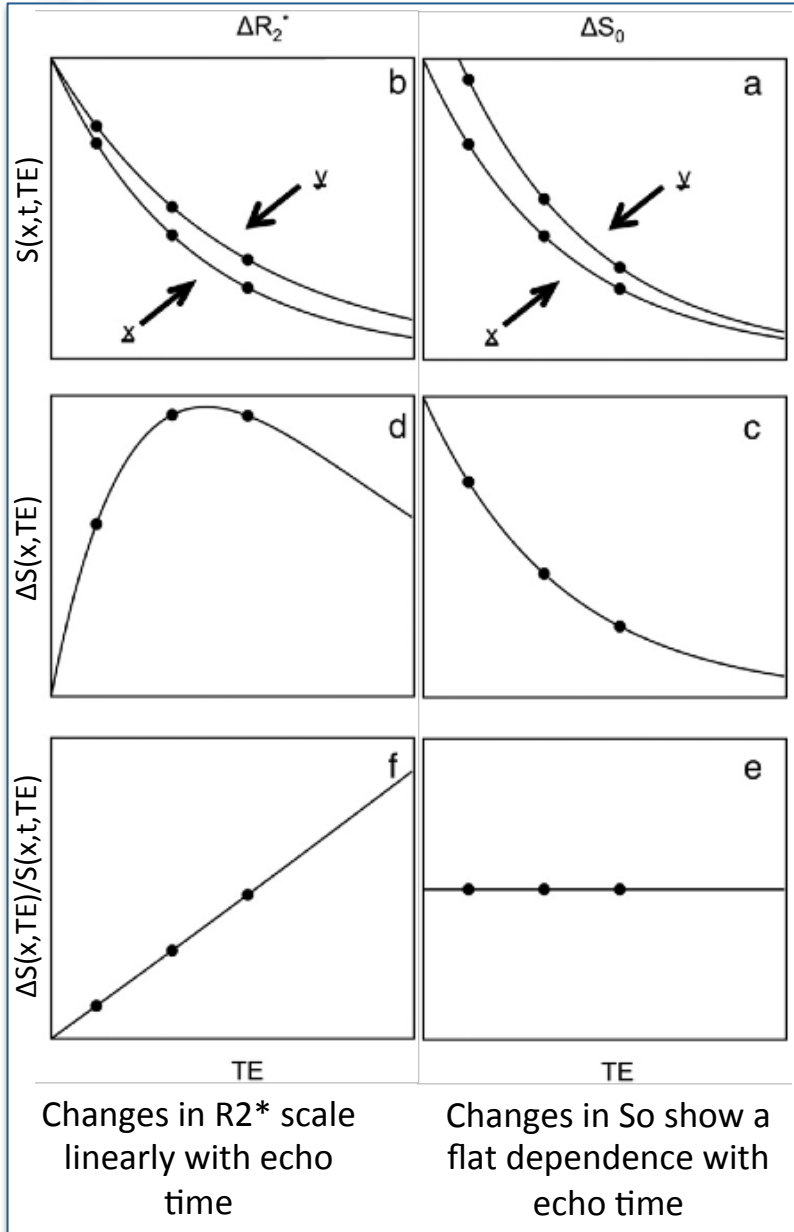




$$S(x, t, TE) = S_o(x, t) e^{-R_2^*(x, t) \cdot TE}$$

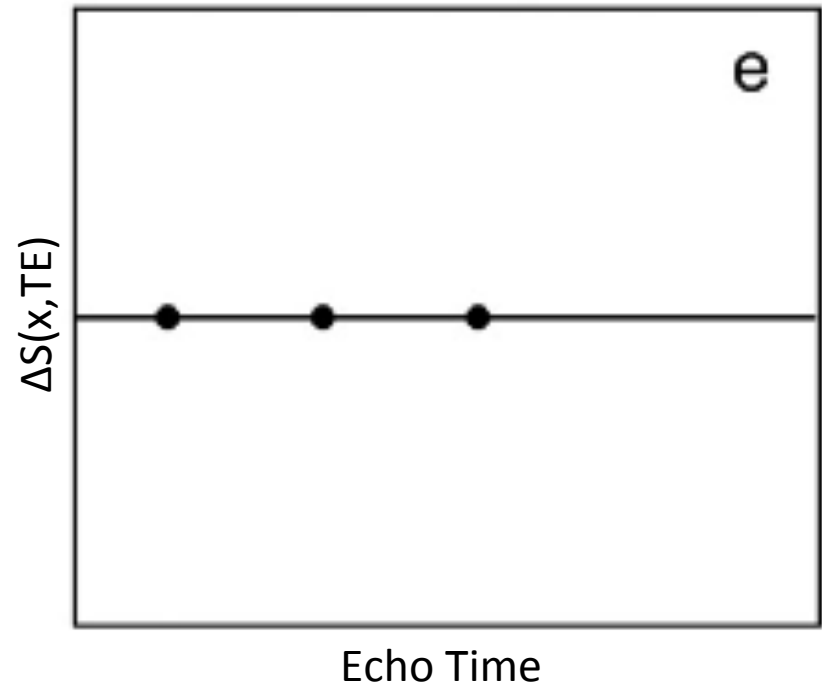
In term of signal percent change, changes in S_0 have a flat dependence with echo time



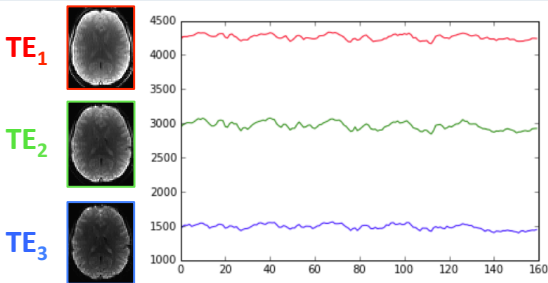


$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)TE}$$

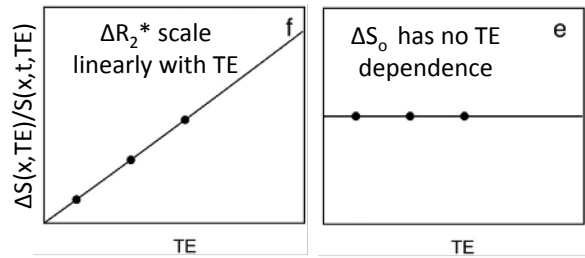
In term of signal percent change, changes in S_o have a flat dependence with echo time



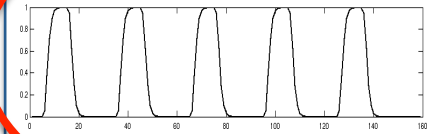
MULTI-ECHO DATASET



TE-DEPENDENCE MODEL

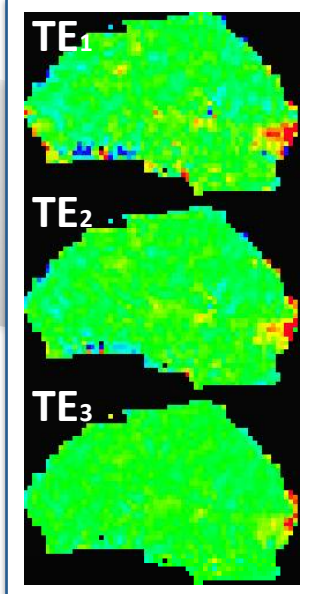


TIMESERIES OF INTEREST

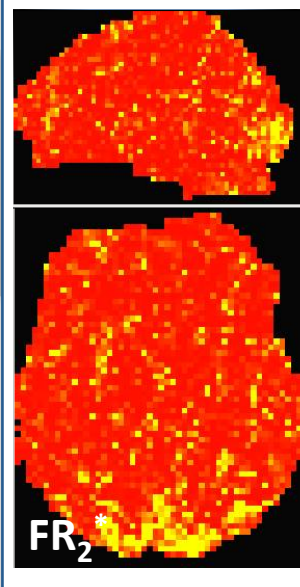


Task Paradigm

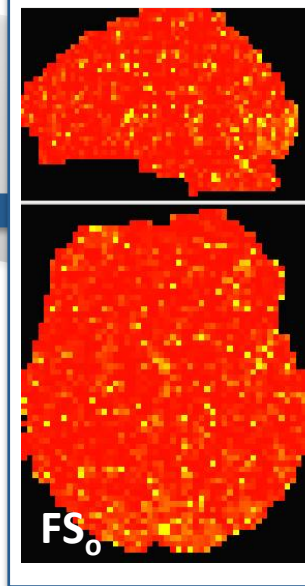
[1] Voxel-wise Fit against all TEs



[2] Voxel-wise Goodness of Fit to R2* Model



[3] Voxel-wise Goodness of Fit to S0 Model



[4] Compute Avg. Metric for each model

$$\kappa = \frac{\sum_{AllVoxels} z_v^2 F_{v,R_2^*}}{\sum_{AllVoxels} z_v^2} = 98.41$$

$$\rho = \frac{\sum_{AllVoxels} z_v^2 F_{v,S_0}}{\sum_{AllVoxels} z_v^2} = 26.02$$

❖ WHAT IS MULTI-ECHO (ME) FMRI

❖ WHAT CAN YOU DO WITH ME TIMESERIES

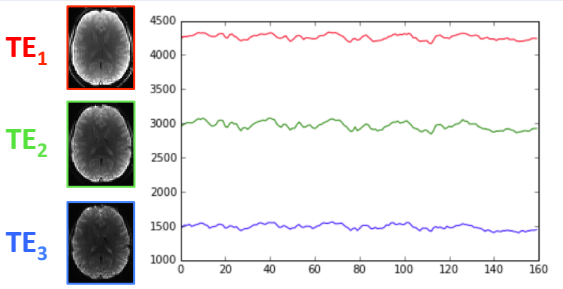
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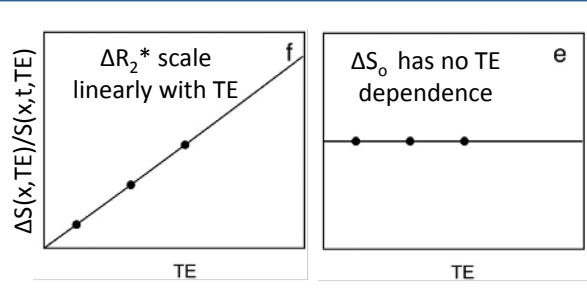
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❖ ME-ICA Applications

MULTI-ECHO DATASET

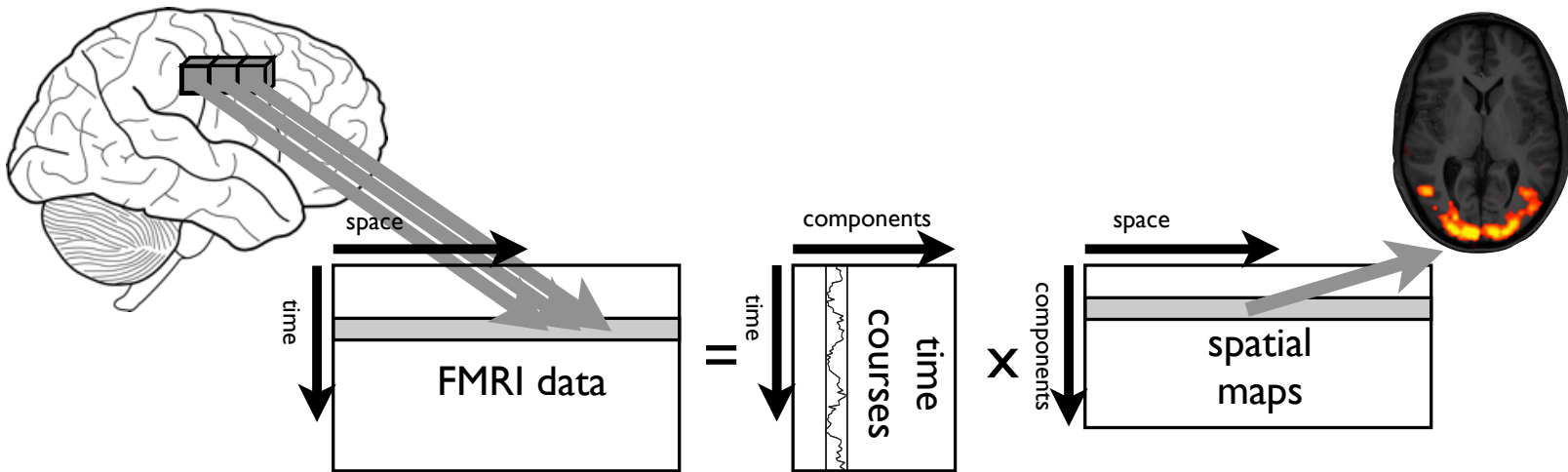


TE-DEPENDENCE MODEL



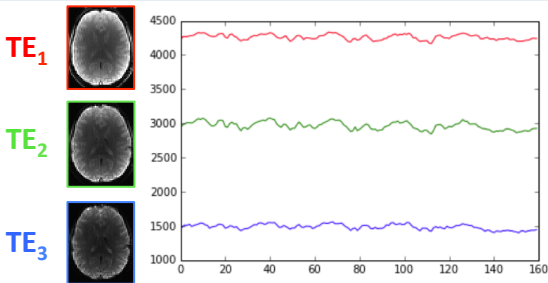
TIMESERIES OF INTEREST

ICA Representative Timeseries

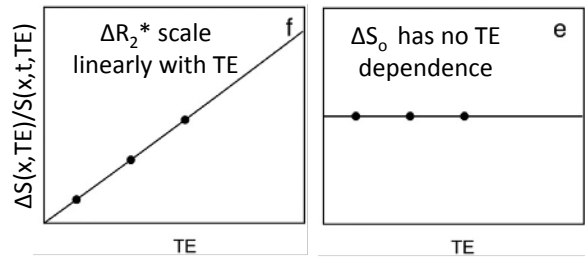


Data is represented as a 2D matrix and decomposed into factor matrices (or modes)

MULTI-ECHO DATASET



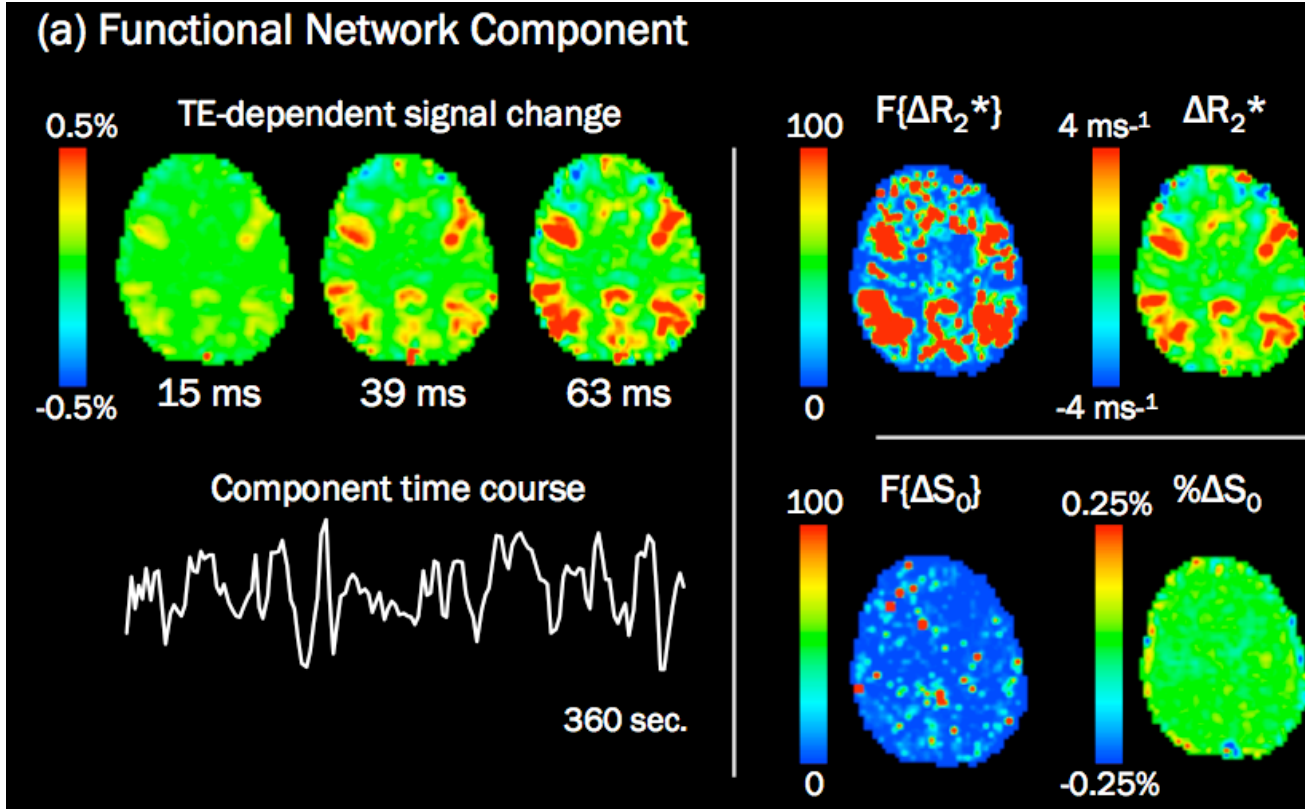
TE-DEPENDENCE MODEL



TIMESERIES OF INTEREST

ICA Representative Timeseries

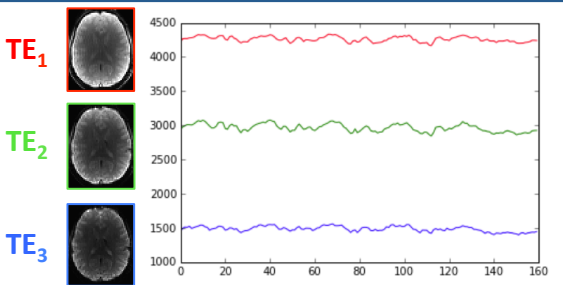
(a) Functional Network Component



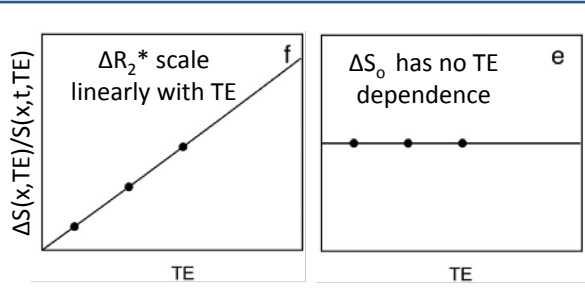
Kappa (κ) = 210

Rho (ρ) = 10

MULTI-ECHO
DATASET



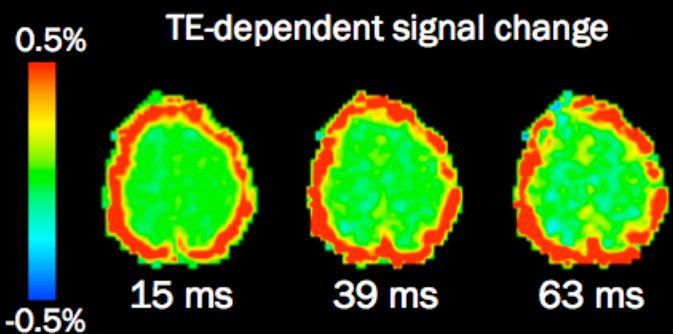
TE-DEPENDENCE
MODEL



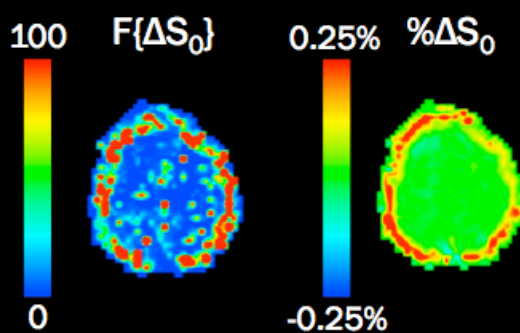
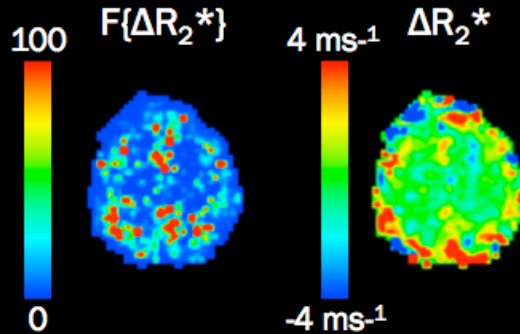
TIMESERIES OF INTEREST

ICA Representative
Timeseries

(b) Artifact Component



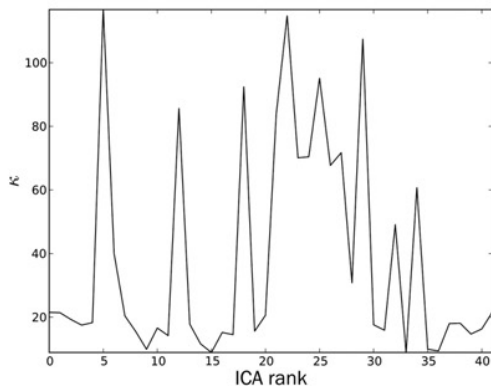
Component time course



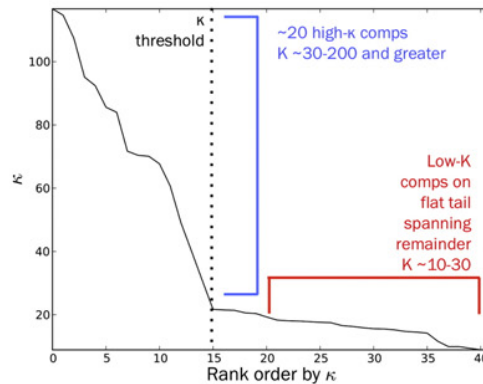
Kappa (κ) = 32

Rho (ρ) = 81

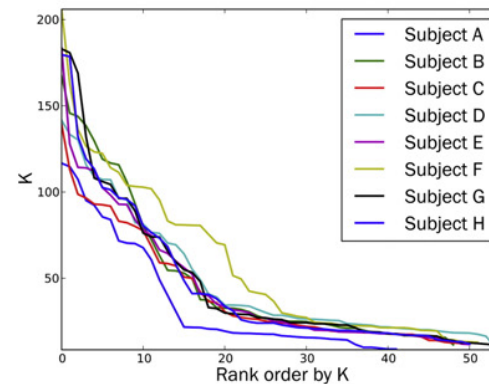
a κ vs. ICA rank



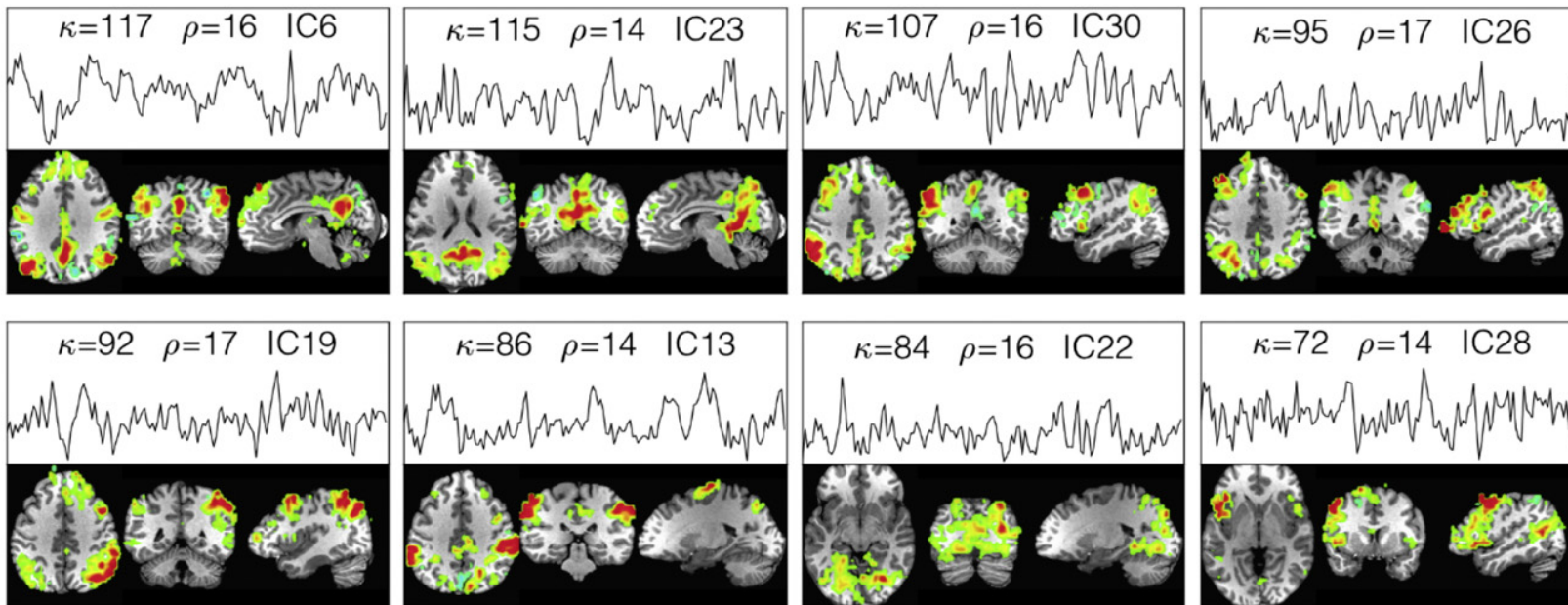
b κ spectrum



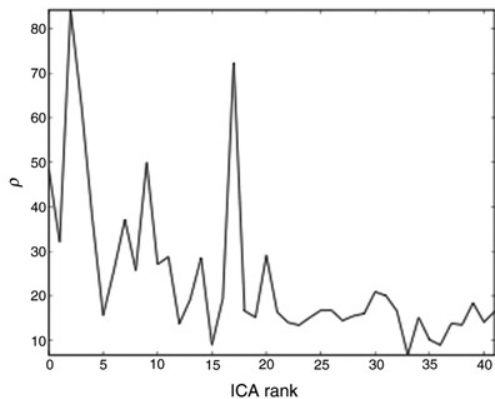
c κ spectra across subjects



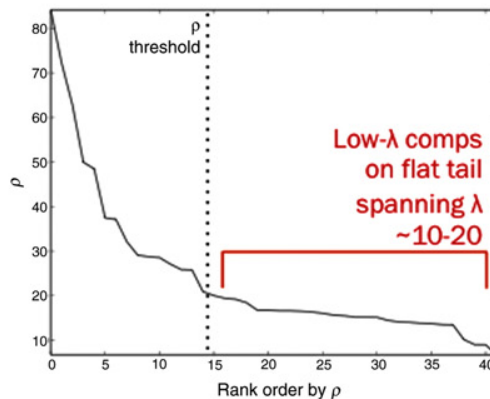
d ΔR_2^* maps of top κ ranked components for a representative subject



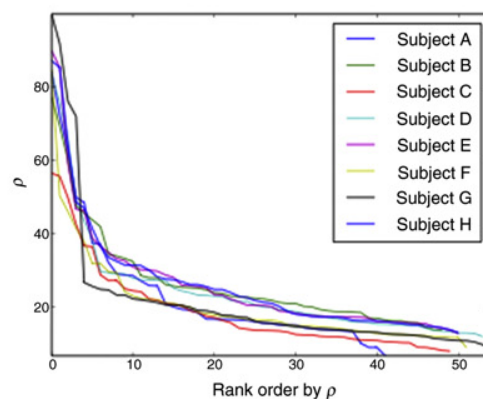
a ρ vs. ICA rank



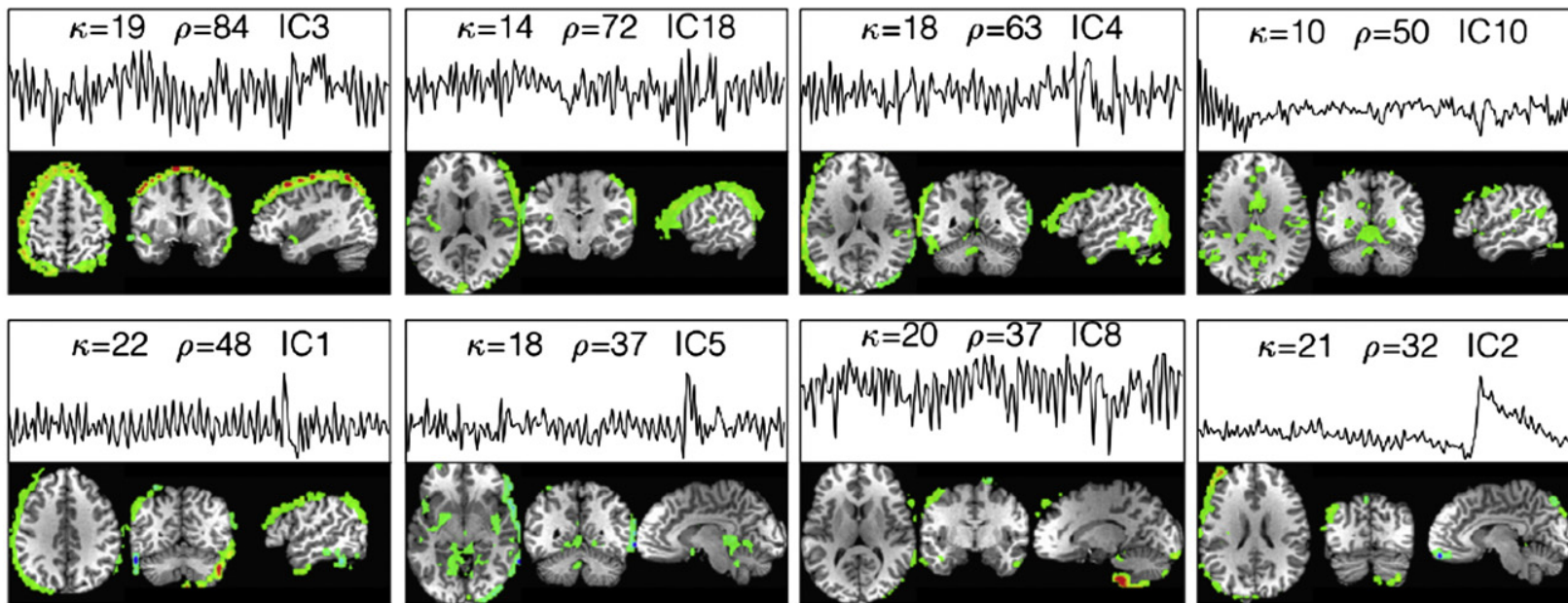
b ρ -spectrum

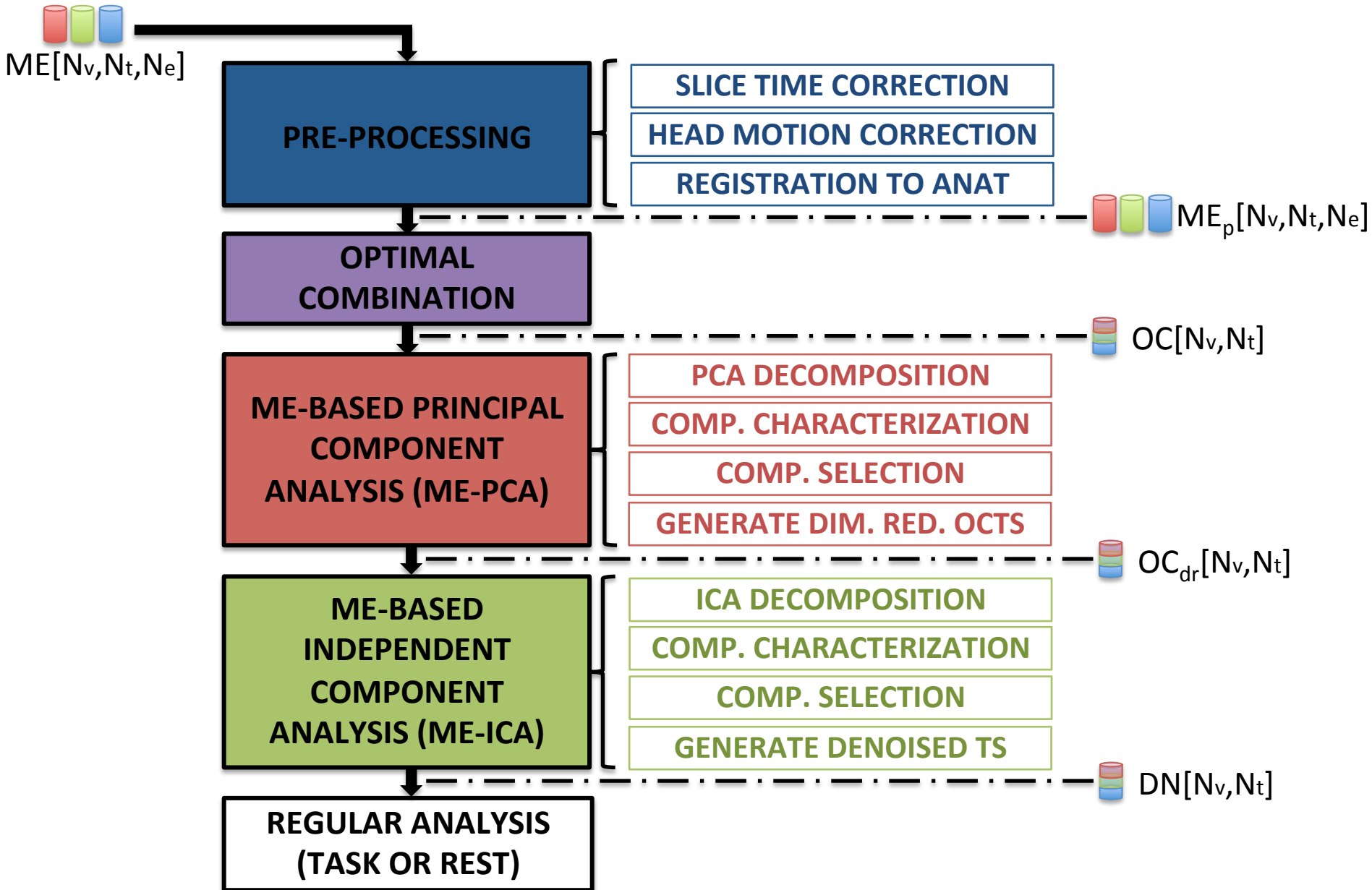


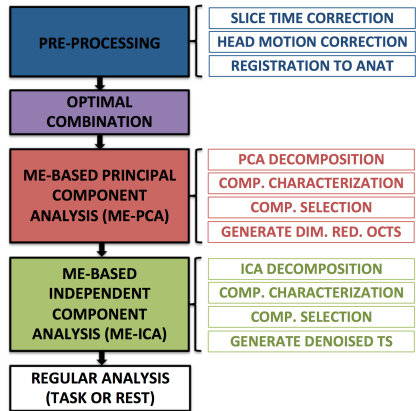
c ρ -spectrum across subjects



d ΔS_0 maps of top ρ -ranked components for a representative subject







ME-PCA

- Uses PCA Decomposition (orthogonality).
- Yet, estimation of model order (Ncomp) is not based on variance, but on κ and ρ thresholds.
 - $\kappa_{thr} = f(\kappa_{elbow}, \kappa_{daw})$; Default $\kappa_{daw} = 10$
 - $\rho_{thr} = f(\rho_{elbow}, \rho_{daw})$; Default $\rho_{daw} = 1$
 - SELECTION RULE: $\kappa > \kappa_{thr}$ are kept
 - SELECTION RULE: $\rho > \rho_{thr}$ are kept

ME-ICA

- Uses fast-ICA algorithm (spatial independence).
- Component Characterization includes:

- Variance Explained

- κ ("BOLD likeliness")

- ρ ("Non-BOLD likeliness")

- Nvoxels that significantly fit the S_0 model

- Nvoxels that significantly fit the R_2^* model

- Spatial overlap (D) between ICA map and FR_2^* map

- Spatial overlap (D) between ICA map and FS_0 map

- Other...

$\left. \begin{array}{l} \kappa \\ \rho \end{array} \right\} \rightarrow \text{If } \kappa_c < \rho_c \rightarrow \text{Discard } c$

$\left. \begin{array}{l} N_{so,c} \\ N_{R2,c} \end{array} \right\} \rightarrow \text{If } N_{so,c} < N_{R2,c} \rightarrow \text{Discard } c$

$\left. \begin{array}{l} D_{so,c} \\ D_{R2,c} \end{array} \right\} \rightarrow \text{If } D_{so,c} < D_{R2,c} \rightarrow \text{Discard } c$



Denoised Time series

INPUTS

- Minimum: fMRI Datasets for all echoes, echo times
- Extras: Anatomical, Pre-processing options, kdaw, rdaw,

OUTPUTS

- T2* Static Map: *t2v.nii*
- So Static Map: *s0v.nii*
- Optimally Combined time series: *ts_OC.nii*
- Denoised time series: *dn_ts_OC.nii*
- Spatial Maps for all ICA components: *betas_OC.nii*
- Spatial Maps for Accepted Components only: *betas_hik_OC.nii*
- Time series for all PCA Components: *mepca_mix.1D*
- Time series for all ICA Components: *meica_mix.1D*
- Summary of ICA Decomposition: *comp_table.txt*
 - List of accepted components
 - List of rejected components
 - List of Mid-k components
 - List of ignored components
 - Kappa and Rho values for all components
 - Total Variance Explained by the ICA decomposition

ME-ICA Software available with AFNI: <http://afni.nimh.nih.gov/afni>

Latest experimental versions (P. Kundu) available at: <https://bitbucket.org/prantik/me-ica.git>

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Your ME-ICA Report!

The program meica.py was created to form an algorithmic method for performing independent component analysis on multi-echo data and then algorithmically deciding which components represent BOLD-like phenomena.

The following content is a report that has taken information provided by meica.py and summarizes a few of the results.

This report form was created by the Section on Functional Imaging Methods in the NIMH. The creators of this report form are Benjamin Gutierrez, Prantik Kundu, Daniel Handwerker, Javier Gonzalez-Castillo, Souheil Inati, and Peter Bandettini.

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file:///spin1/users/SFIMJGC/TALK_fMRIclassME/PrCsData/SBJ02/D03_Meica/SBJ02_S02Run10/meica.Report.SBJ02_S02Run10/html/diagnostics.html#tsnr

❖ WHAT IS MULTI-ECHO (ME) FMRI

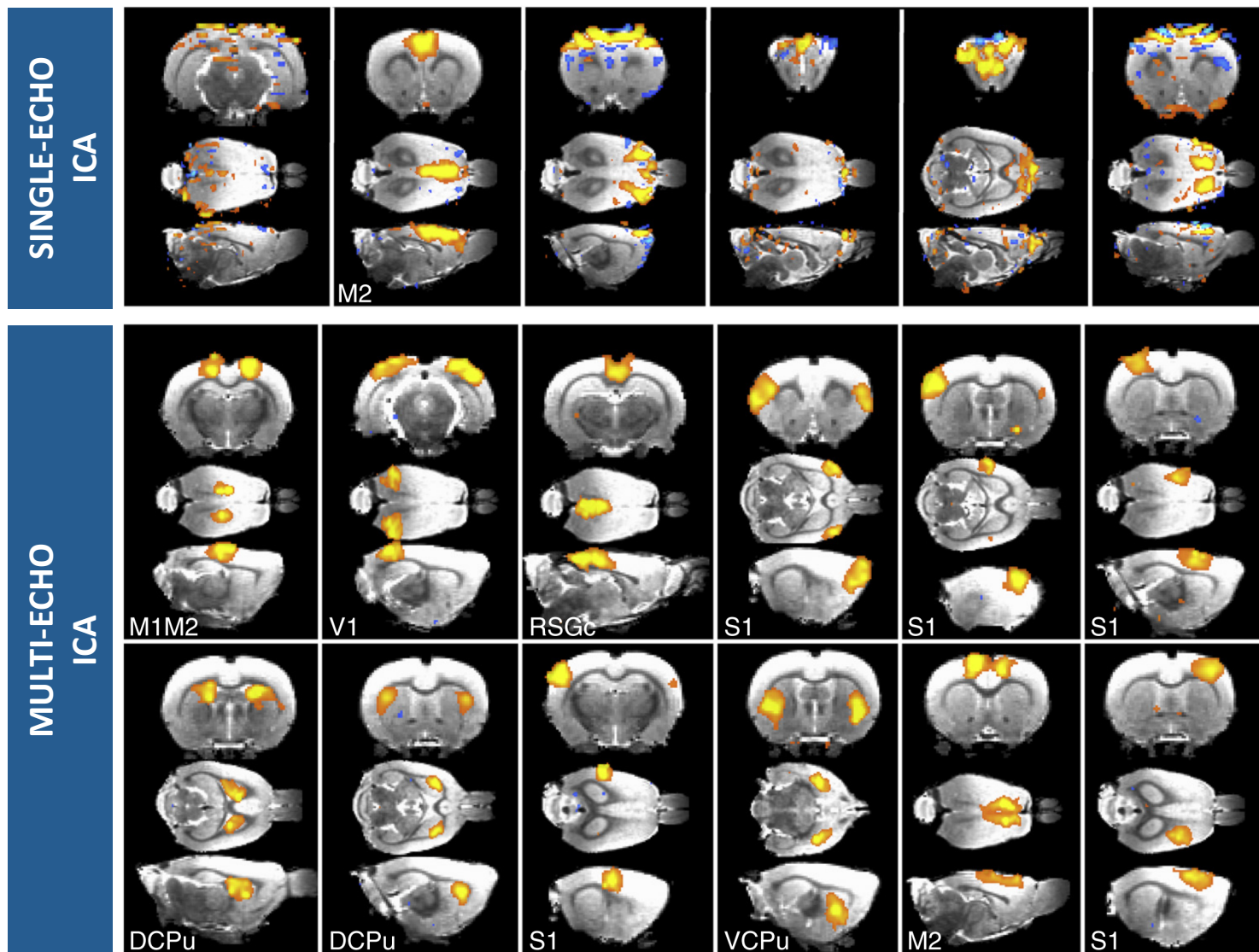
❖ WHAT CAN YOU DO WITH ME TIMESERIES

- Compute static S_0 and T_2^* Maps
- Compute voxel-wise time-series of S_0 (Non-BOLD) and T_2^* (BOLD)
- Combine echoes to improve SNR/spatially equalize functional contrast
- Echo Time Dependence Analysis

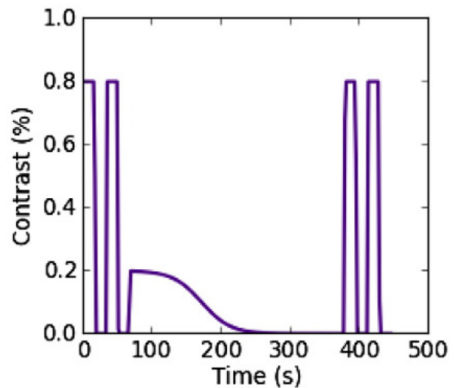
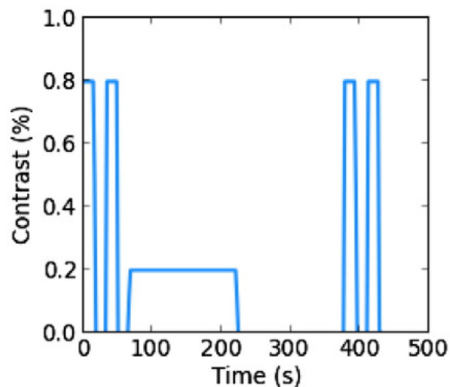
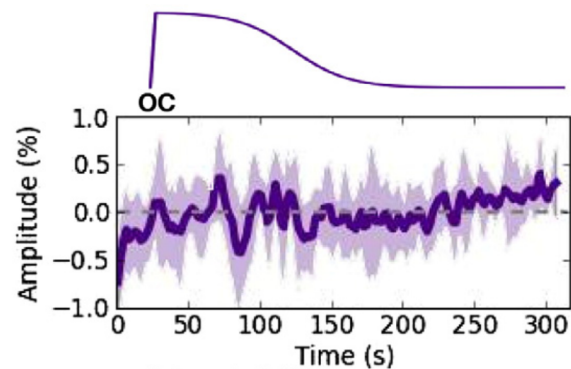
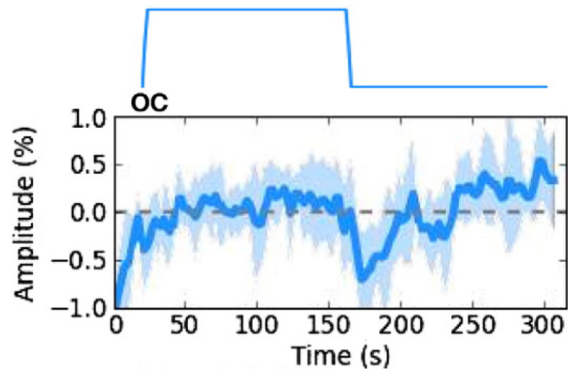
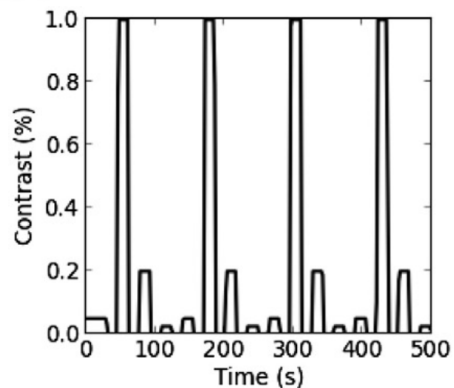
❖ ME-ICA Denoising

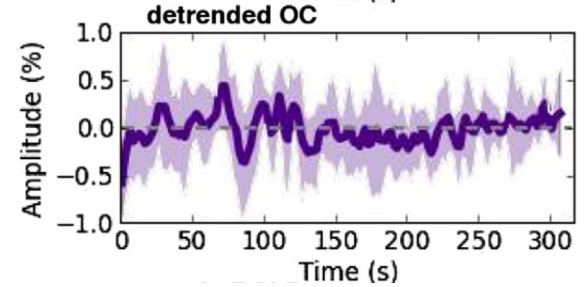
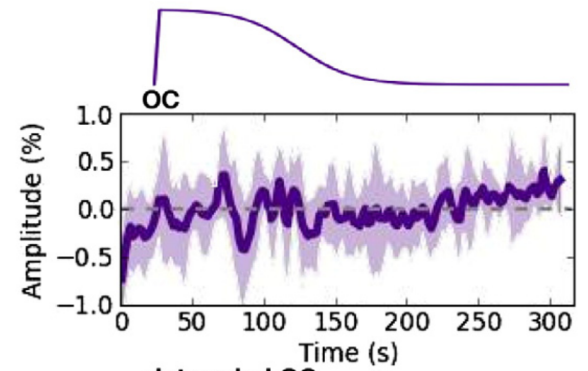
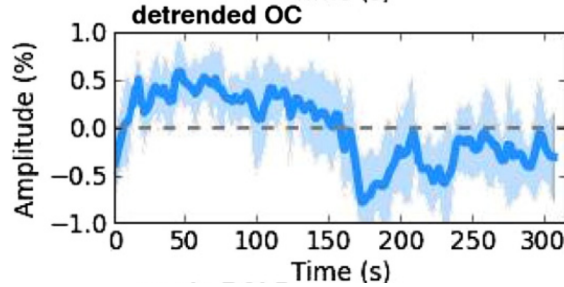
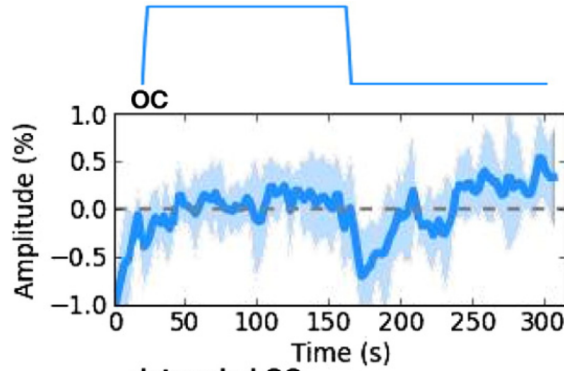
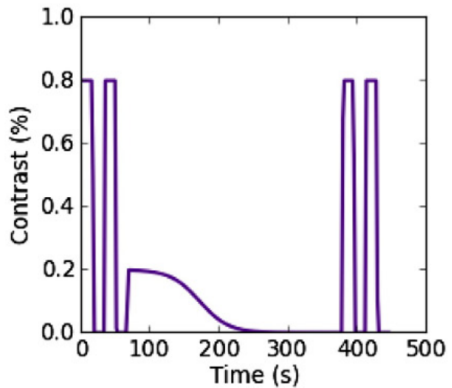
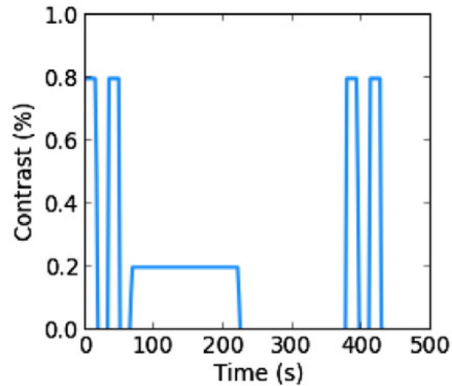
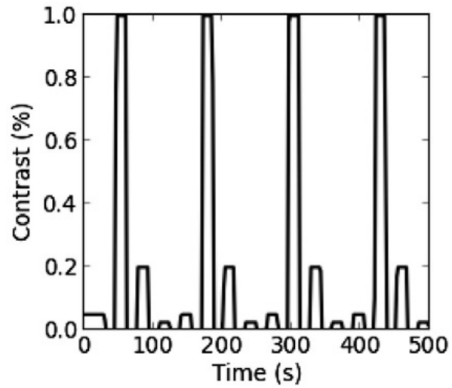
- ME-ICA Pipeline
- ME-ICA Outputs
- ME-ICA Web Reporting Tool

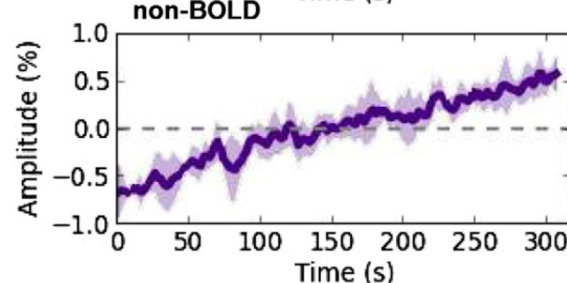
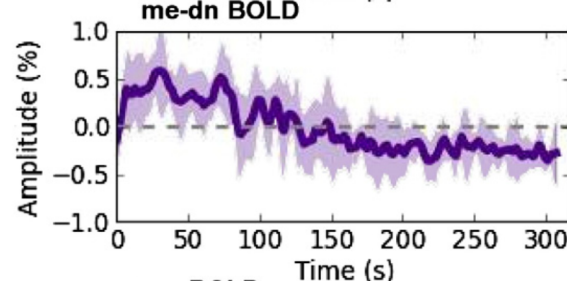
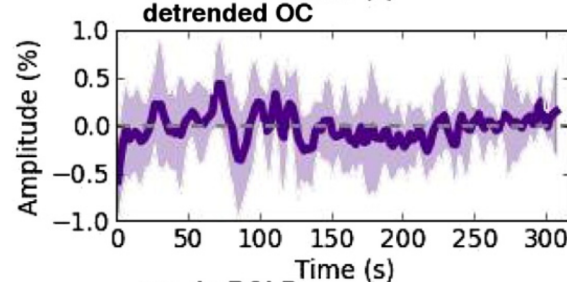
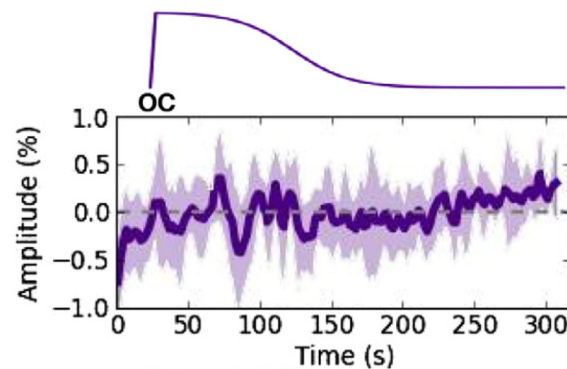
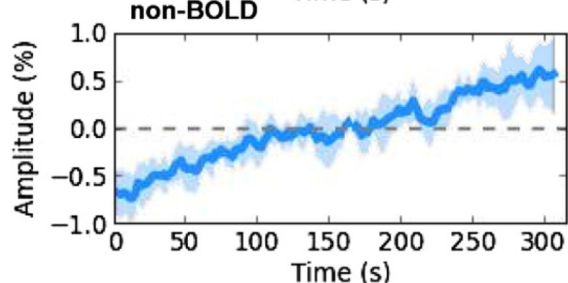
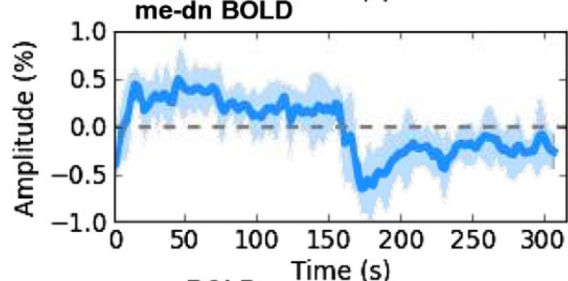
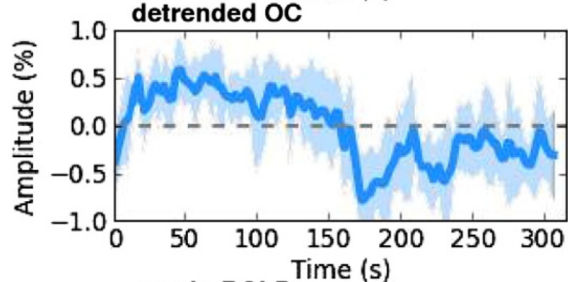
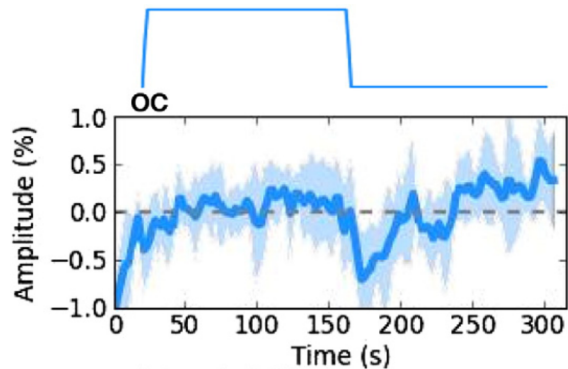
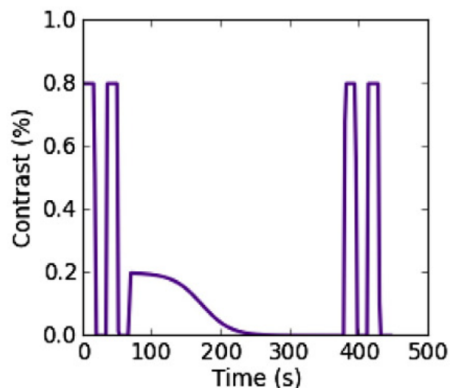
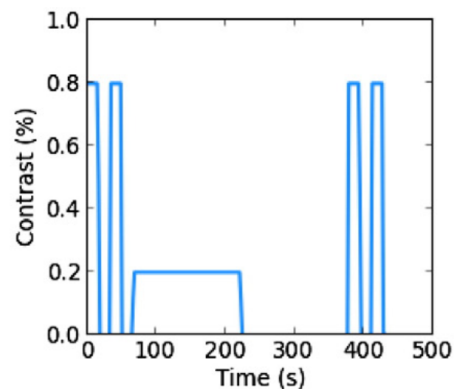
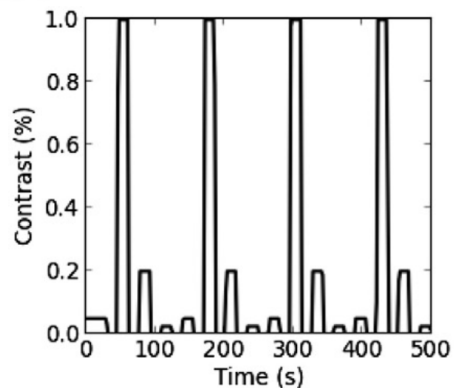
❖ ME-ICA Applications



Scanner 11.7T | 0.5x0.5x0.5mm | TR = 3s |
TE=8.25/20.25/32.35 ms | 400 volumes | Rats





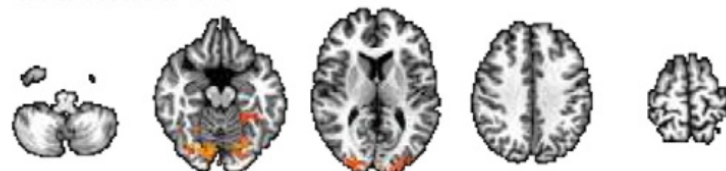




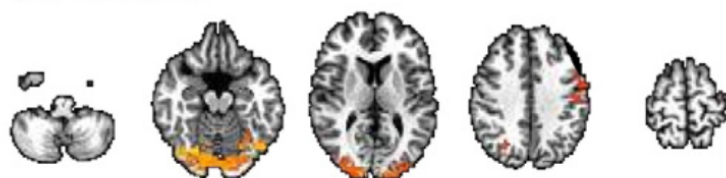
OC



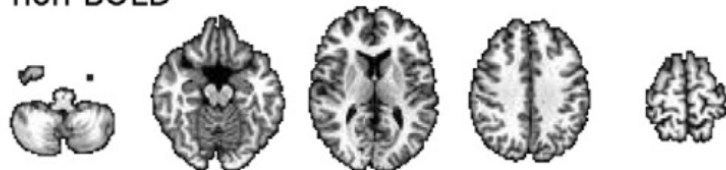
detrended OC



me-dn BOLD



non-BOLD

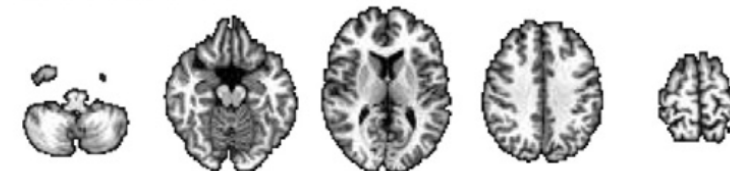


b)

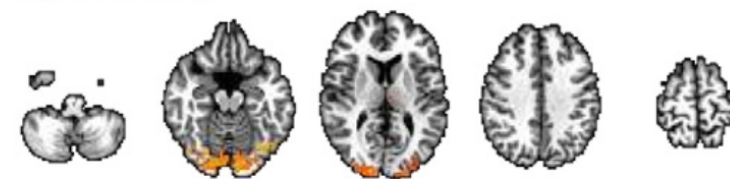
OC



detrended OC

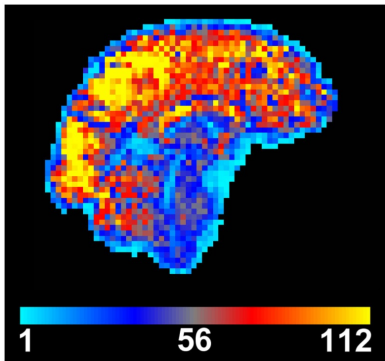
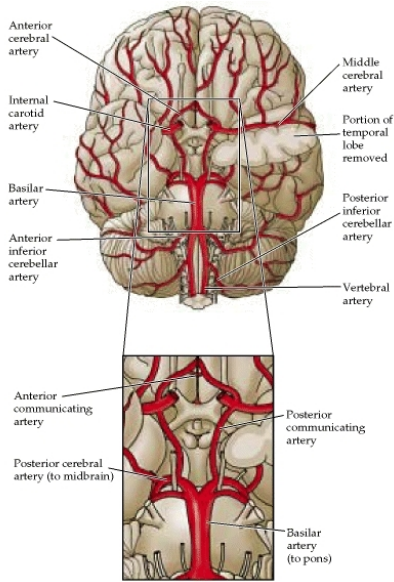


me-dn BOLD

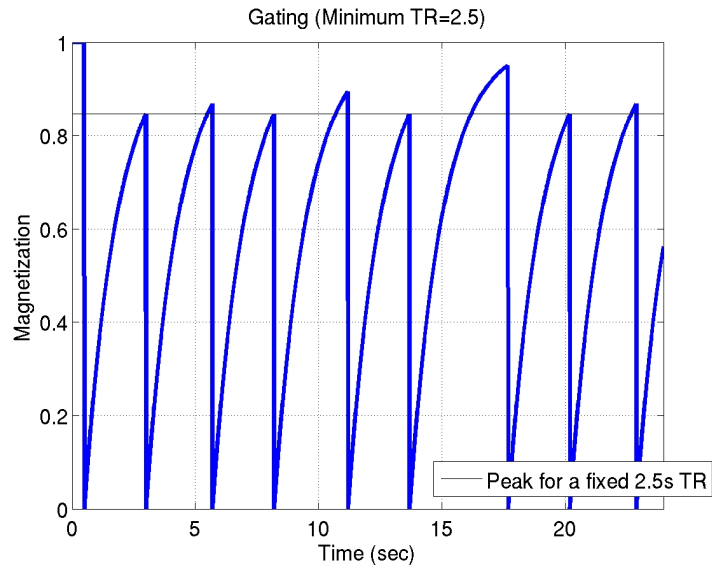
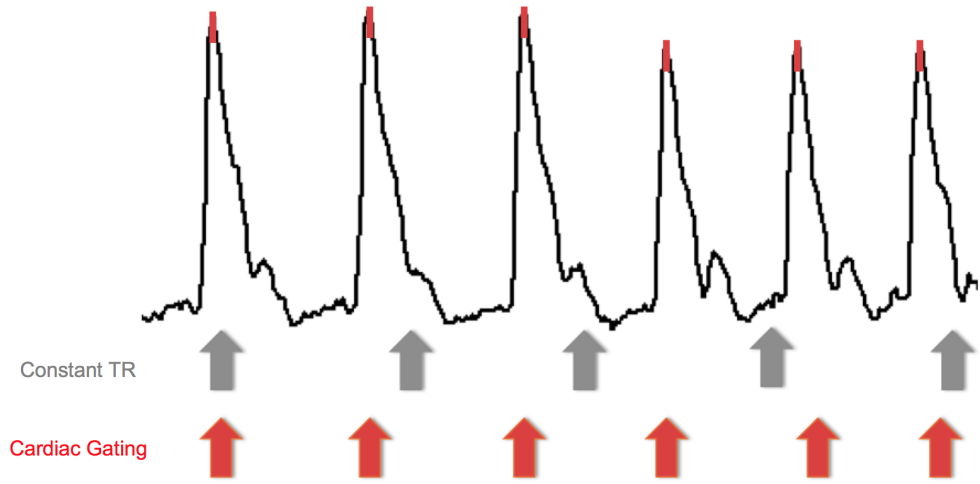


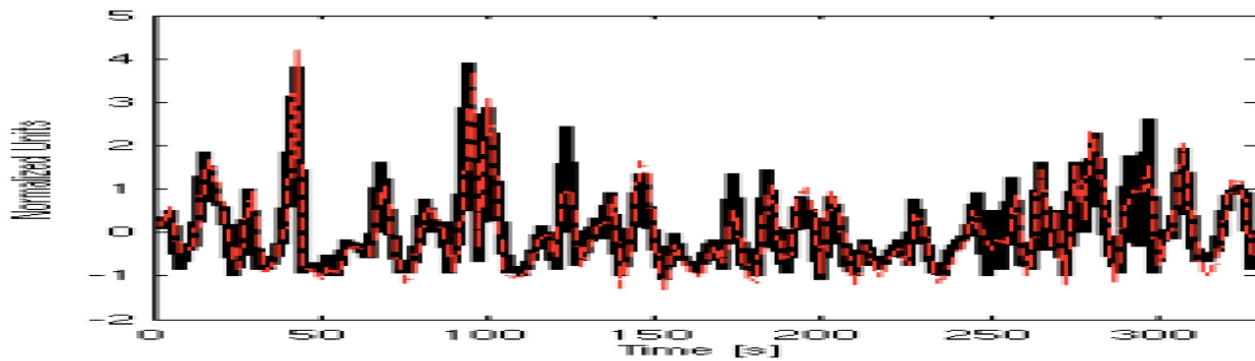
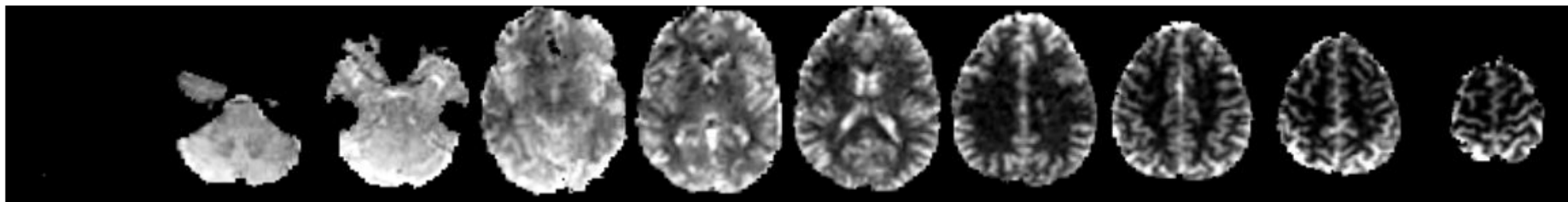
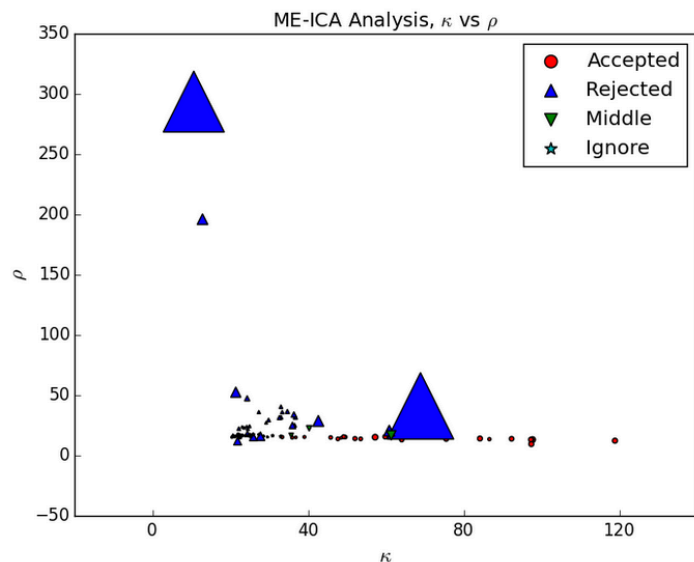
non-BOLD



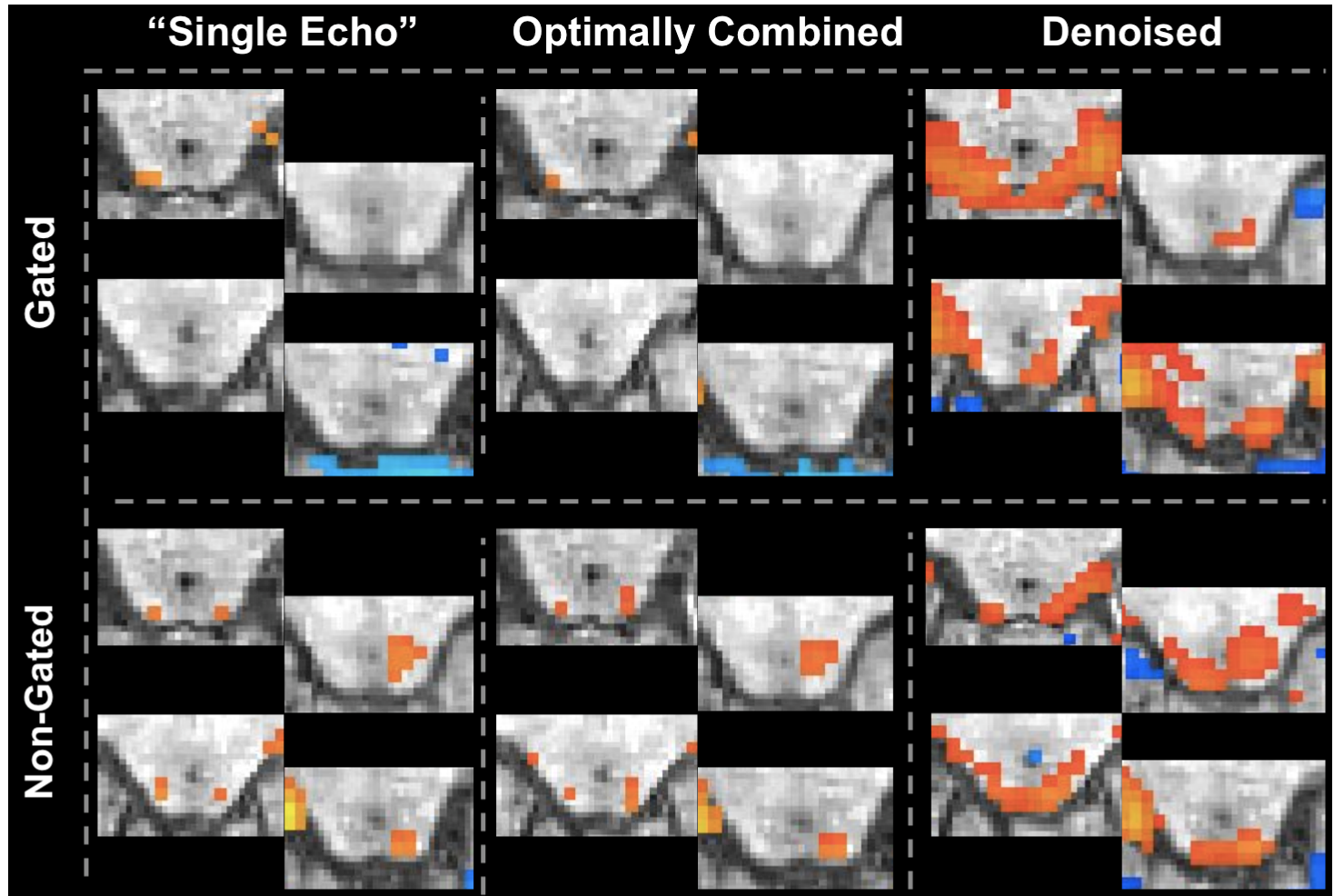


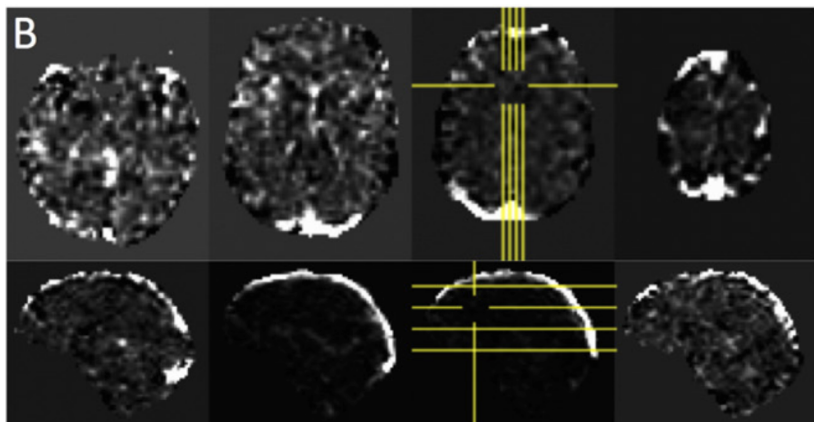
Brooks et al. 2014



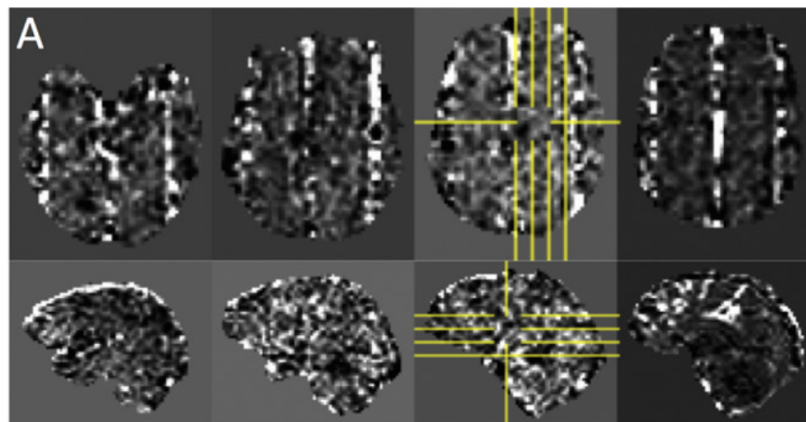


--- Component TS
 — ΔTR

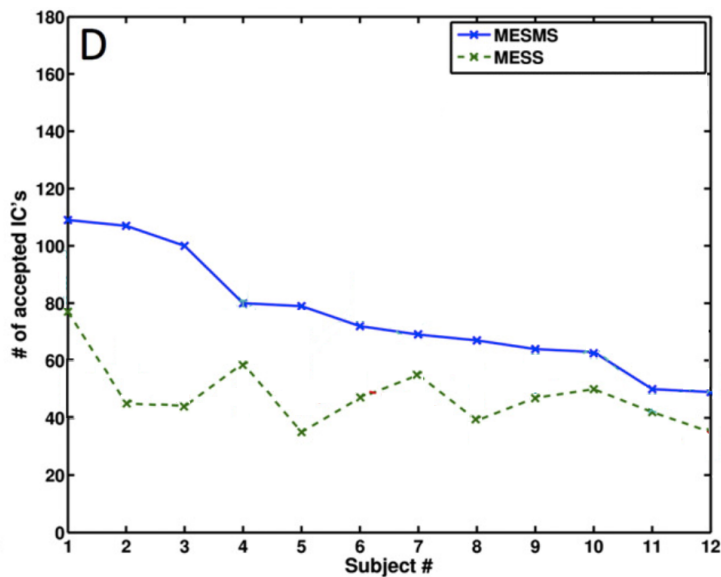




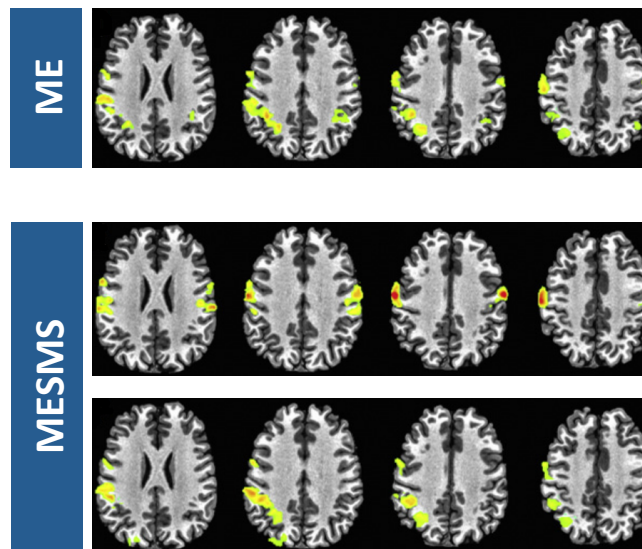
Non-BOLD Component: Vascular Pulsation



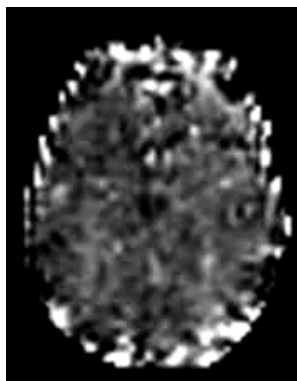
Non-BOLD Component: MSS Artifact



Number of BOLD-like components significantly larger for MESMS

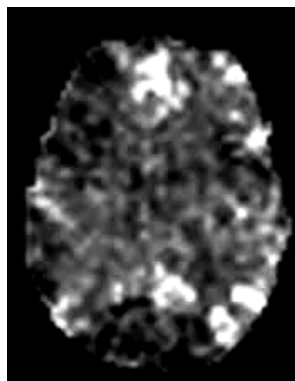


- ❑ Multi-echo fMRI allows to capture additional information with minimal costs in terms of temporal and spatial resolution.
- ❑ Such additional information can be used to:
 - ❑ Increase CNR in drop-out regions (e.g., Optimal Combination of Echoes).
 - ❑ Automatically separate BOLD-like from Non-BOLD-like components (ME-ICA).
- ❑ ME-ICA is a promising denoising methodology that combines ICA with TE-Dependence Analysis:
 - ❑ Will not clean every single artifact in the data.
 - ❑ Still under development.
 - ❑ Can substantially improve the SNR of the data → Quality of the results.



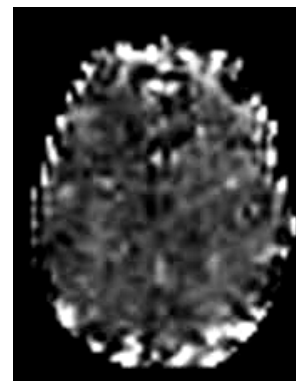
ME-fMRI

=



ACCEPTED

+



REJECTED

+

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 Hang Joon Jo
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 Dave Jangraw
 Meghan Robinson
 Colin Hoy
 Laura Buchanan
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