Multi-echo EPI for task-based and resting-state fMRI

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Section on Functional Imaging Methods, NIMH, NIH

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Agenda

❖ WHAT IS MULTI-ECHO (ME) FMRI

*** WHAT CAN YOU DO WITH ME TIMESERIES**

- Compute static S₀ and T₂* Maps
- Compute voxel-wise time-series of S₀ (Non-BOLD) and T₂* (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



Where to go for additional information...

NeuroImage 154 (2017) 59-80



Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage



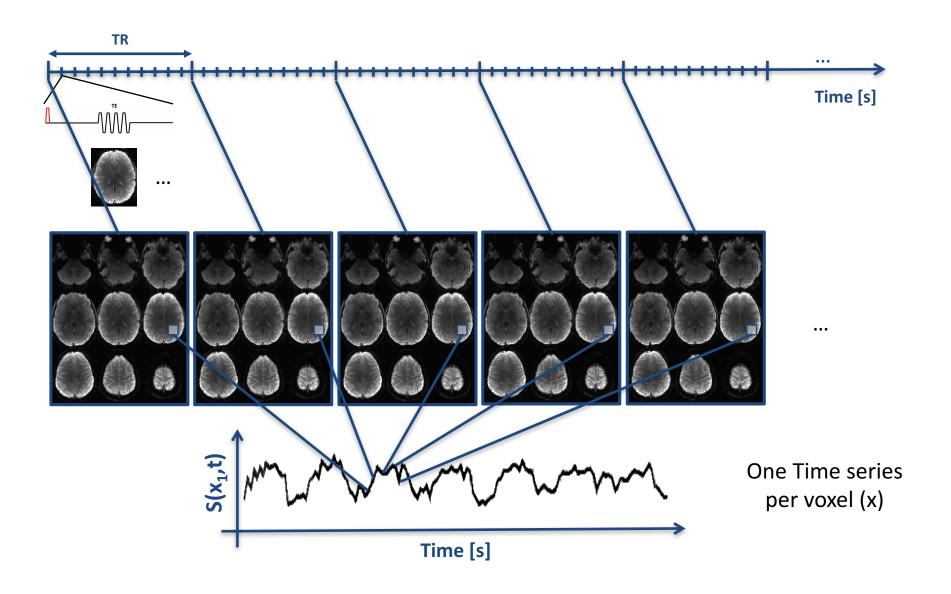
Multi-echo fMRI: A review of applications in fMRI denoising and analysis of BOLD signals



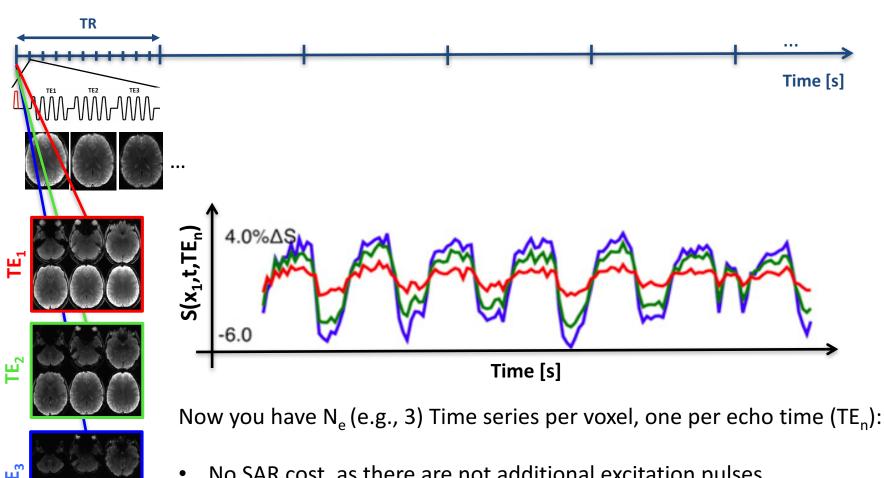
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- ^a Departments of Radiology and Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY, USA
- ^b Behavioral and Clinical Neuroscience Institute, University of Cambridge, Cambridge, UK
- ^c Department of Psychology and Center for Applied Neuroscience, University of Cyprus, Nicosia, Cyprus
- ^d Department of Cognitive Neuroscience, Maastricht University, Maastricht, NL, The Netherlands
- ^e Section on Functional Imaging Methods, National Institute of Mental Health, Bethesda, MD, USA

Single-Echo fMRI (a.k.a. Your regular fMRI)



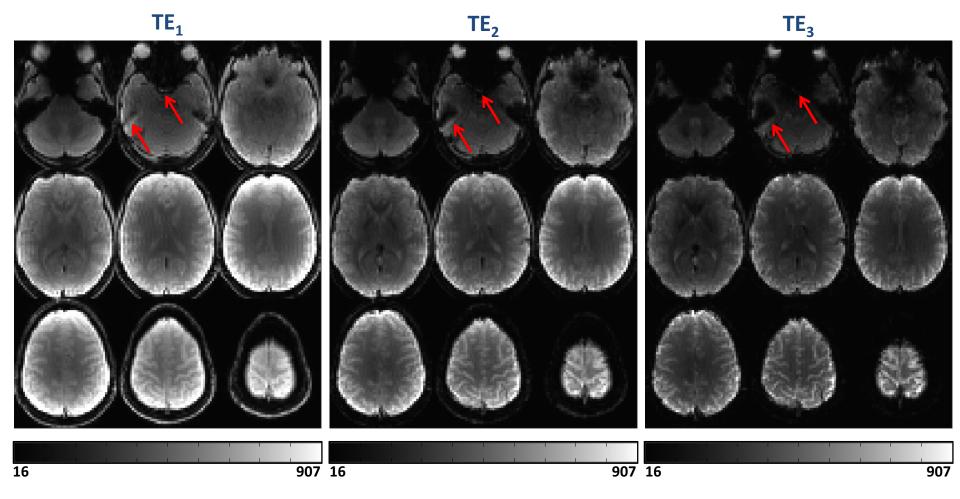
Multi-Echo fMRI



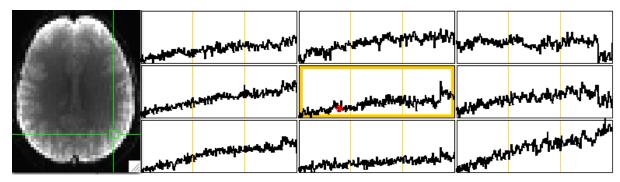
- No SAR cost, as there are not additional excitation pulses.
- Slight lost in temporal resolution to fit the third echo.
- Slight lost in spatial resolution to make sure you have signal in last echo.



Multi-Echo fMRI (II)



Signal Model



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

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

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

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

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

Captures local fluctuations in field inhomogeneity (including BOLD)

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

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



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ME-ICA Applications

How to Compute Spatial Maps of $\overline{S_o}$ and $\overline{T_2}^*$

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

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

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

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:

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

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

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

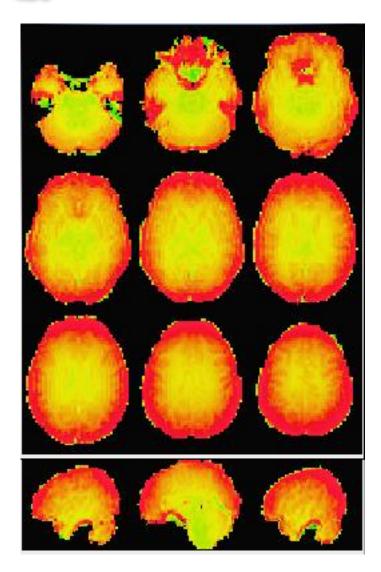
$$y(x,TE) = a(x) * TE + b(x)$$

Linear system of equations for 3 echoes

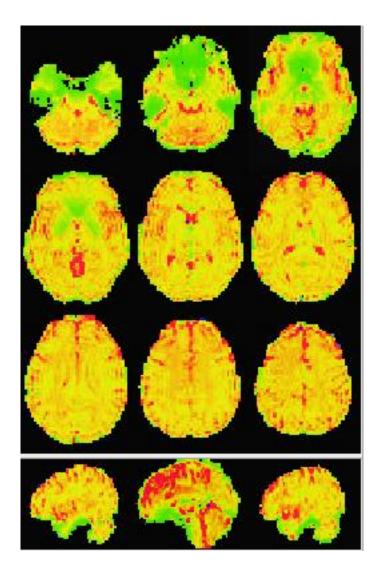
$$\begin{cases} \log(\overline{S(x,TE_1)}) = -\overline{R_2^*(x)} \cdot TE_1 + \log(\overline{S_o(x)}) \\ \log(\overline{S(x,TE_2)}) = -\overline{R_2^*(x)} \cdot TE_2 + \log(\overline{S_o(x)}) \\ \log(\overline{S(x,TE_3)}) = -\overline{R_2^*(x)} \cdot TE_3 + \log(\overline{S_o(x)}) \end{cases}$$



How to Compute Spatial Maps of $\overline{S_o}$ and $\overline{T_2}^*$



Static So Map (s0v.nii)



Static T₂* Map (t2sv.nii)



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FIM

How to Compute Time series of ΔS_o and ΔR_2^* fluctuations

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

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

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

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

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

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

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

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

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

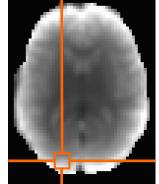
$$\Delta \rho(x,t) = \Delta S_o(x,t) / \overline{S_o(x)} \\
\Delta \kappa(x,t) = \Delta R_2^*(x,t) \cdot \overline{TE}$$

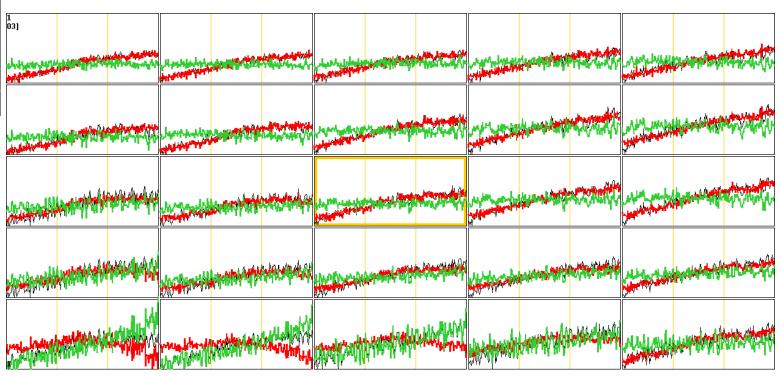
$$\Rightarrow S(x,t,TE) \approx \overline{S(x,TE)} \cdot \left[1 + \Delta \rho(x,t) - \frac{TE}{\overline{TE}} \Delta \kappa(x,t)\right] \tag{5}$$

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



How to Compute Time series of ΔS_o and ΔR_2^* fluctuations

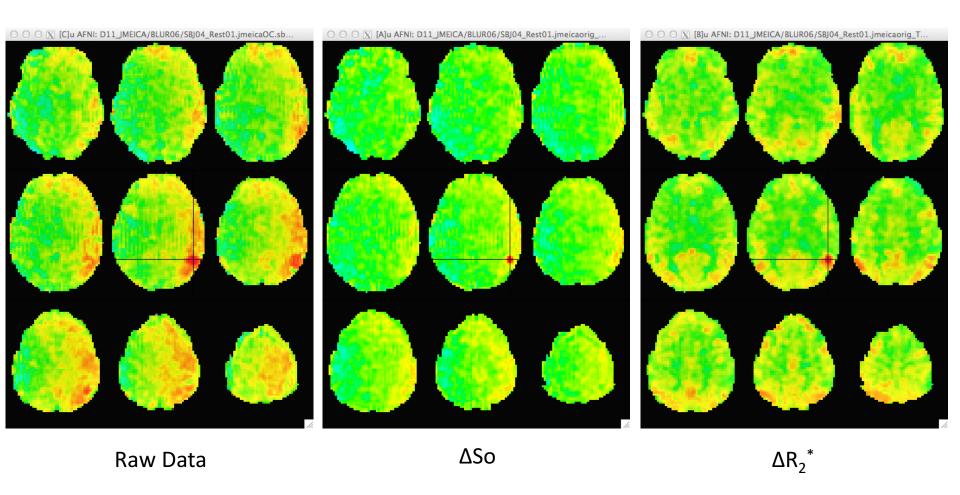




$$\longrightarrow S(x,t,TE_2) \longrightarrow \Delta S_o(x,t) \longrightarrow \Delta R_2^*(x,t)$$



How to Compute Time series of ΔS_o and ΔR_2^* fluctuations



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



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Combination of Multi-Echo Time series

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

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

 $\hat{S}(x,t) = \sum_{n=1}^{N} S(x,t,TE_n)$ • Noisy data at longer echoes reduce the overall gain in sensitivity.

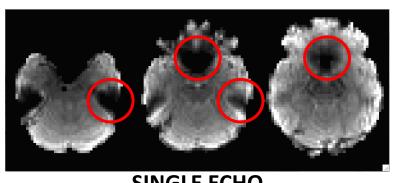
Weighted Summation

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

$$T_n = \frac{TE_n e^{-TE_n/T_{2,v}^*}}{\sum_{n=0}^{\infty} TE_n e^{-TE_n/T_{2,v}^*}}$$

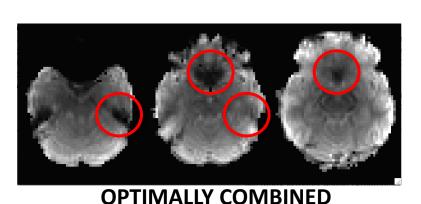
 $\hat{S}(x,t) = \sum_{n=1}^{N} S(x,t,TE_n) \cdot w_v(TE_n)$ • Helps to spatially maximize CNR and also to recover some signal level in regions affected by drop-out. $w_v(TE_n) = \frac{TE_n e^{-TE_n/T_{2,v}^*}}{\sum_n TE_n \cdot e^{-TE_n/T_{2,v}^*}}$

Posse et al., MRM 1999



SINGLE ECHO







Combination of Multi-Echo Time series

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

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

 $\hat{S}(x,t) = \sum_{n=1}^{N} S(x,t,TE_n)$ • Noisy data at longer echoes reduce the overall gain in sensitivity.

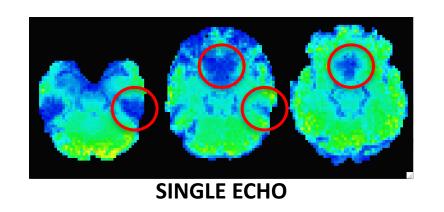
Weighted Summation

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

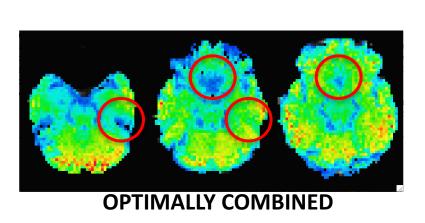
$$w_{v}(TE_{n}) = \frac{TE_{n}e^{-TE_{n}/T_{2,v}^{*}}}{\sum_{n}TE_{n} \cdot e^{-TE_{n}/T_{2,v}^{*}}}$$

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









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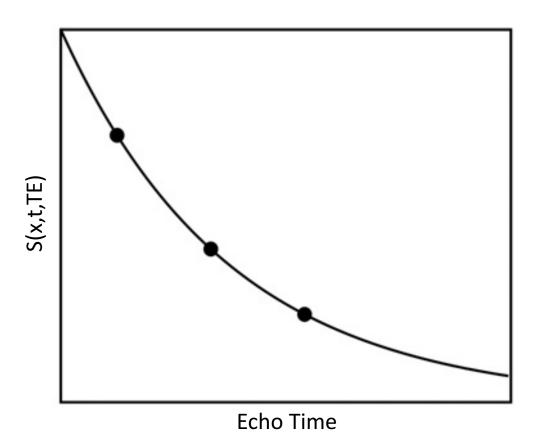
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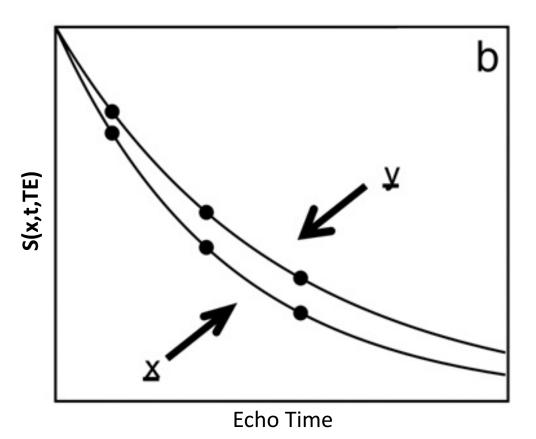
$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

Let's assume that a given voxel (x) and time (t) So(x,t)=5000 and T2*(x,t)=30ms



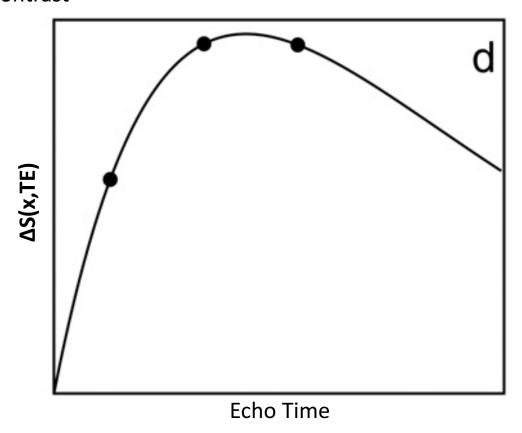
$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

Let's assume now, that a local change in oxygenation happens (T₂* effect)



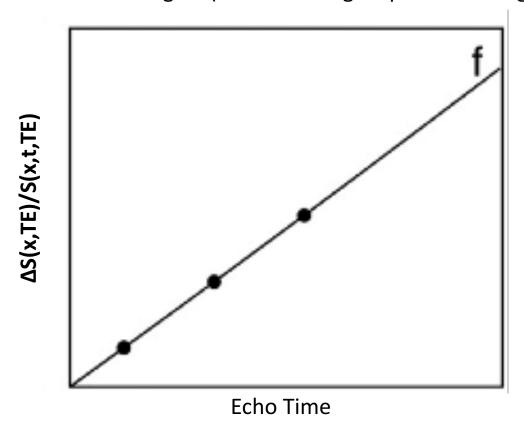
$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

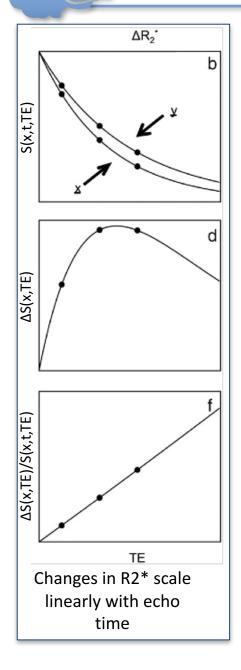
We could then use the difference between two curves to examine which is the optimal TE to maximize BOLD contrast



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

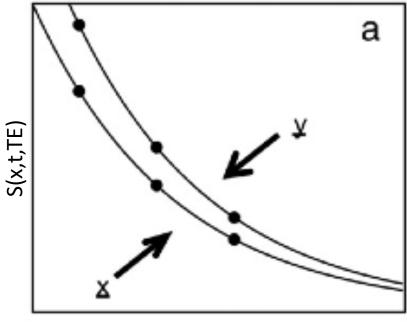
Most importantly for our discussion, for T₂* signal changes, there is a linear relationship between echo time and measured signal (in terms of signal percent change)



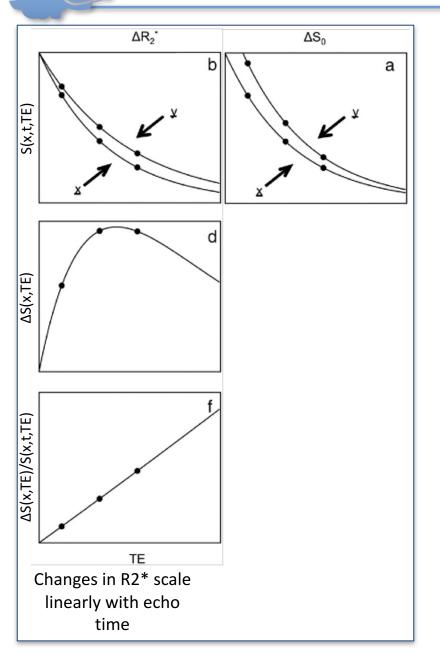


$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

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

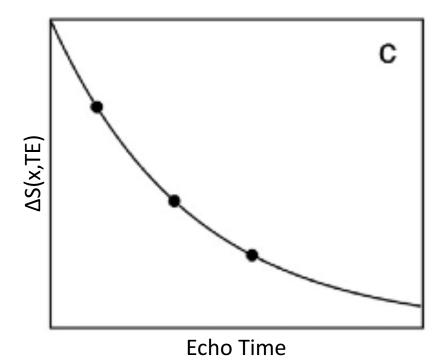


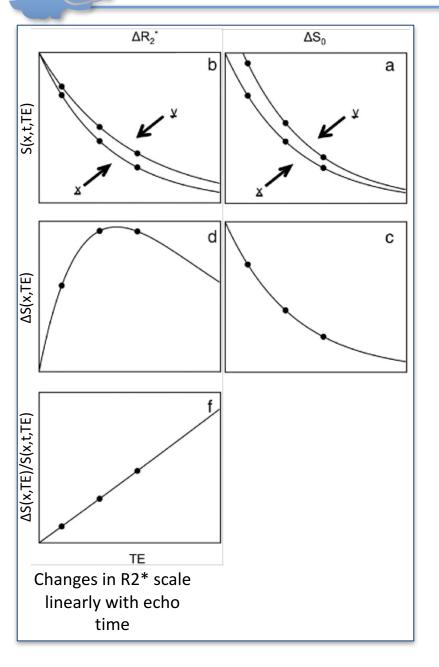
Echo Time



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

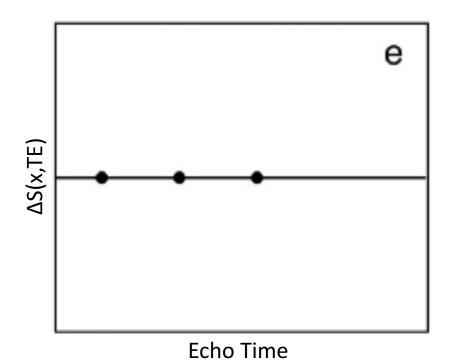
This time the difference between both curves looks very different

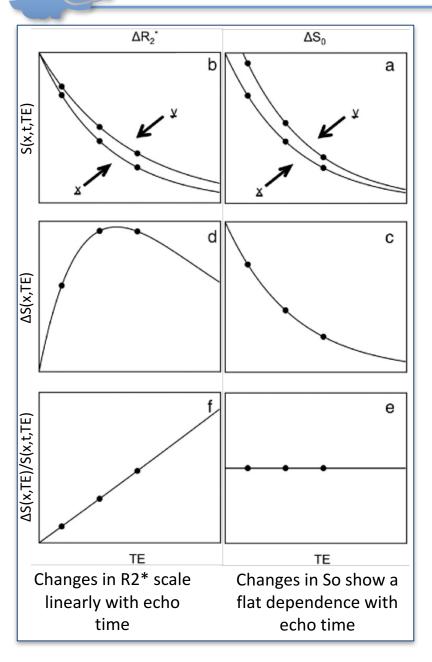




$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

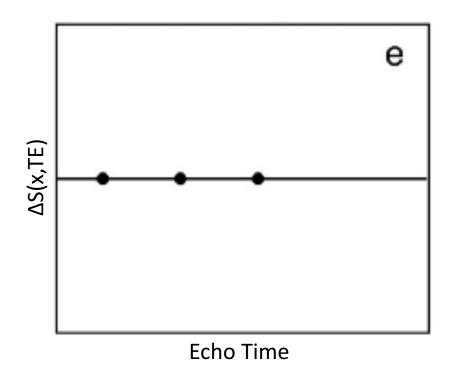
In term of signal percent change, changes in So have a flat dependence with echo time



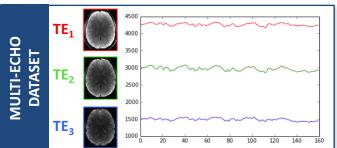


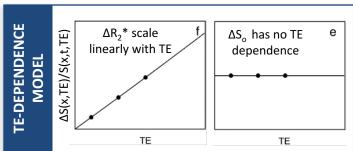
$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

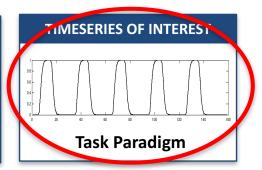
In term of signal percent change, changes in So have a flat dependence with echo time



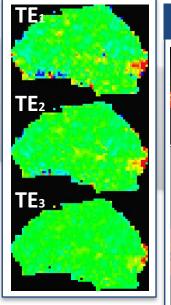






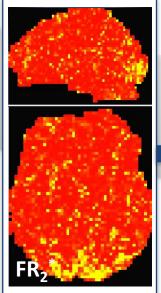




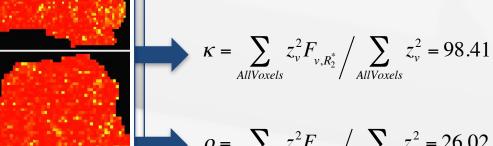


[2] Voxel-wise Goodness of Fit to R2* Model

FS_o



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



$$\rho = \sum_{AllVoxels} z_v^2 F_{v,S_o} / \sum_{AllVoxels} z_v^2 = 26.02$$

[4] Compute Avg. Metric for each model



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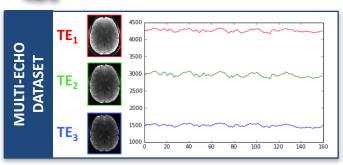
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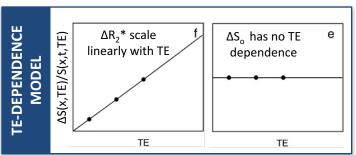
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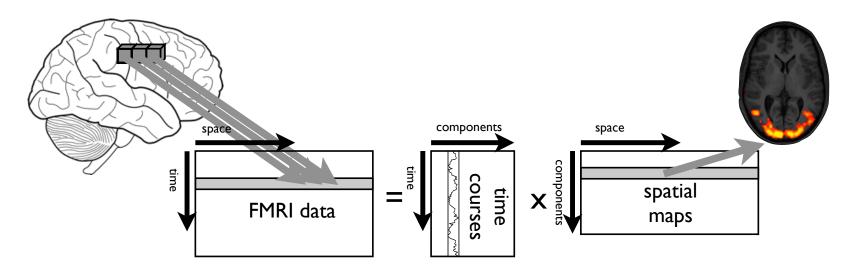
ME-ICA Applications





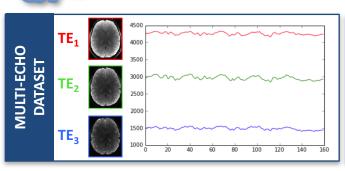


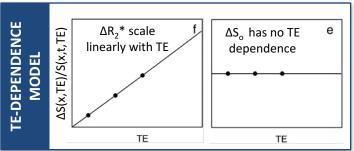
ICA Representative
Timeseries



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

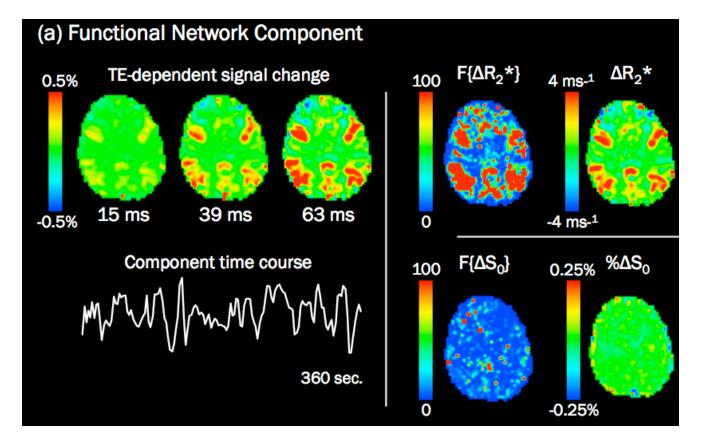






TIMESERIES OF INTEREST

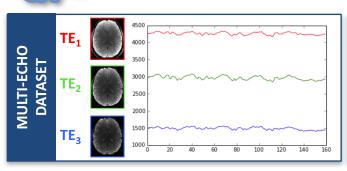
ICA Representative Timeseries

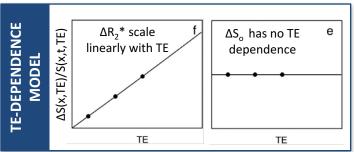


Карра (
$$\kappa$$
) = 210

Rho (
$$\rho$$
) = 10

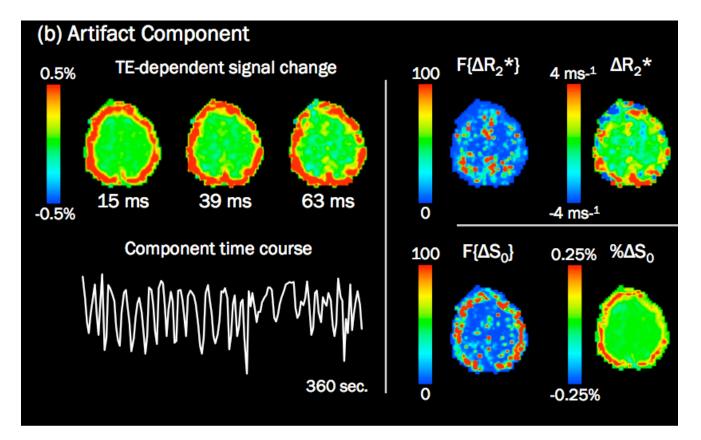






TIMESERIES OF INTEREST

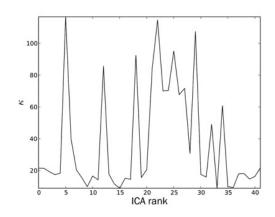
ICA Representative Timeseries



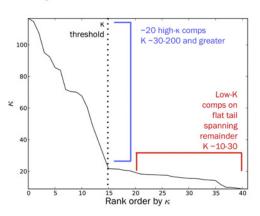
Kappa (
$$\kappa$$
) = 32

Rho (
$$\rho$$
) = 81

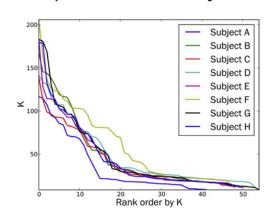
a κ vs. ICA rank



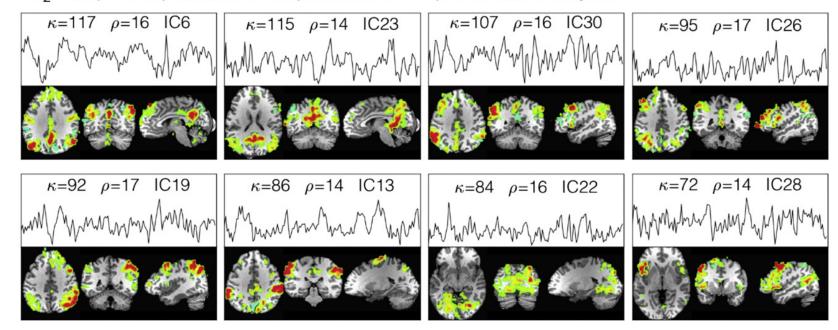
b κ spectrum

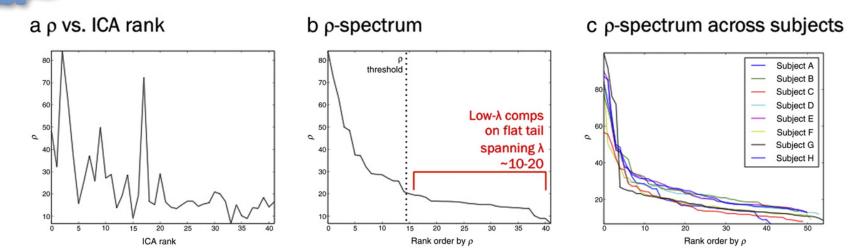


c κ spectra across subjects

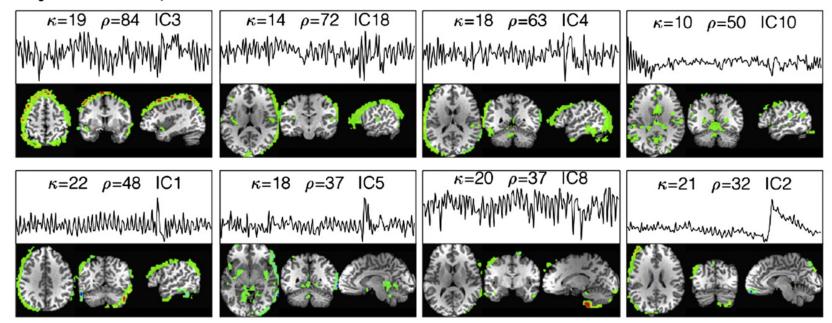


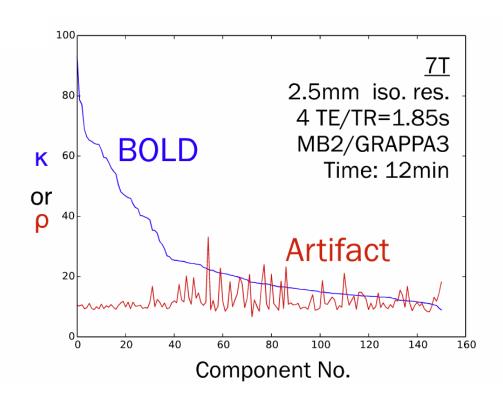
d ΔR_2^* maps of top κ ranked components for a representative subject

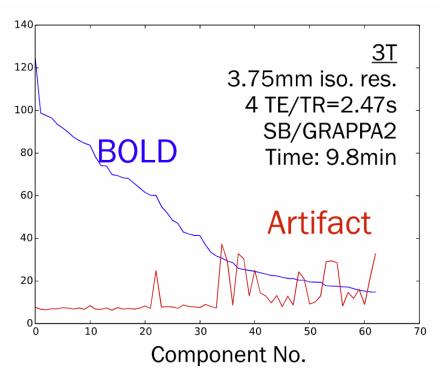




d ΔS_0 maps of top ρ -ranked components for a representative subject

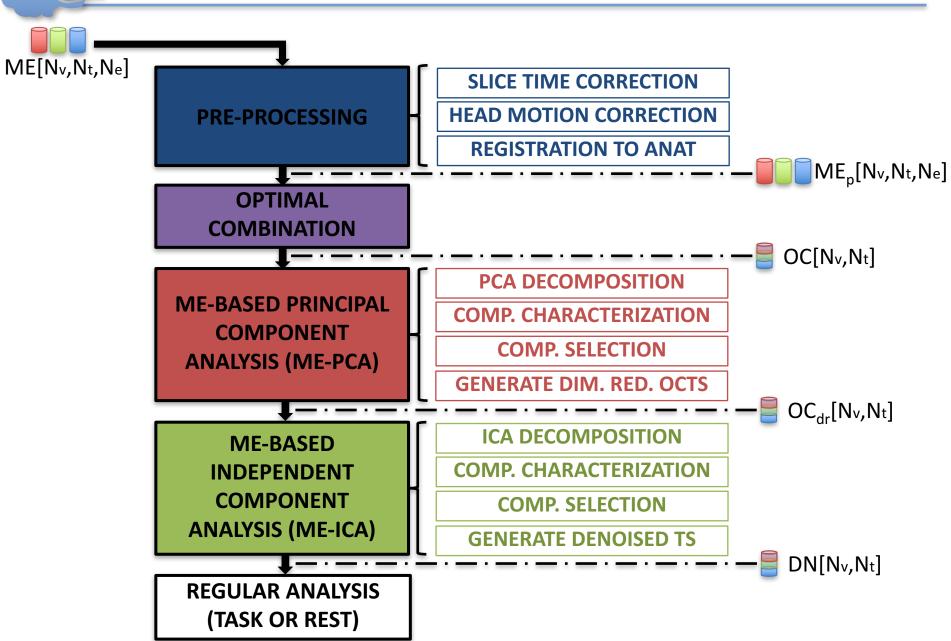


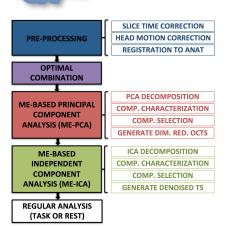




FIM

ME-ICA Denoising: Pipeline





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 $\rho_{daw} = 1$

- <u>SELECTION RULE</u>: $\kappa > \kappa_{thr}$ are kept
- <u>SELECTION RULE</u>: $\rho > \rho_{thr}$ are kept
- Uses fast-ICA algorithm (spatial independence).
- Component Characterization includes:
 - Variance Explained
 - к ("BOLD likeliness")
 - ρ ("Non-BOLD likeliness")
- \rightarrow If $\kappa_c < \rho_c \rightarrow$ Discard c
- Nvoxels that significantly fit the S_o model If $N_{so,c} < N_{R2,c} \rightarrow Discard c$ Nvoxels that significantly fit the R₂* model
- Spatial overlap (D) between ICA map and FR₂* map
- Spatial overlap (D) between ICA map and FS_o map
- Other...



➤ If $D_{so,c} < D_{R2,c}$ → Discard c

FIM

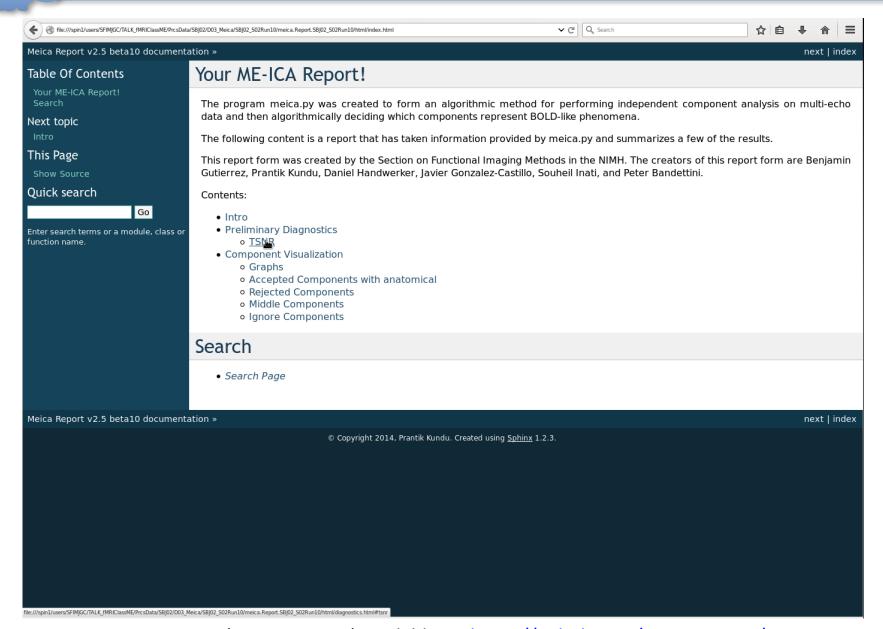
ME-ICA Denoising: Primary Inputs / Outputs

INPUTS	Minimum: fMRI Datasets for all echoes, echo timesExtras: Anatomical, Pre-processing options, kdaw, rdaw,
OUTPUTS	□ T2* 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 □ 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/prantikk/me-ica.git



ME-ICA Denoising: Web Reporting Tool



(Ben Gutierrez) available at: https://github.com/BenGutierrez/Meica Report



Agenda

❖ WHAT IS MULTI-ECHO (ME) FMRI

*** WHAT CAN YOU DO WITH ME TIMESERIES**

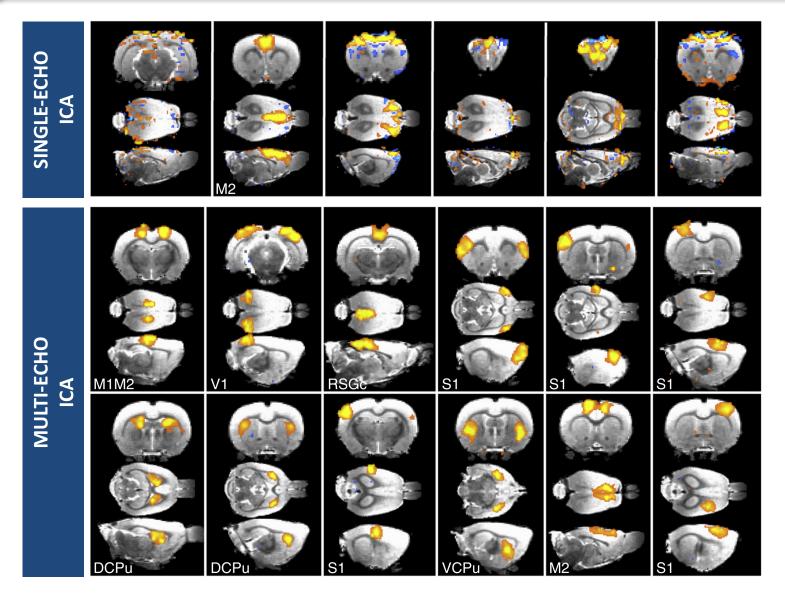
- Compute static S₀ and T₂* Maps
- Compute voxel-wise time-series of S₀ (Non-BOLD) and T₂* (BOLD)
- Combine echoes to improve SNR/spatially equalize functional contrast
- Echo Time Dependence Analysis

❖ ME-ICA Denoising

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

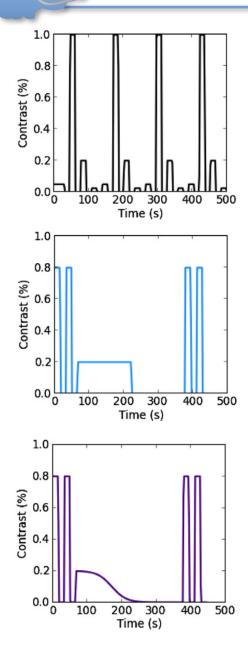
ME-ICA Applications

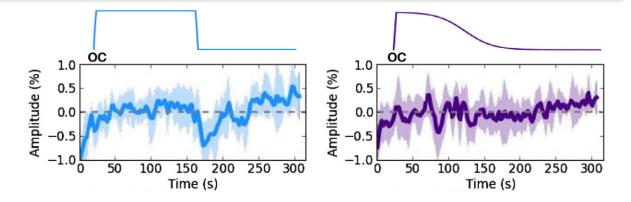
Suitability for ultra-high field fMRI animal studies



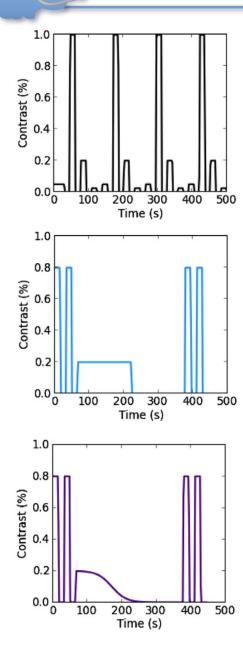
Scanner 11.7T | 0.5x0.5x0.5mm | TR = 3s | TE=8.25/20.25/32.35 ms | 400 volumes | Rats

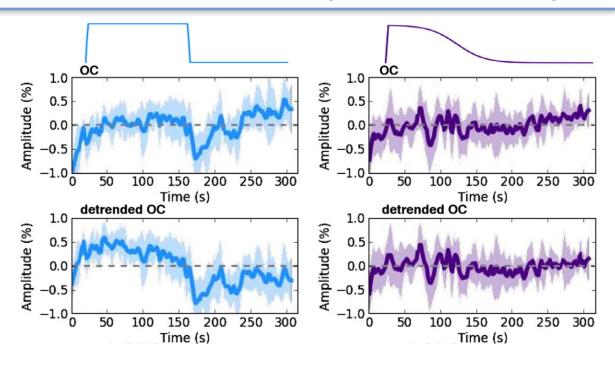


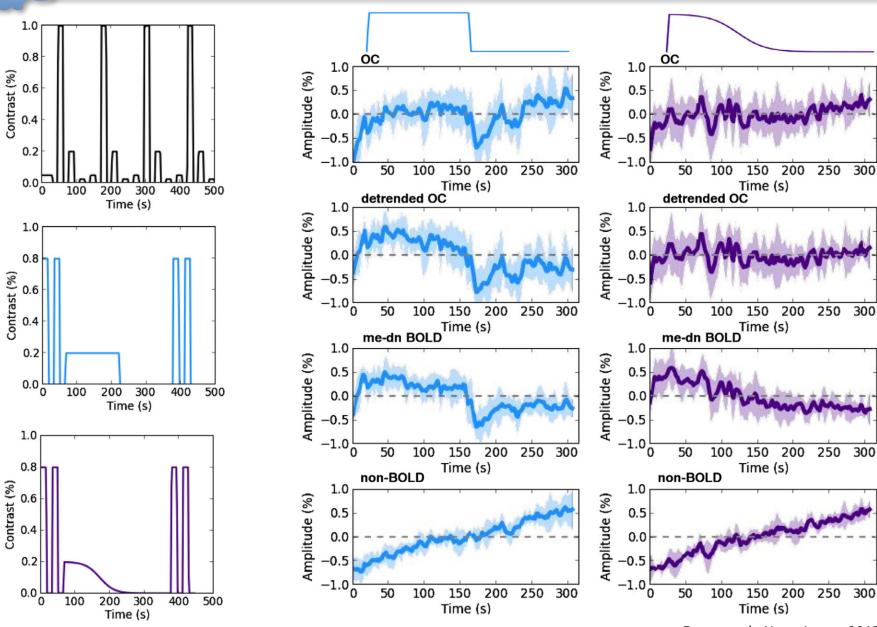






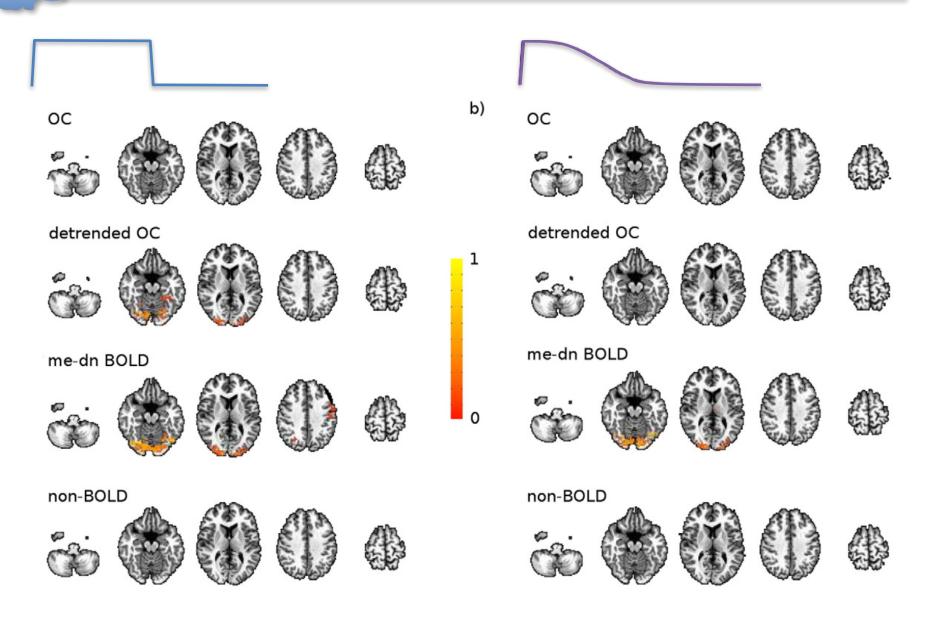






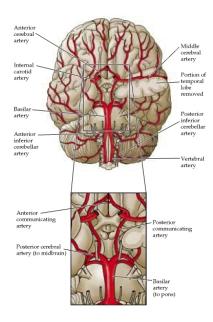
Evans et al., NeuroImage 2015

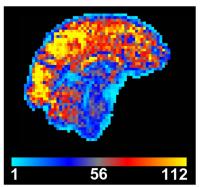




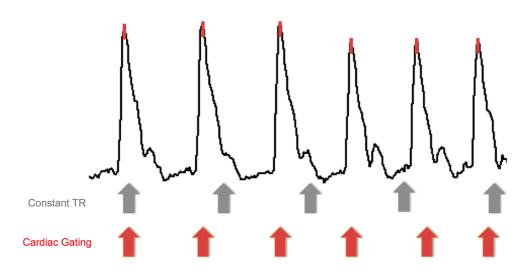


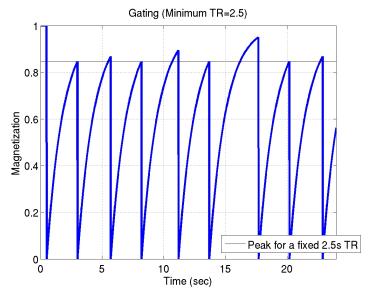
Alternative Approach for Brainstem Imaging: Gated fMRI + ME-ICA





Brooks et al. 2014







5

43

=

50

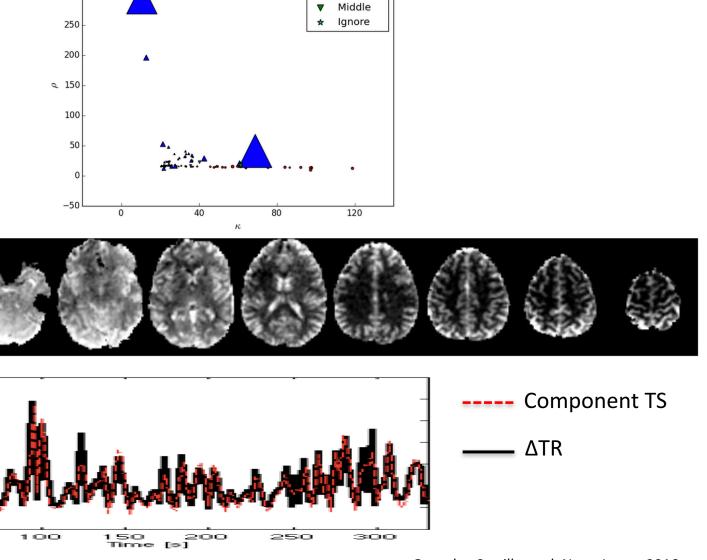
Normalized Units

Alternative Approach for Brainstem Imaging: Gated fMRI + ME-ICA

ME-ICA Analysis, κ vs ρ

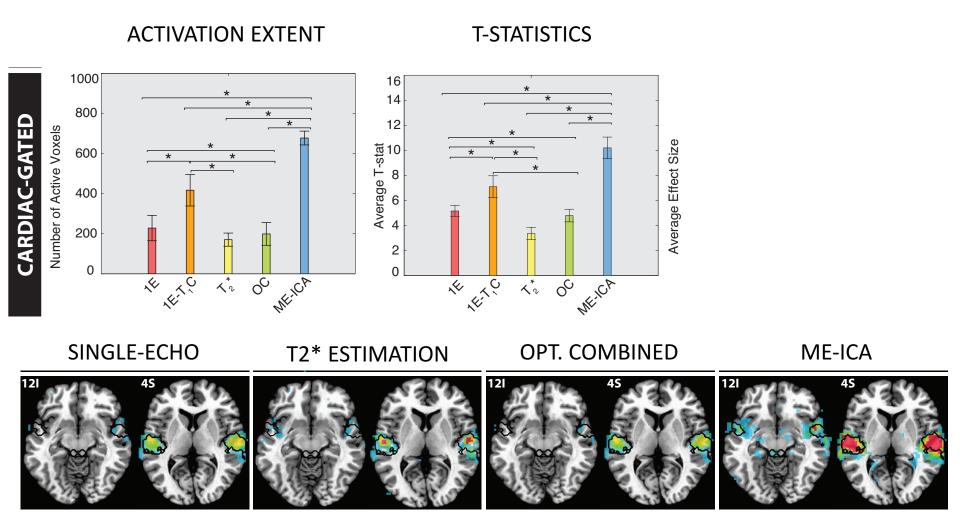
350

300



Accepted Rejected

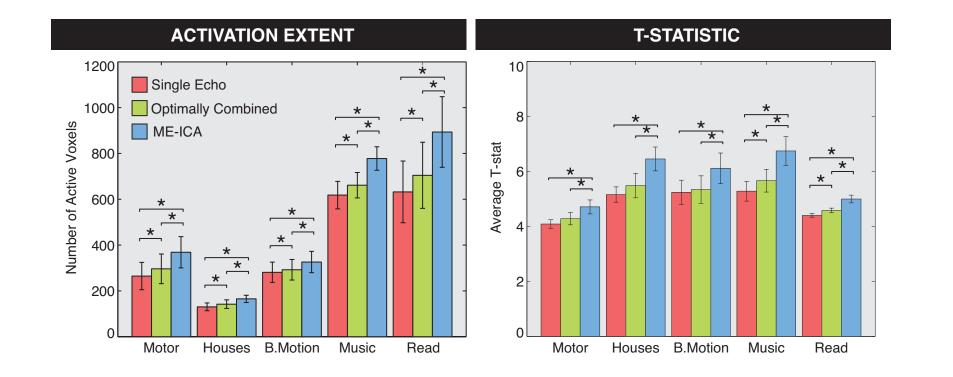
Alternative Approach for Brainstem Imaging: Gated fMRI + ME-ICA





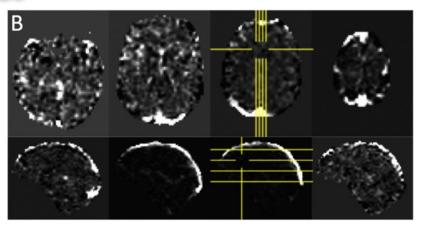
ME+ICA for Rapid Event Related fMRI



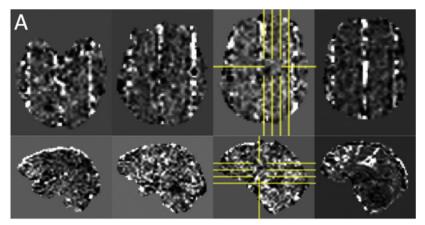




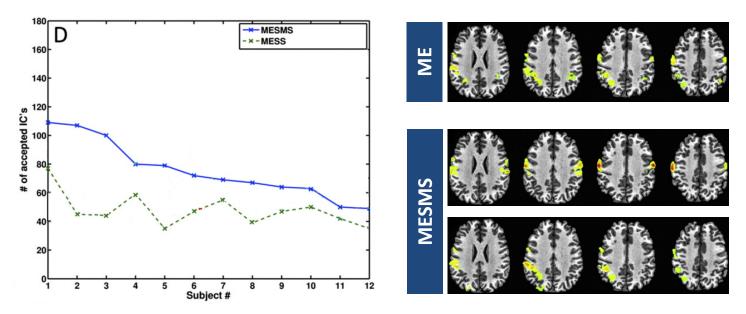
Multi-Echo & Simultaneous Multi-Slice (MESMS)



Non-BOLD Component: Vascular Pulsation



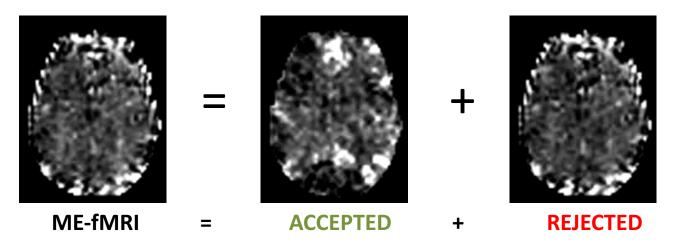
Non-BOLD Component: MSS Artifact



Number of BOLD-like components significantly larger for MESMS

Conclusions

- ☐ 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.
 - \Box Can substantially improve the SNR of the data \rightarrow Quality of the results.





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