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

### Javier González-Castillo

Section on Functional Imaging Methods, NIMH, NIH

July 2018, National Institutes of Health, Bethesda, MD









# Agenda

# **❖ WHAT IS MULTI-ECHO (ME) FMRI**

# **BASIC OPERATIONS WITH ME DATA**

- Compute static S<sub>o</sub> and T<sub>2</sub>\* Maps
- Compute voxel-wise time-series of S<sub>o</sub> (Non-BOLD) and T<sub>2</sub>\* (BOLD)
- Combine echoes to improve SNR/spatially equalize functional contrast
- Echo Time Dependence Analysis

## **❖** ADVANCE AUTOMATIC DENOISING WITH ME-ICA

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

# **EVENT DECONVOLUTION WITH ME-SPFM**

- What are fMRI Deconvolution Methods
- ME Formulation for fMRI Deconvolution based on SPFM
- Example / Validation Experiments



# 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



Prantik Kundu<sup>a,\*</sup>, Valerie Voon<sup>b</sup>, Priti Balchandani<sup>a</sup>, Michael V. Lombardo<sup>c</sup>, Benedikt A. Poser<sup>d</sup>, Peter A. Bandettini<sup>c</sup>

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

Intro to ME Signal Model+ ME-ICA Denoising

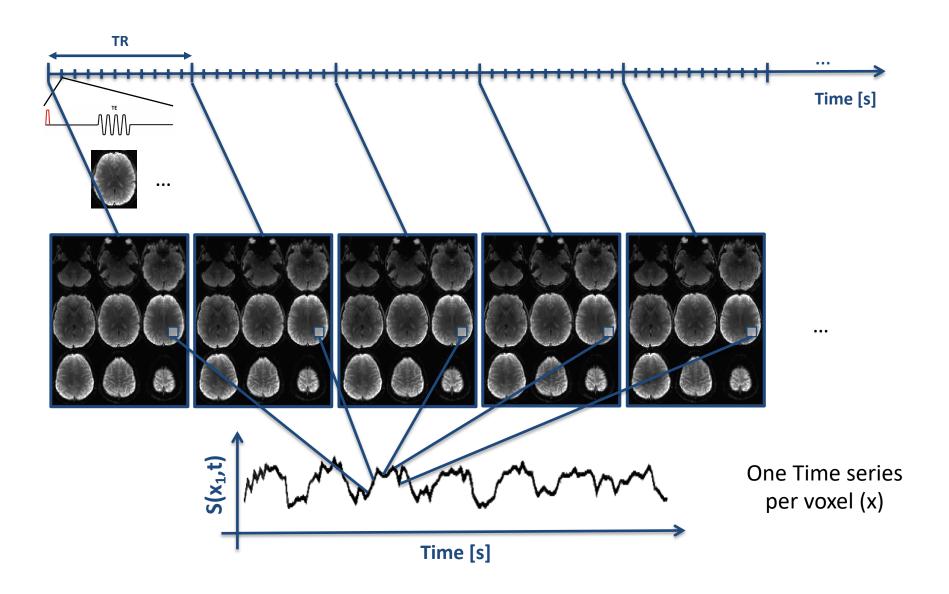
2018 IEEE 15th International Symposium on Biomedical Imaging (ISBI 2018) April 4-7, 2018, Washington, D.C., USA

#### A TEMPORAL DECONVOLUTION ALGORITHM FOR MULTIECHO FUNCTIONAL MRI

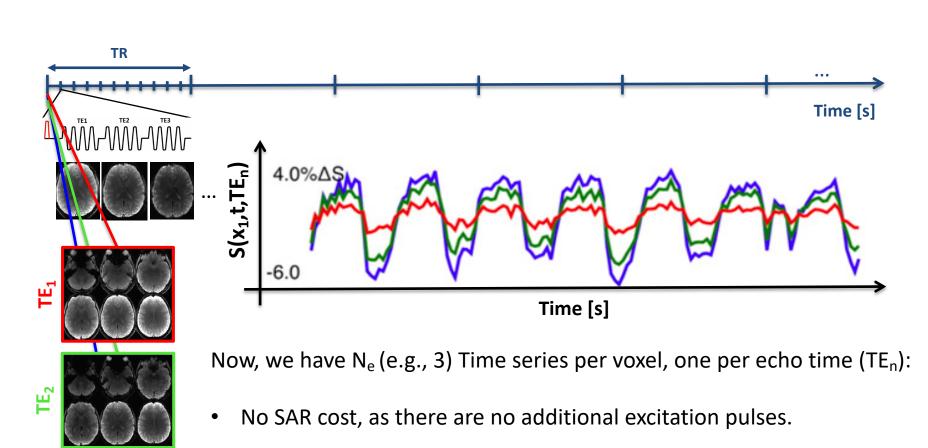
César Caballero Gaudes<sup>1</sup>, Peter A. Bandettini<sup>2,3</sup>, Javier Gonzalez-Castillo<sup>2</sup>

<sup>1</sup>Basque Center on Cognition, Brain and Language, San Sebastian, Spain <sup>2</sup>Section on Functional Imaging Methods, NIMH, NIH, Bethesda, MD, USA <sup>3</sup>Functional MRI Core, NIH, Bethesda, MD, USA ME Formulation for fMRI Deconvolution of Sparse Events

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



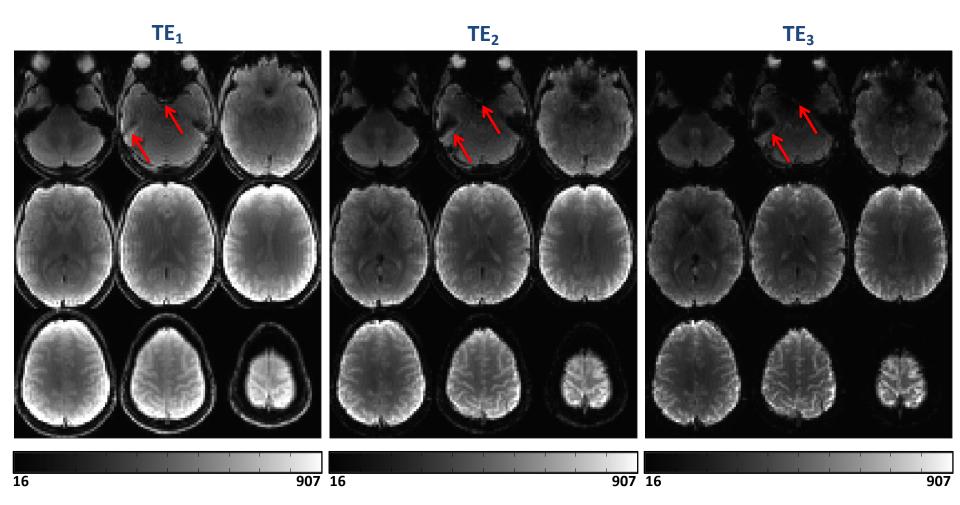
# Multi-Echo fMRI



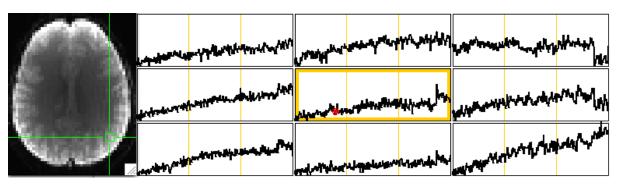
- Slight lost in temporal resolution (easy to overcome with Multi-Band).
- Slight lost in spatial resolution: to ensure sufficient signal levels in last echo.



# 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

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

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

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

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

Captures local fluctuations in field



# Agenda

# **❖ WHAT IS MULTI-ECHO (ME) FMRI**

# **BASIC OPERATIONS WITH ME DATA**

- Compute static S<sub>o</sub> and T<sub>2</sub>\* Maps
- Compute voxel-wise time-series of S<sub>o</sub> (Non-BOLD) and T<sub>2</sub>\* (BOLD)
- Combine echoes to improve SNR/spatially equalize functional contrast
- Echo Time Dependence Analysis

## **❖** ADVANCE AUTOMATIC DENOISING WITH ME-ICA

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

# **EVENT DECONVOLUTION WITH ME-SPFM**

- What are fMRI Deconvolution Methods
- ME Formulation for fMRI Deconvolution based on SPFM
- Example / Validation Experiments

# 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:

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

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

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

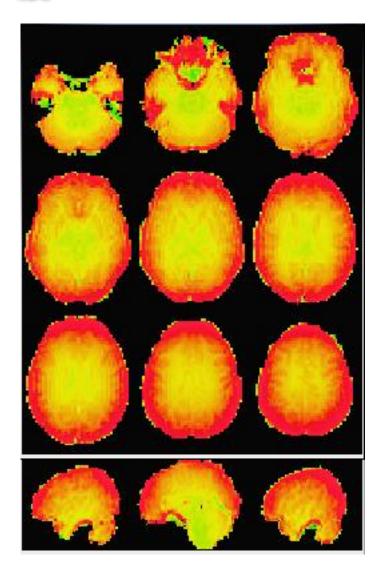
$$y(x,TE) = a(x) * TE + b(x)$$

Linear system of equations for 3 echoes

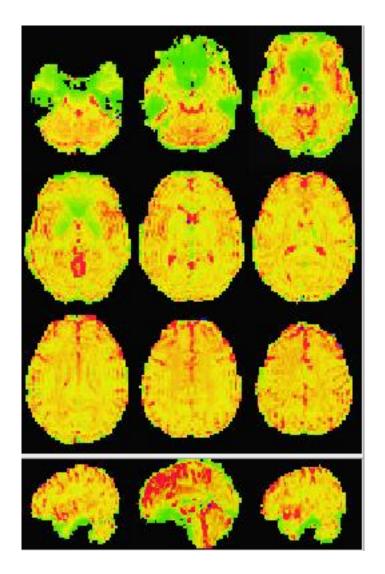
$$\begin{cases}
\log(\overline{S(x,TE_1)}) = -\overline{R_2^*(x)} \cdot TE_1 + \log(\overline{S_o(x)}) \\
\log(\overline{S(x,TE_2)}) = -\overline{R_2^*(x)} \cdot TE_2 + \log(\overline{S_o(x)}) \\
\log(\overline{S(x,TE_3)}) = -\overline{R_2^*(x)} \cdot TE_3 + \log(\overline{S_o(x)})
\end{cases}$$



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



Static So Map (s0v.nii)



Static T<sub>2</sub>\* Map (t2sv.nii)



# Agenda

# ❖ WHAT IS MULTI-ECHO (ME) FMRI

# **BASIC OPERATIONS WITH ME DATA**

- Compute static S<sub>o</sub> and T<sub>2</sub>\* Maps
- Compute voxel-wise time-series of S<sub>o</sub> (Non-BOLD) and T<sub>2</sub>\* (BOLD)
- Combine echoes to improve SNR/spatially equalize functional contrast
- Echo Time Dependence Analysis

## **❖** ADVANCE AUTOMATIC DENOISING WITH ME-ICA

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

# **EVENT DECONVOLUTION WITH ME-SPFM**

- What are fMRI Deconvolution Methods
- ME Formulation for fMRI Deconvolution based on SPFM
- Example / Validation Experiments



# How to Compute Time series of $\Delta S_o$ and $\Delta R_2^*$ fluctuations

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

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

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

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

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

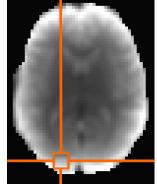
$$\Delta \rho(x,t) = \Delta S_o(x,t) / \overline{S_o(x)} \\
\Delta \kappa(x,t) = \Delta R_2^*(x,t) \cdot \overline{TE}$$

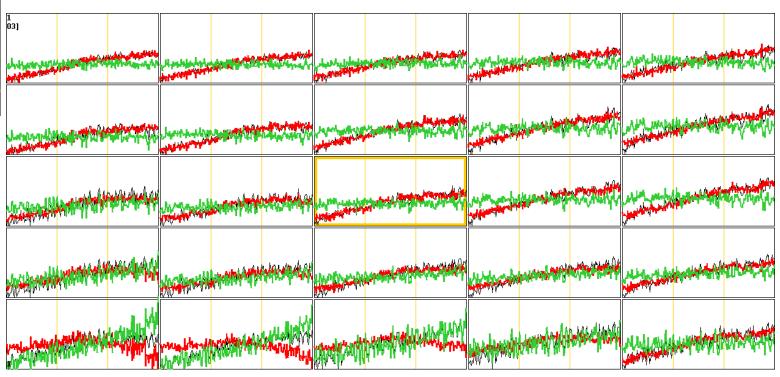
$$\Rightarrow S(x,t,TE) \approx \overline{S(x,TE)} \cdot \left[1 + \Delta \rho(x,t) - \frac{TE}{\overline{TE}} \Delta \kappa(x,t)\right] \tag{5}$$

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



# How to Compute Time series of $\Delta S_o$ and $\Delta R_2^*$ fluctuations

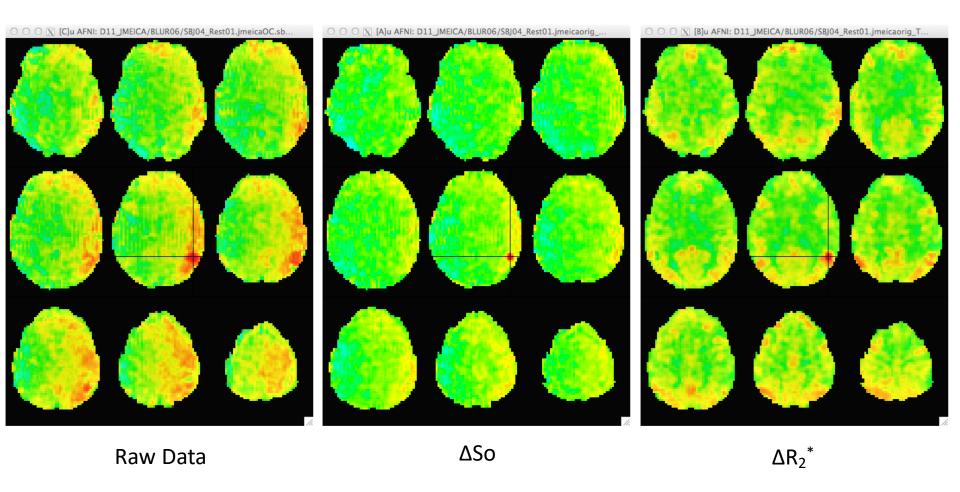




$$\longrightarrow S(x,t,TE_2) \longrightarrow \Delta S_o(x,t) \longrightarrow \Delta R_2^*(x,t)$$



# How to Compute Time series of $\Delta S_o$ and $\Delta R_2^*$ fluctuations



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



# Agenda

# ❖ WHAT IS MULTI-ECHO (ME) FMRI

# **BASIC OPERATIONS WITH ME DATA**

- Compute static S<sub>o</sub> and T<sub>2</sub>\* Maps
- Compute voxel-wise time-series of S<sub>o</sub> (Non-BOLD) and T<sub>2</sub>\* (BOLD)
- Combine echoes to improve SNR/spatially equalize functional contrast
- Echo Time Dependence Analysis

# **❖** ADVANCE AUTOMATIC DENOISING WITH ME-ICA

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

# **EVENT DECONVOLUTION WITH ME-SPFM**

- What are fMRI Deconvolution Methods
- ME Formulation for fMRI Deconvolution based on SPFM
- Example / Validation Experiments



# **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.

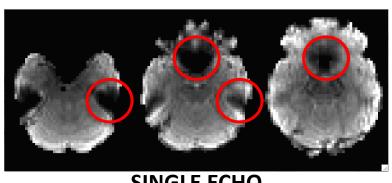
#### **Weighted Summation**

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

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

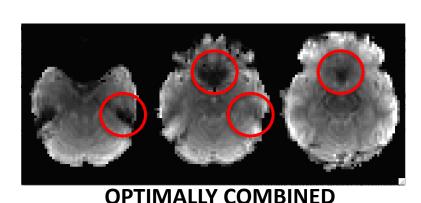
$$w_{v}(TE_{n}) = \frac{TE_{n}e^{-TE_{n}/T_{2,v}^{*}}}{\sum_{n}TE_{n} \cdot e^{-TE_{n}/T_{2,v}^{*}}}$$

Posse et al., MRM 1999



SINGLE ECHO







# **Combination of Multi-Echo Time series**

We have N<sub>e</sub> 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.

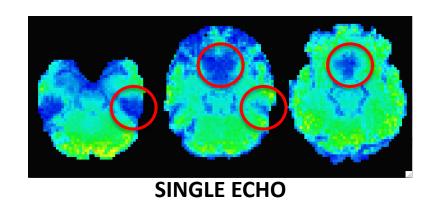
#### **Weighted Summation**

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

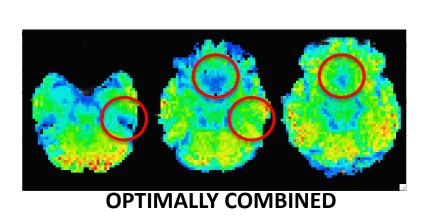
$$w_{v}(TE_{n}) = \frac{TE_{n}e^{-TE_{n}/T_{2,v}^{*}}}{\sum_{n}TE_{n} \cdot e^{-TE_{n}/T_{2,v}^{*}}}$$

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









# Agenda

# ❖ WHAT IS MULTI-ECHO (ME) FMRI

# **BASIC OPERATIONS WITH ME DATA**

- Compute static S<sub>o</sub> and T<sub>2</sub>\* Maps
- Compute voxel-wise time-series of S<sub>o</sub> (Non-BOLD) and T<sub>2</sub>\* (BOLD)
- Combine echoes to improve SNR/spatially equalize functional contrast
- Echo Time Dependence Analysis

## **❖ ADVANCE AUTOMATIC DENOISING WITH ME-ICA**

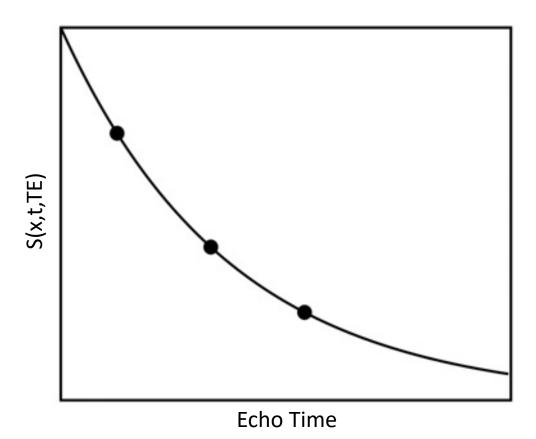
- ME-ICA Pipeline
- ME-ICA Outputs
- ME-ICA Web Reporting Tool

# **EVENT DECONVOLUTION WITH ME-SPFM**

- What are fMRI Deconvolution Methods
- ME Formulation for fMRI Deconvolution based on SPFM
- Example / Validation Experiments

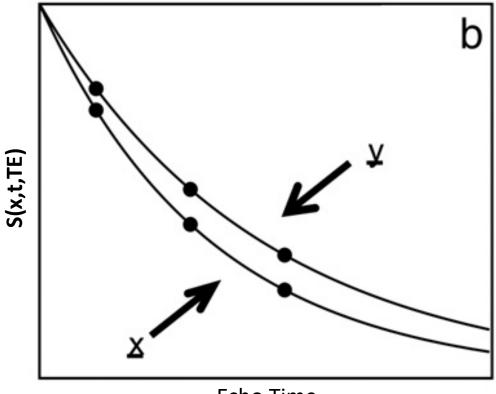
$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

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



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

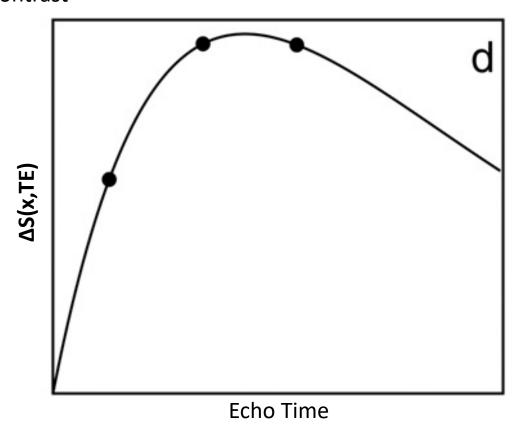
Let's assume now, that a local change in oxygenation happens (T<sub>2</sub>\* effect)



Echo Time

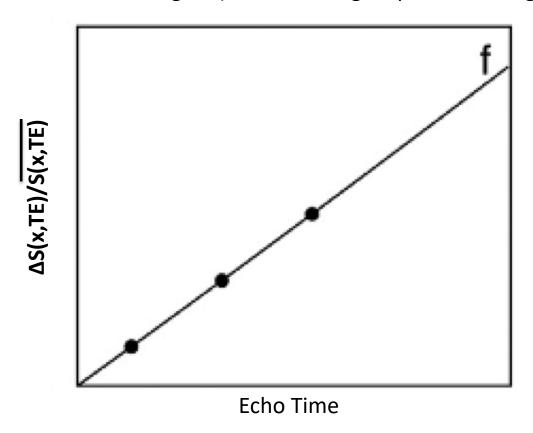
$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

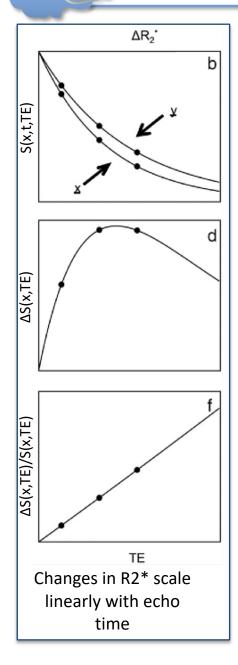
We could then use the difference between two curves to examine which is the optimal TE to maximize BOLD contrast



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

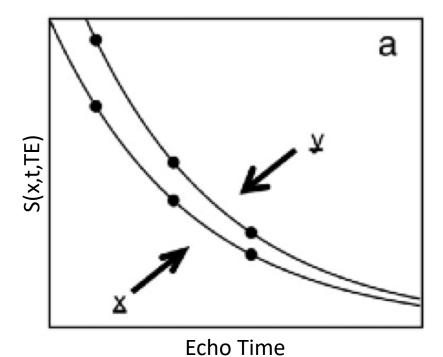
Most importantly for our discussion, for T<sub>2</sub>\* signal changes, there is a linear relationship between echo time and measured signal (in terms of signal percent change)

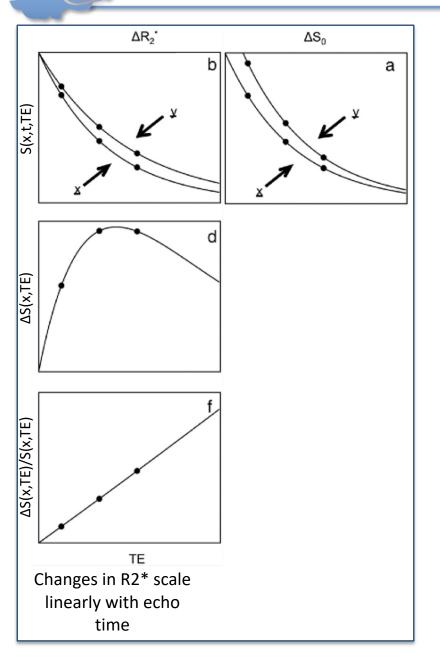




$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

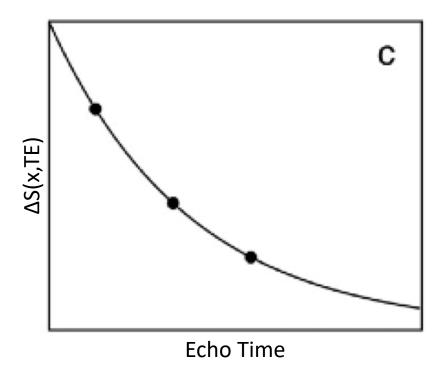
Let's now examine what happens when there is a change in  $S_o$  (T1 effect)

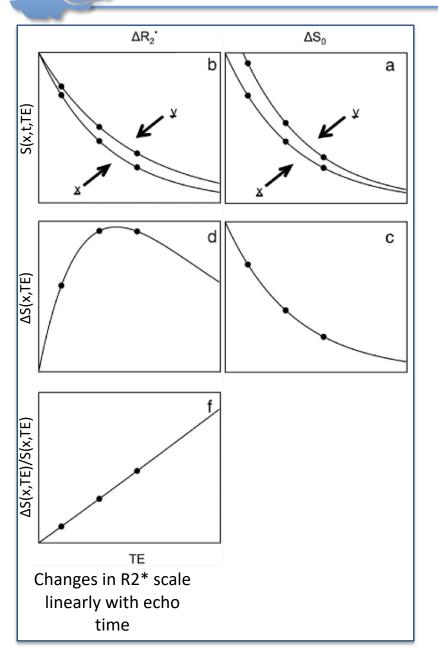




$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

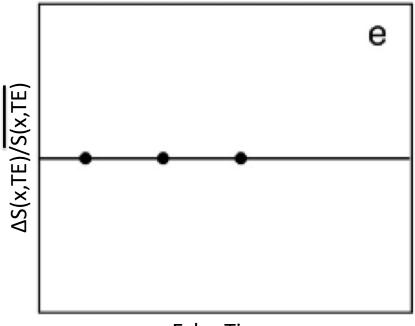
This time the difference between both curves looks very different



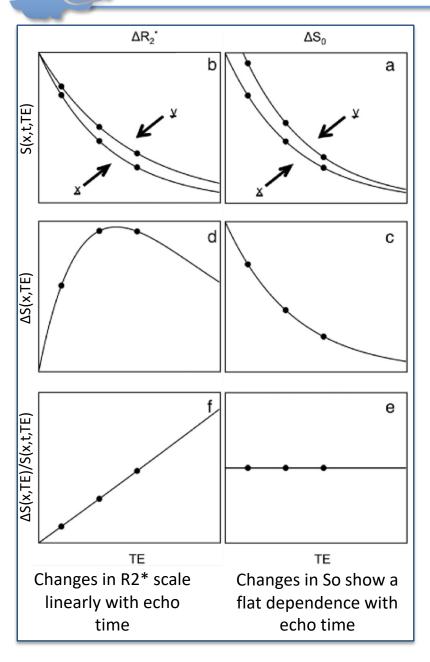


$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

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

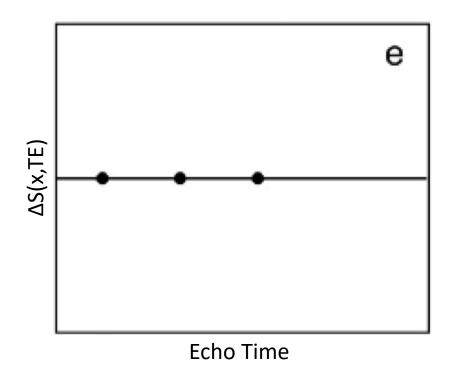


**Echo Time** 

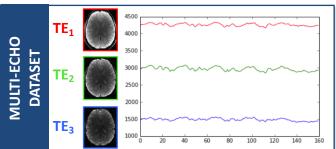


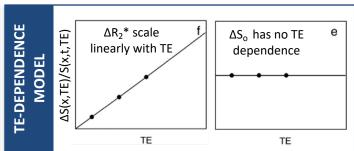
$$S(x,t,TE) = S_o(x,t)e^{-R_2^*(x,t)\cdot TE}$$

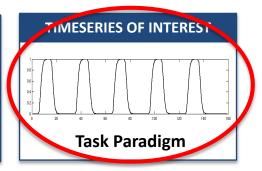
In term of signal percent change, changes in So have a flat dependence with echo time



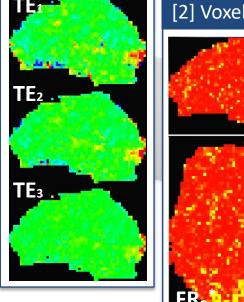




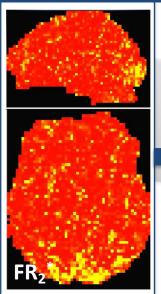




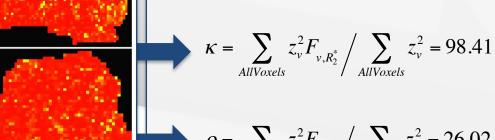




[2] Voxel-wise Goodness of Fit to R2\* Model



[3] Voxel-wise Goodness of Fit to S<sub>0</sub> 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



# Agenda

# ❖ WHAT IS MULTI-ECHO (ME) FMRI

# **BASIC OPERATIONS WITH ME DATA**

- Compute static S<sub>o</sub> and T<sub>2</sub>\* Maps
- Compute voxel-wise time-series of S<sub>o</sub> (Non-BOLD) and T<sub>2</sub>\* (BOLD)
- Combine echoes to improve SNR/spatially equalize functional contrast
- Echo Time Dependence Analysis

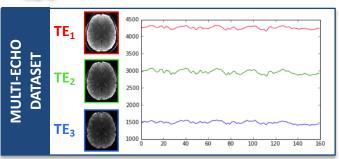
# **ADVANCE AUTOMATIC DENOISING WITH ME-ICA**

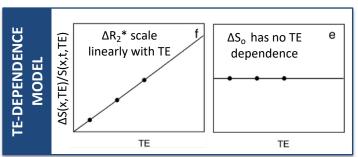
- ME-ICA Pipeline
- ME-ICA Outputs
- ME-ICA Web Reporting Tool

# **EVENT DECONVOLUTION WITH ME-SPFM**

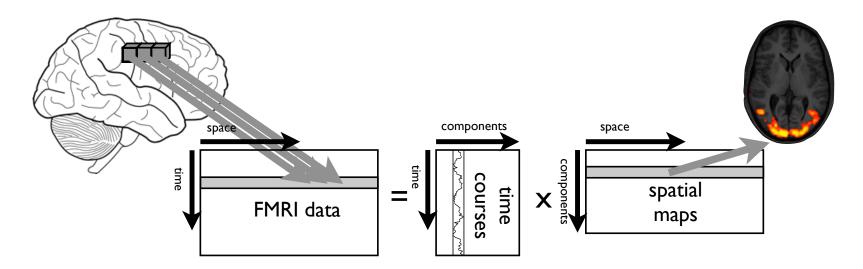
- What are fMRI Deconvolution Methods
- ME Formulation for fMRI Deconvolution based on SPFM
- Example / Validation Experiments





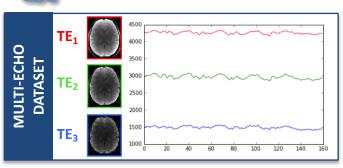


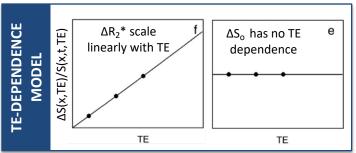
# ICA Representative Timeseries



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

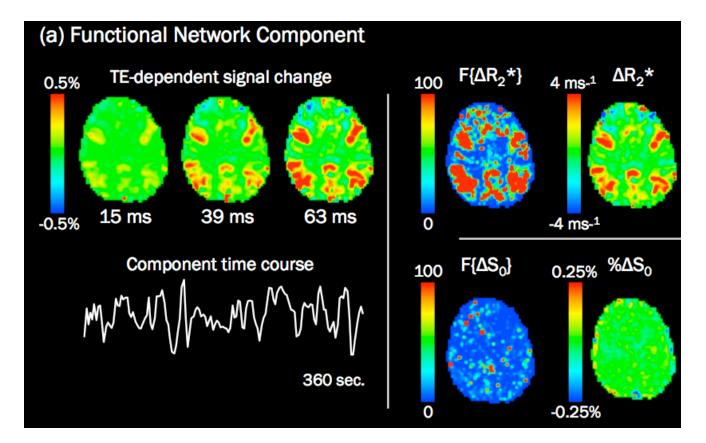






#### **TIMESERIES OF INTEREST**

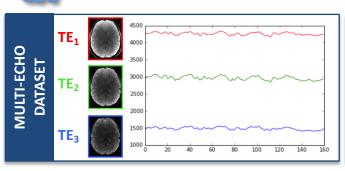
ICA Representative Timeseries

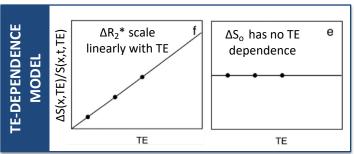


Карра (
$$\kappa$$
) = 210

Rho (
$$\rho$$
) = 10

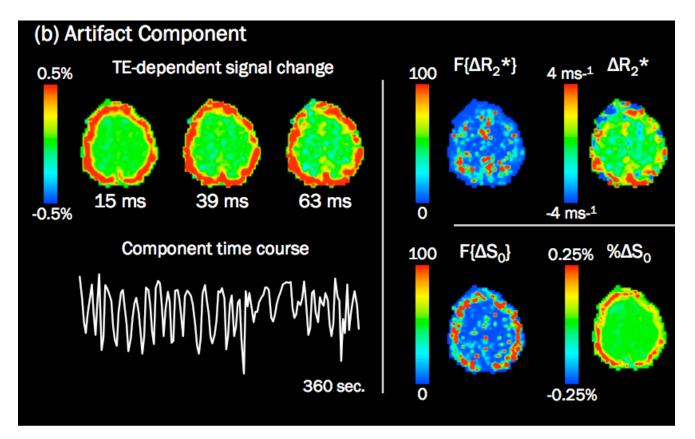






#### **TIMESERIES OF INTEREST**

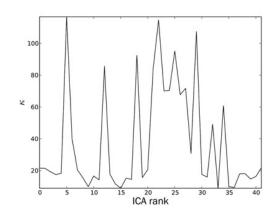
ICA Representative Timeseries



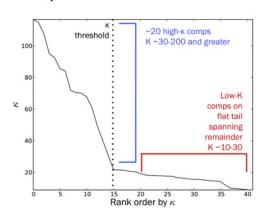
Kappa (
$$\kappa$$
) = 32

Rho (
$$\rho$$
) = 81

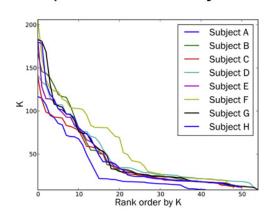
a κ vs. ICA rank



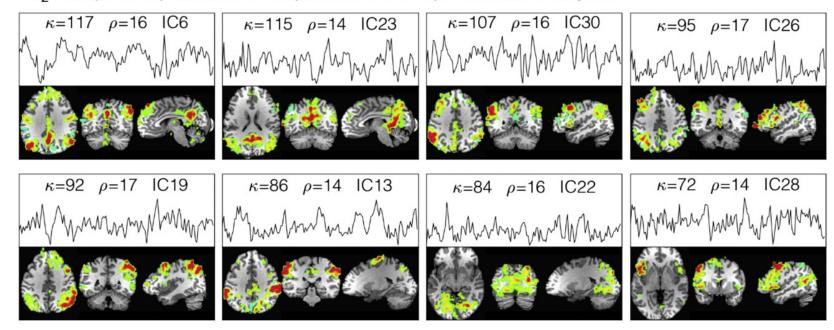
b κ spectrum

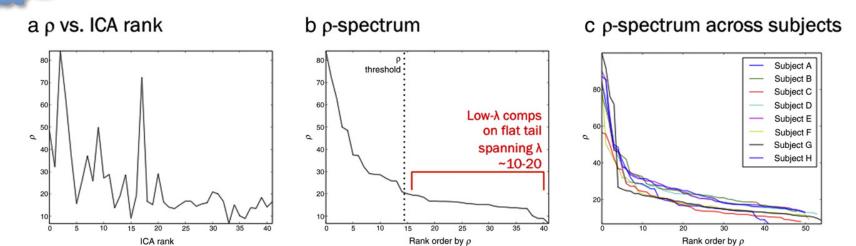


c κ spectra across subjects

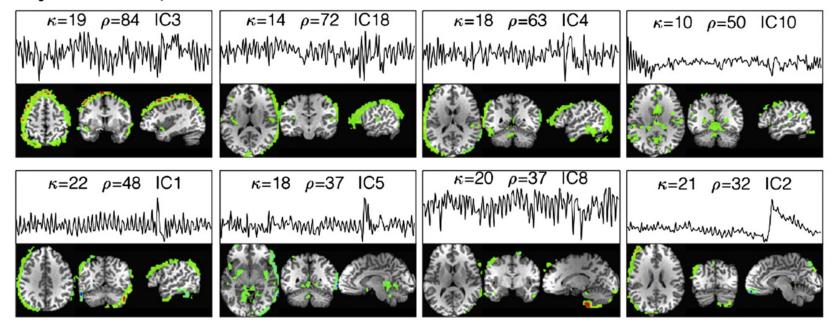


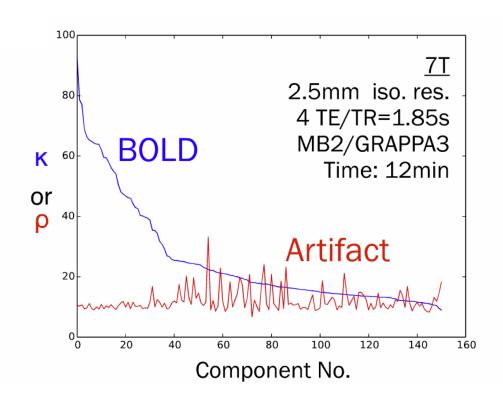
d  $\Delta R_2^*$  maps of top  $\kappa$  ranked components for a representative subject

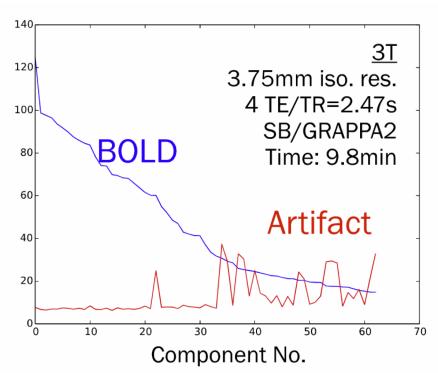




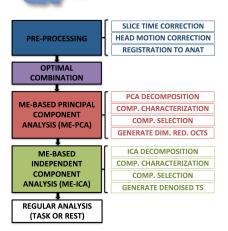
#### d $\Delta S_0$ maps of top $\rho$ -ranked components for a representative subject





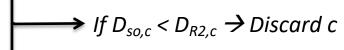


#### **ME-ICA Denoising: Pipeline** FIM $ME[N_{V},N_{t},N_{e}]$ **SLICE TIME CORRECTION HEAD MOTION CORRECTION PRE-PROCESSING REGISTRATION TO ANAT** $ME_p[N_v,N_t,N_e]$ **OPTIMAL COMBINATION** $OC[N_V,N_t]$ **PCA DECOMPOSITION ME-BASED PRINCIPAL** COMP. CHARACTERIZATION **COMPONENT COMP. SELECTION ANALYSIS (ME-PCA) GENERATE DIM. RED. OCTS** $OC_{dr}[N_{V},N_{t}]$ ICA DECOMPOSITION **ME-BASED** INDEPENDENT COMP. CHARACTERIZATION **COMPONENT** COMP. SELECTION **ANALYSIS (ME-ICA) GENERATE DENOISED TS** $DN[N_v,N_t]$ **REGULAR ANALYSIS** (TASK OR REST) Kundu et al., NeuroImage 2012



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
  - <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<sub>o</sub> model
- Nvoxels that significantly fit the R<sub>2</sub>\* model
- Spatial overlap (D) between ICA map and FR<sub>2</sub>\* map
- Spatial overlap (D) between ICA map and FS<sub>o</sub> map



If  $N_{so.c} < N_{R2.c} \rightarrow Discard c$ 

Other...



# FIM

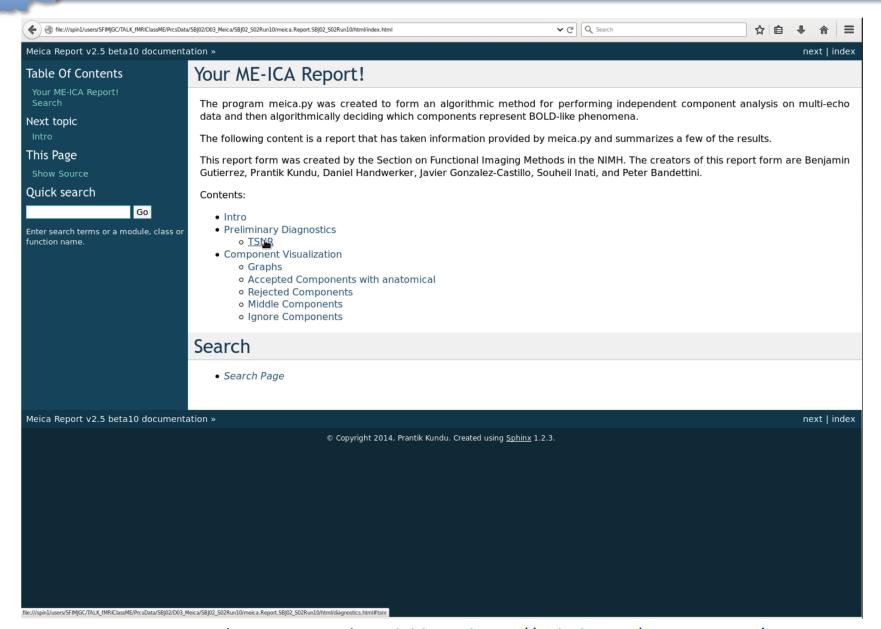
### **ME-ICA Denoising: Primary Inputs / Outputs**

INPUTS	<ul><li>Minimum: fMRI Datasets for all echoes, echo times</li><li>Extras: Anatomical, Pre-processing options, kdaw, rdaw,</li></ul>
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 □ Total Variance Explained by the ICA decomposition

ME-ICA Software available with AFNI: <a href="http://afni.nimh.nih.gov/afni">http://afni.nimh.nih.gov/afni</a> Latest updates available at: <a href="https://github.com/ME-ICA">https://github.com/ME-ICA</a>



### ME-ICA Denoising: Web Reporting Tool





## Agenda

### ❖ WHAT IS MULTI-ECHO (ME) FMRI

### **BASIC OPERATIONS WITH ME DATA**

- Compute static S<sub>o</sub> and T<sub>2</sub>\* Maps
- Compute voxel-wise time-series of S<sub>0</sub> (Non-BOLD) and T<sub>2</sub>\* (BOLD)
- Combine echoes to improve SNR/spatially equalize functional contrast
- Echo Time Dependence Analysis

### **❖** ADVANCE AUTOMATIC DENOISING WITH ME-ICA

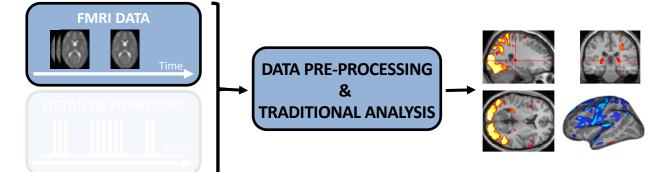
- ME-ICA Pipeline
- ME-ICA Outputs
- ME-ICA Web Reporting Tool

### **EVENT DECONVOLUTION WITH ME-SPFM**

- What are fMRI Deconvolution Methods
- ME Formulation for fMRI Deconvolution based on SPFM
- Example / Validation Experiments



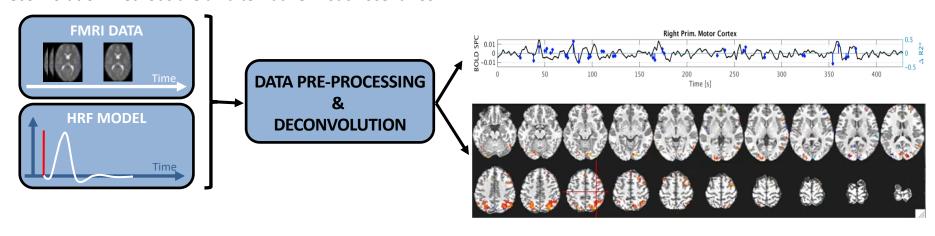
## What are deconvolution methods?



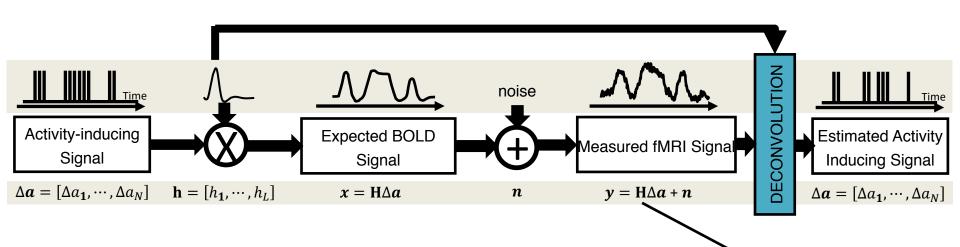
There are experimental scenarios where event timing might be missing:

- Naturalistic paradigms
- Clinical studies (e.g., interictal events)
- Resting State

Deconvolution methods are an alternative in such scenarios:



### Deconvolution Formulation for Singe-Echo fMRI



If one assumes the underlying activity-inducing signal to consist of brief, sparse events, then the formulated deconvolution problem can be solved using LASSO regularization:

Error Minimization Term 
$$\Delta \widehat{a} = \arg\min_{\Delta a} \frac{1}{2} \|y - \mathbf{H} \Delta a\|_{2}^{2} + \lambda \|\Delta a\|_{1}$$
 L1-Norm Regularization (Sparseness)

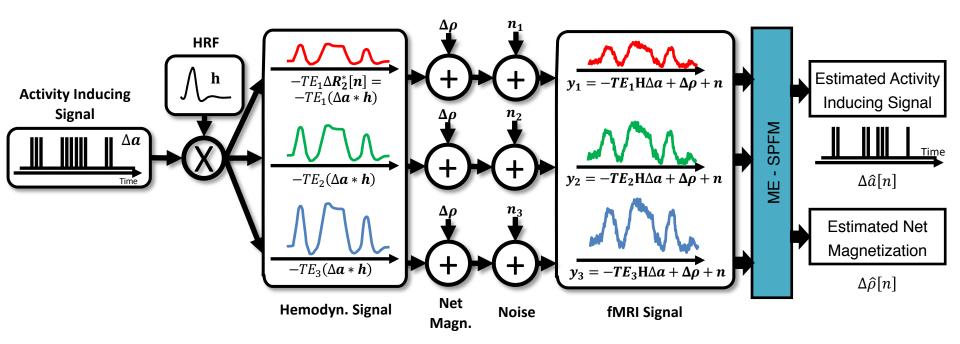
Single Echo Sparse Free
Paradigm Mapping Algorithm

AFNII

3dPFM



### **Deconvolution Formulation for Multi-Echo fMRI**



$$\overline{y} \stackrel{\text{def}}{=} \begin{bmatrix} y_1 \\ \vdots \\ y_K \end{bmatrix} = \begin{bmatrix} I \\ \vdots \\ I \end{bmatrix} \triangle \rho - \begin{bmatrix} TE_1 H \\ \vdots \\ TE_K H \end{bmatrix} \triangle a$$

$$\overline{I} \qquad \overline{H}$$

Assuming sparsity in both unknowns, we can solve using LASSO regularization

$$\Delta \widehat{\boldsymbol{a}}, \Delta \widehat{\boldsymbol{\rho}} = \arg\min_{\Delta \boldsymbol{a}, \Delta \boldsymbol{\rho}} \frac{1}{2} \| \overline{\boldsymbol{y}} - \overline{\mathbf{H}} \Delta \boldsymbol{a} - \overline{\mathbf{I}} \Delta \boldsymbol{\rho} \|_{2}^{2} + \lambda_{1} \| \Delta \boldsymbol{a} \|_{1} + \lambda_{2} \| \Delta \boldsymbol{\rho} \|_{1}$$



### Validation Experiments – Data Acquisition

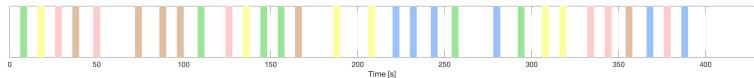
- 10 Subjects (5M/5F)
- GRE EPI @ 3T / 32 Channel Coil

- TE = 16.3/32.2/48.1 ms
- TR = 2 seconds

- Resolution = 3 x 3 x 4 mm<sup>3</sup>
- ASSET = 2

Rapid Event Related with 5 different tasks / 6 trials per task per run / events are approx. 4 seconds long

#### SCHEMATIC OF ONE FUNCTIONAL RUN





Listen to an audio clip and select instrument being played from the ones displayed on the screen.



Passive viewing of dots patterns resembling different types of biological motion.



Press button at an approx. rate of 0.5Hz (following a counter on the screen).

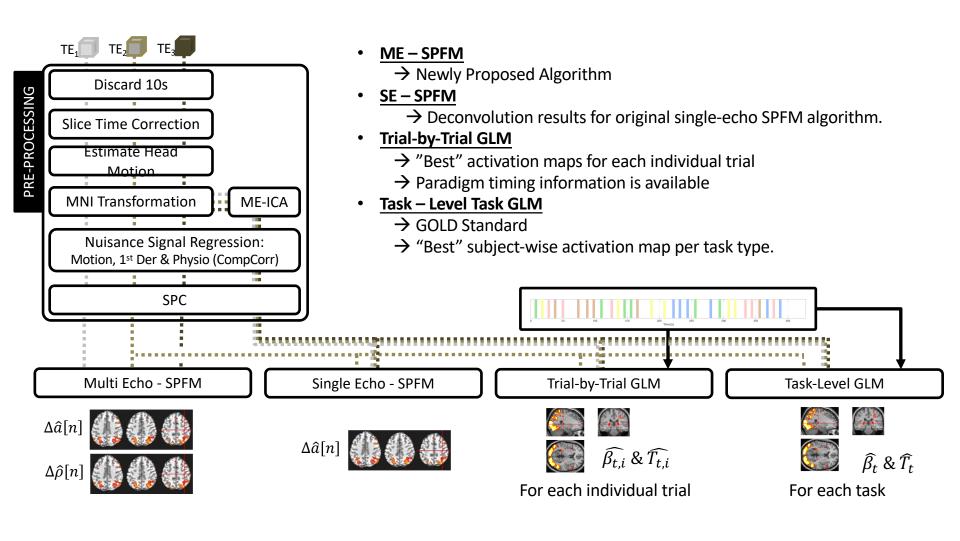
Silently read sentences that appear on the screen one word at a time.



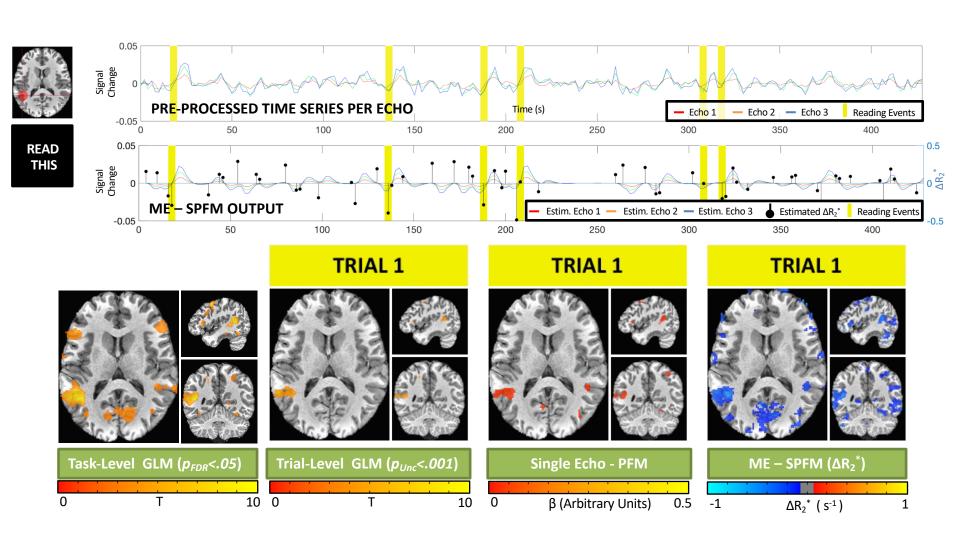
Passive viewing of images of houses

# FIM

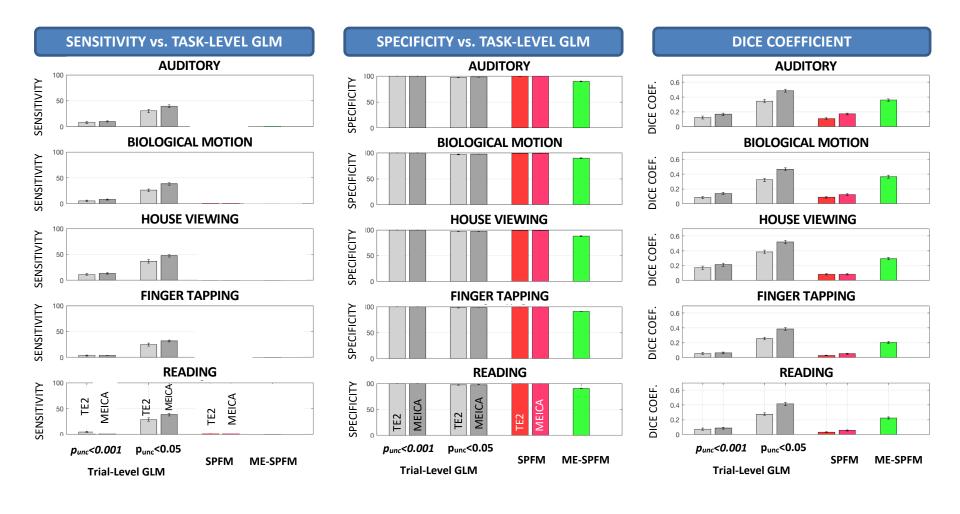
### Validation Experiments – Data Analysis



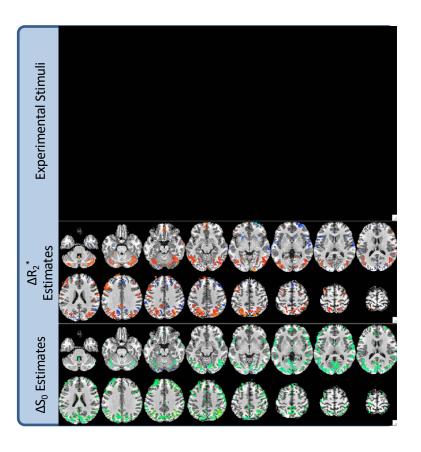
### Validation Experiments – Results (I)



### Validation Experiments – Results (2)



### ME – Deconvolution – Future Work



• Understand the pros/cons of different formulations for the ME deconvolution problem.

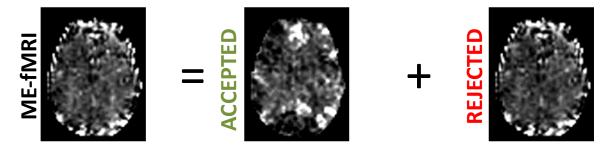
	Models	Sparsity
$\Delta \widehat{\boldsymbol{a}} = \arg\min_{\Delta \boldsymbol{a}} \frac{1}{2} \ \boldsymbol{y} - \mathbf{H} \Delta \boldsymbol{a}\ _{2}^{2} + \lambda \ \Delta \boldsymbol{a}\ _{1}$	$\Delta R_2^*$	$\Delta R_2^*$
$\Delta \widehat{\boldsymbol{a}}, \Delta \widehat{\boldsymbol{\rho}} = \arg\min_{\Delta \boldsymbol{a}, \Delta \boldsymbol{\rho}} \frac{1}{2} \  \boldsymbol{y} - \mathbf{H} \Delta \boldsymbol{a} - \mathbf{I} \Delta \boldsymbol{\rho} \ _{2}^{2} + \lambda_{1} \  \Delta \boldsymbol{a} \ _{1} + \lambda_{2} \  \Delta \boldsymbol{\rho} \ _{1}$	$\Delta R_2^*, \Delta S_0$	$\Delta R_2^*, \Delta S_0$
$\Delta \widehat{\boldsymbol{a}}, \Delta \widehat{\boldsymbol{\rho}} = \arg\min_{\Delta \boldsymbol{a}} \frac{1}{2} \  \boldsymbol{y} - \mathbf{H} \Delta \boldsymbol{a} - \mathbf{I} \Delta \boldsymbol{\rho} \ _{2}^{2} + \lambda \  \Delta \boldsymbol{a} \ _{1}$	$\Delta R_2^*, \Delta S_0$	$\Delta R_2^*$

- Explore the limitations of the algorithm in terms of event duration, temporal overlap of events, etc.
- Adapt the method to accommodate spatial heterogeneity in hemodynamic response shape.
- Explore its application to scientifically and clinically relevant scenarios.

# FIM

### **Conclusions**

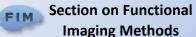
- ☐ Multi-echo fMRI allows to capture additional information with minimal costs in terms of temporal and spatial resolution.
- ☐ Such additional information can be used to:
  - ☐ Increase CNR in drop-out regions (e.g., Optimal Combination of Echoes).
  - ☐ Automatically separate BOLD-like from Non-BOLD-like components (ME-ICA).
  - ☐ Significantly increase the sensitivity of BOLD deconvolution algorithms
- ☐ ME-ICA is a 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.



☐ ME-SPFM can help us reliably detect individual BOLD events without a-priori information about their timing.



### **Acknowledgements/ Questions**



#### Peter A. Bandettini

Daniel A. Handwerker
Dave Jangraw
Laurentius Huber
Emily Finn
Yuhui Chai
Natasha Topolski
Harry Hall



# Scientific and Statistical Computing Core

Robert W. Cox
Paul Taylor
Daniel Glen
Richard Reynolds
Gang Chen



Basque Center on Cognition, Brain and Language

César Caballero-Gaudes Manuel Carreiras





#### Functional MRI Facility

Sean Marrett
Vinai Roopchansingh
Andy Derbishire
Linquing Li

3dMEPFM will be soon available in

