Multi-echo fMRI

Daniel Handwerker

Section on Functional Imaging Methods
National Institute of Mental Health

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National Institute of Mental Health

Multi-echo education book (in progress)

Overview

- General Intro
  - Why care about multi-echo fMRI?
  - A bit of history
  - What is multi-echo fMRI?
- Multi-echo for noise removal
  - General concepts
  - ICA-based denoising (ME-ICA & tedana)
- Considerations for acquisition
- Open questions and continuing work
- Tedana community & how to contribute

Multi-echo education book (in progress)

Why I’m interested in multi-echo fMRI

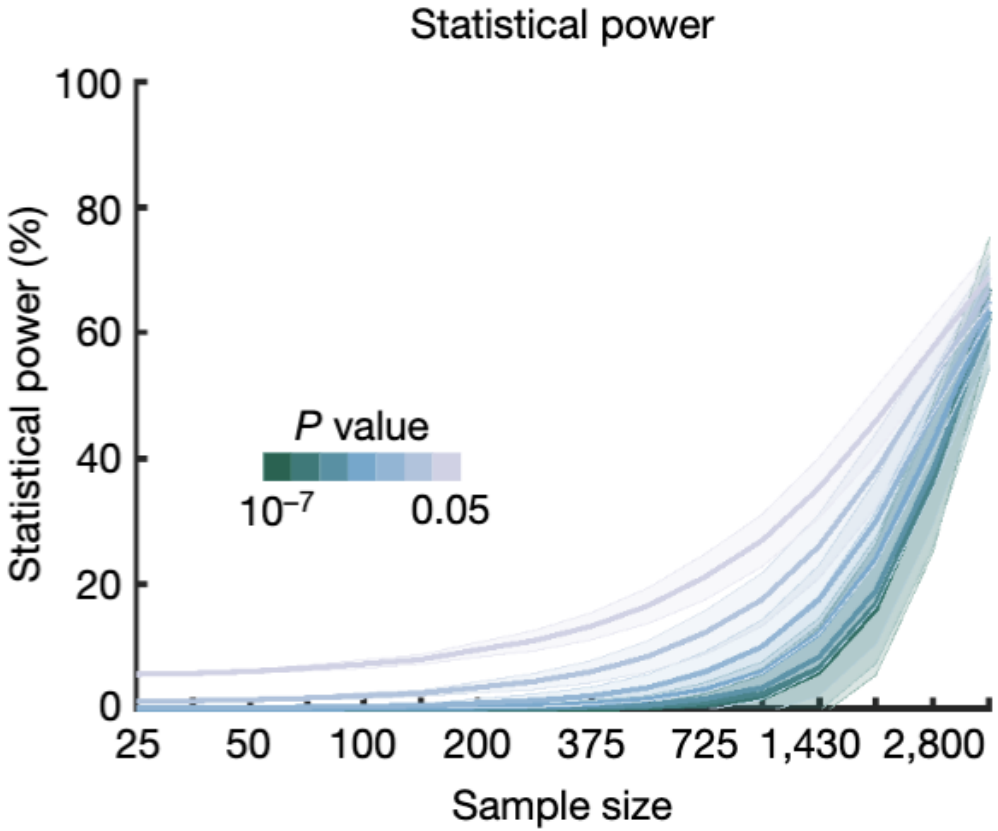
- I want fMRI to directly help people
- Clinically useful scans require better data
- For population studies, better data → lower sample size

- Multi-echo is not the only path to better data

  but it already helps and has the potential to address key road bocks towards better data

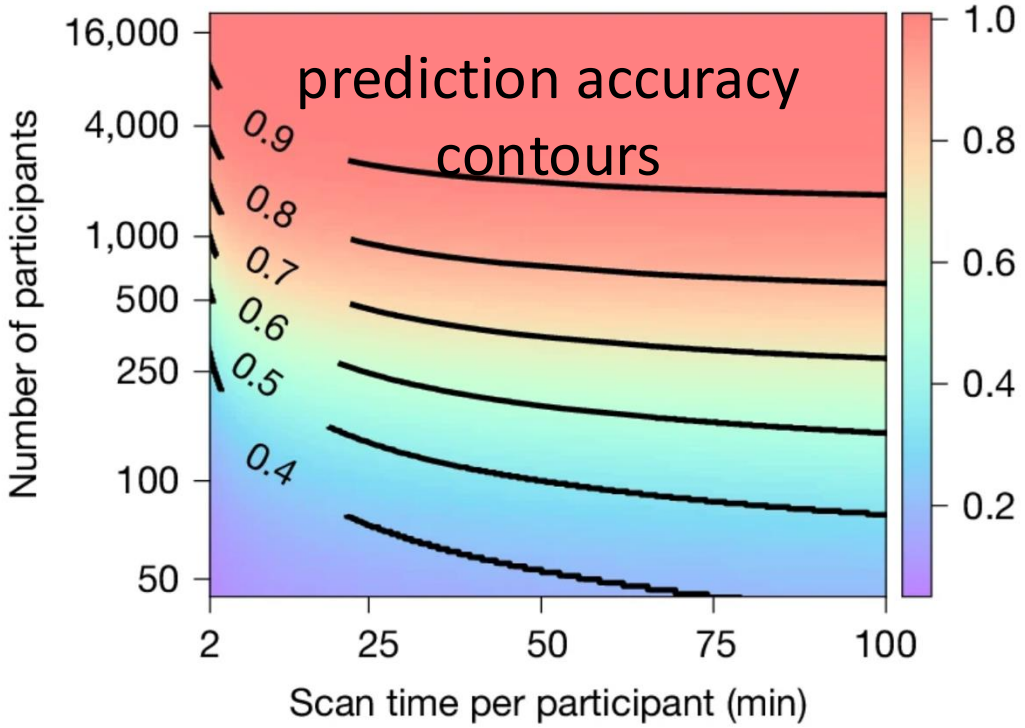
Many paths to better fMRI

How many participants?



Marek, Tervo-Clemmens, et. al. *Nature* 2022
Reproducible brain-wide association studies require thousands of individuals

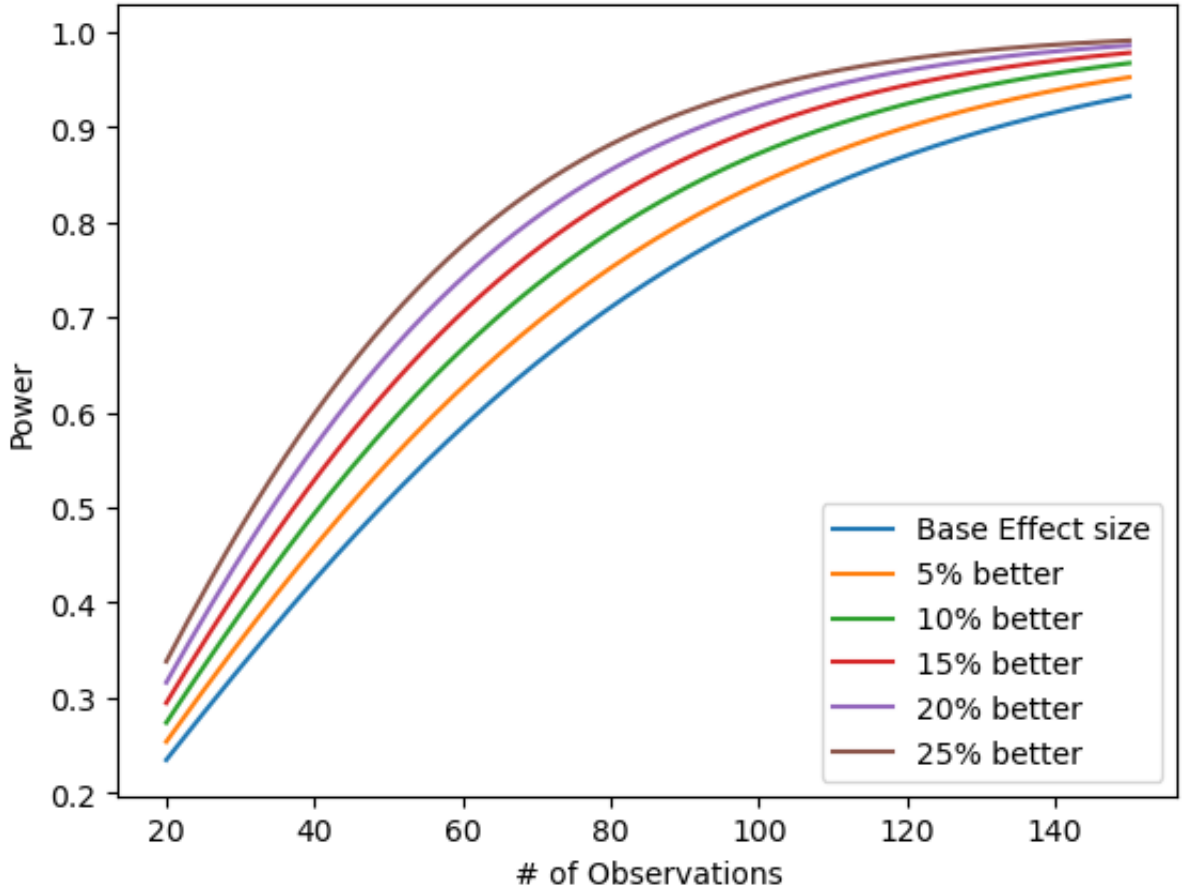
Scan time per participant?

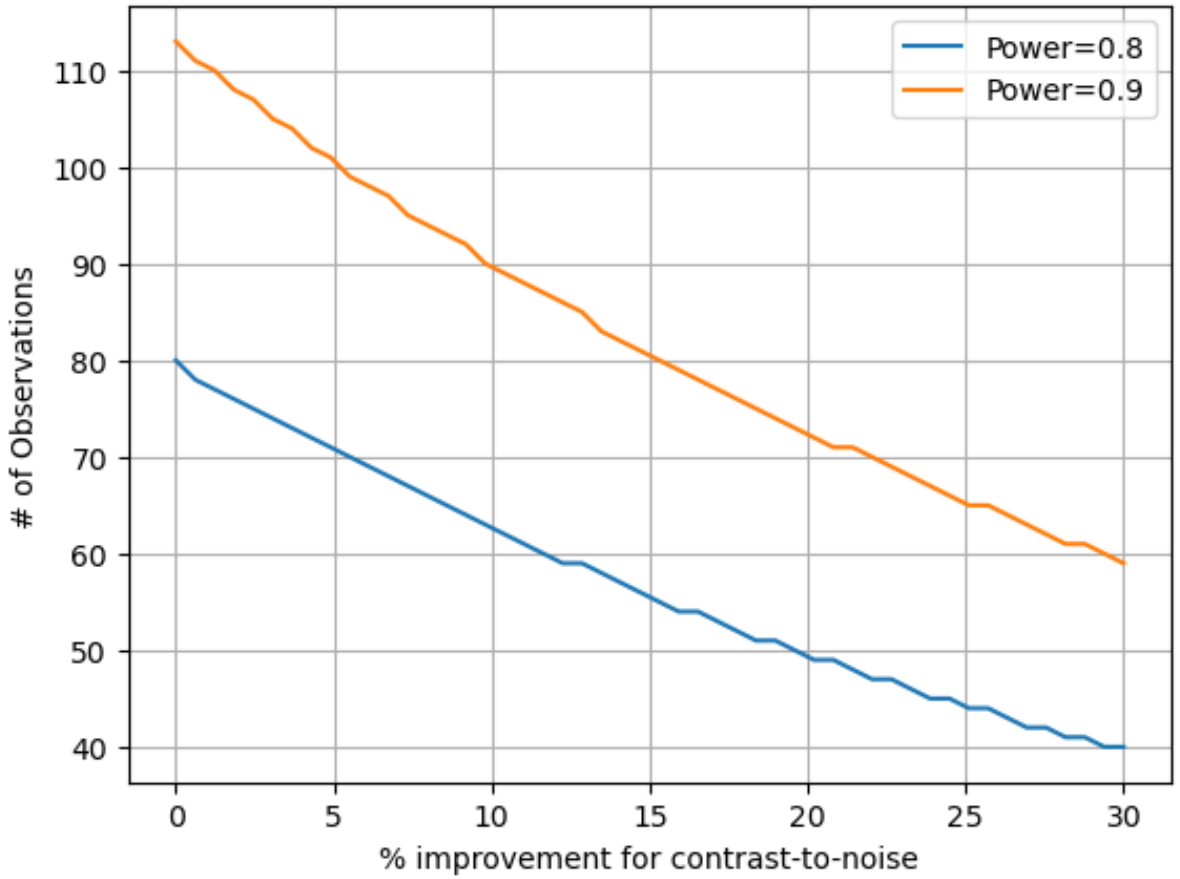


Ooi, Orban, et. al. *Nature* 2024
Longer scans boost prediction and cut costs in brain-wide association studies

Scan duration is one of multiple ways to improve intra-subject data quality

Data quality matters!

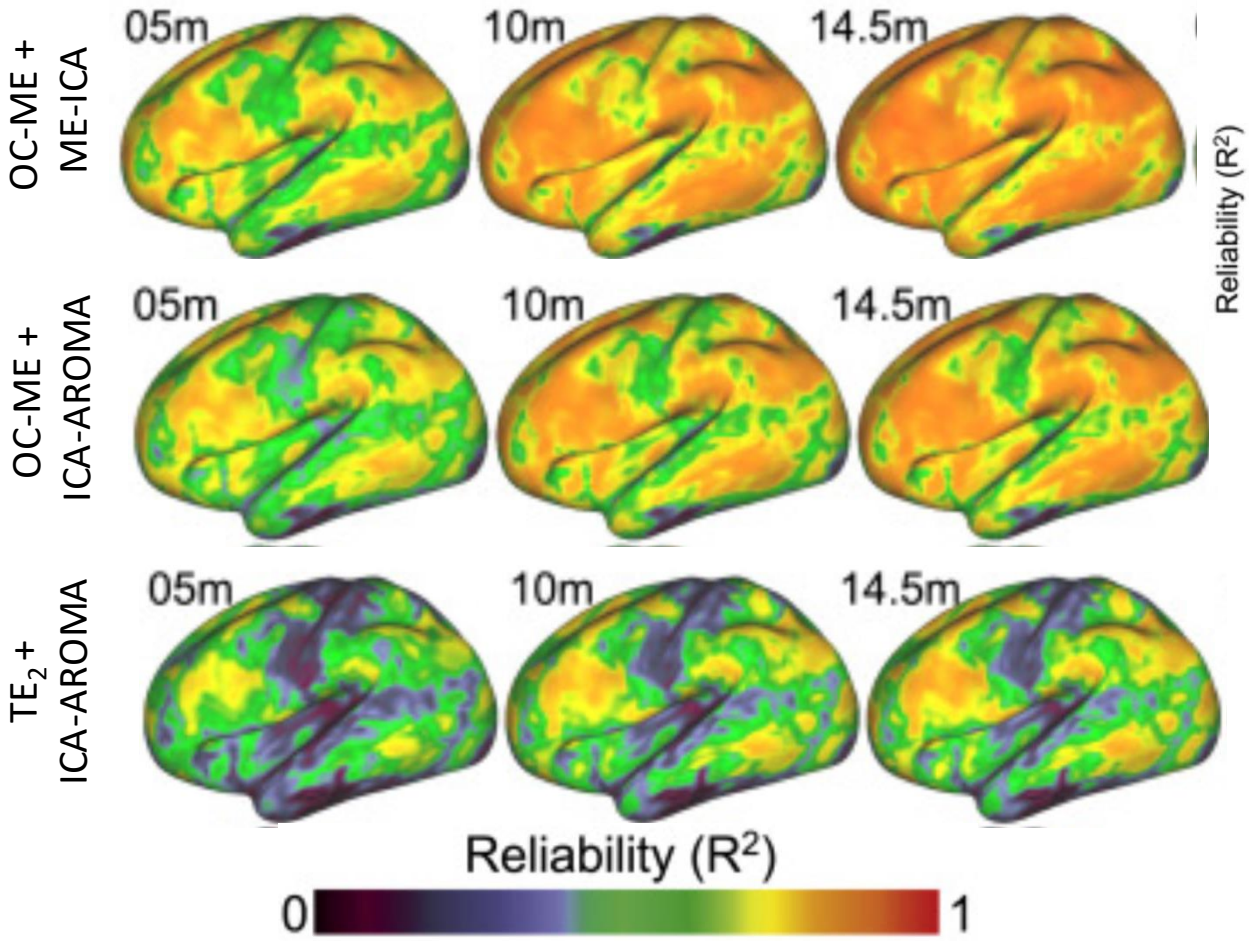




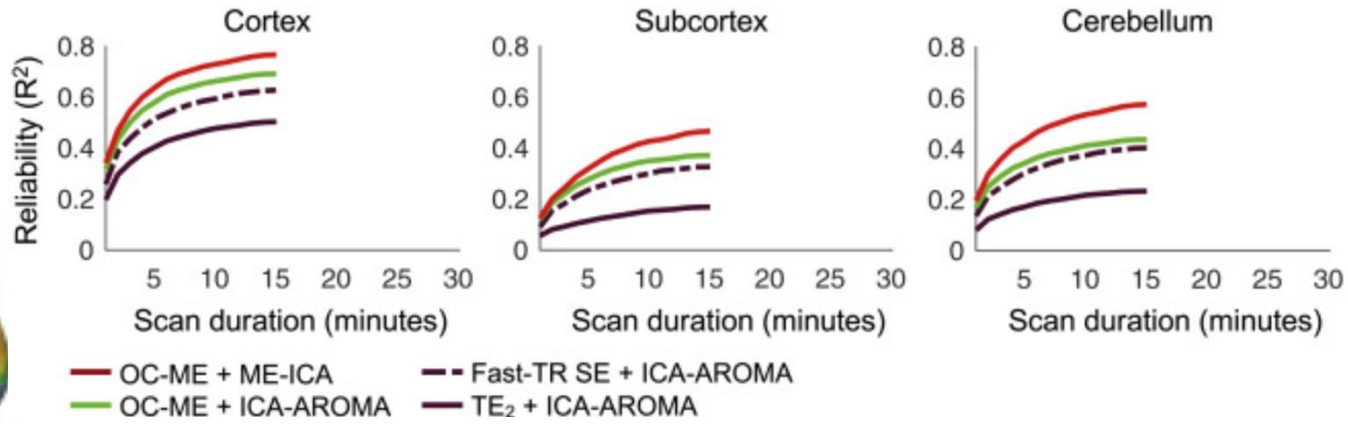
A 10% improvement in contrast-to-noise could mean a statistical power of 0.8 is possible with 63 vs 80 subjects

Multi-echo fMRI improves reliability

Reliability map, sbj ME01



Time x reliability, sbj ME01

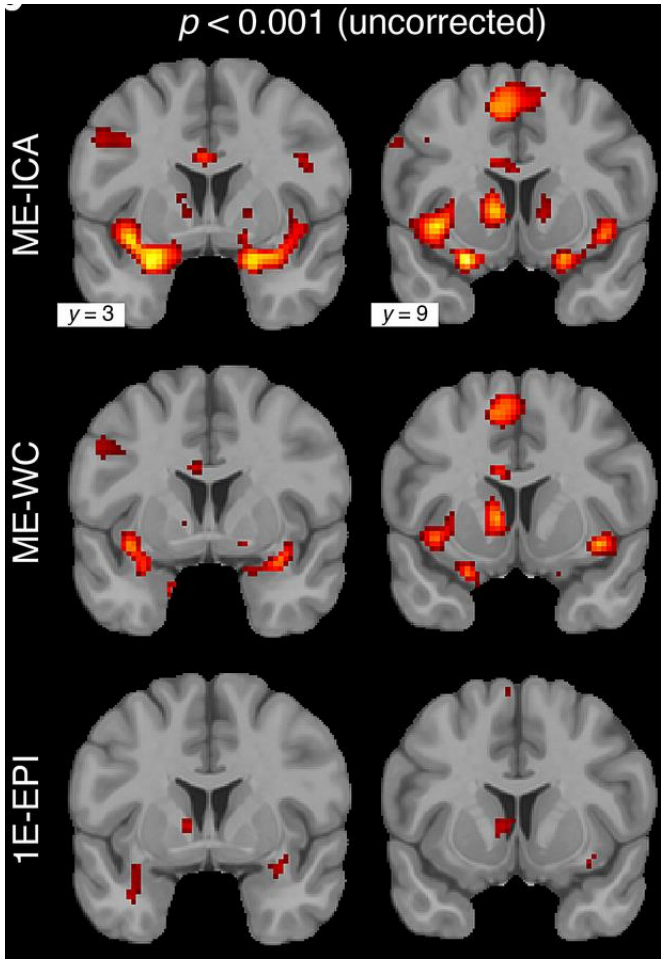


Collecting Multi-echo data + multi-echo denoising is better than multi-echo data without denoising and single-echo data with a shorter-TR

Lynch et al “Rapid Precision Functional Mapping of Individuals using multi-echo fMRI” Cell Reports 2022

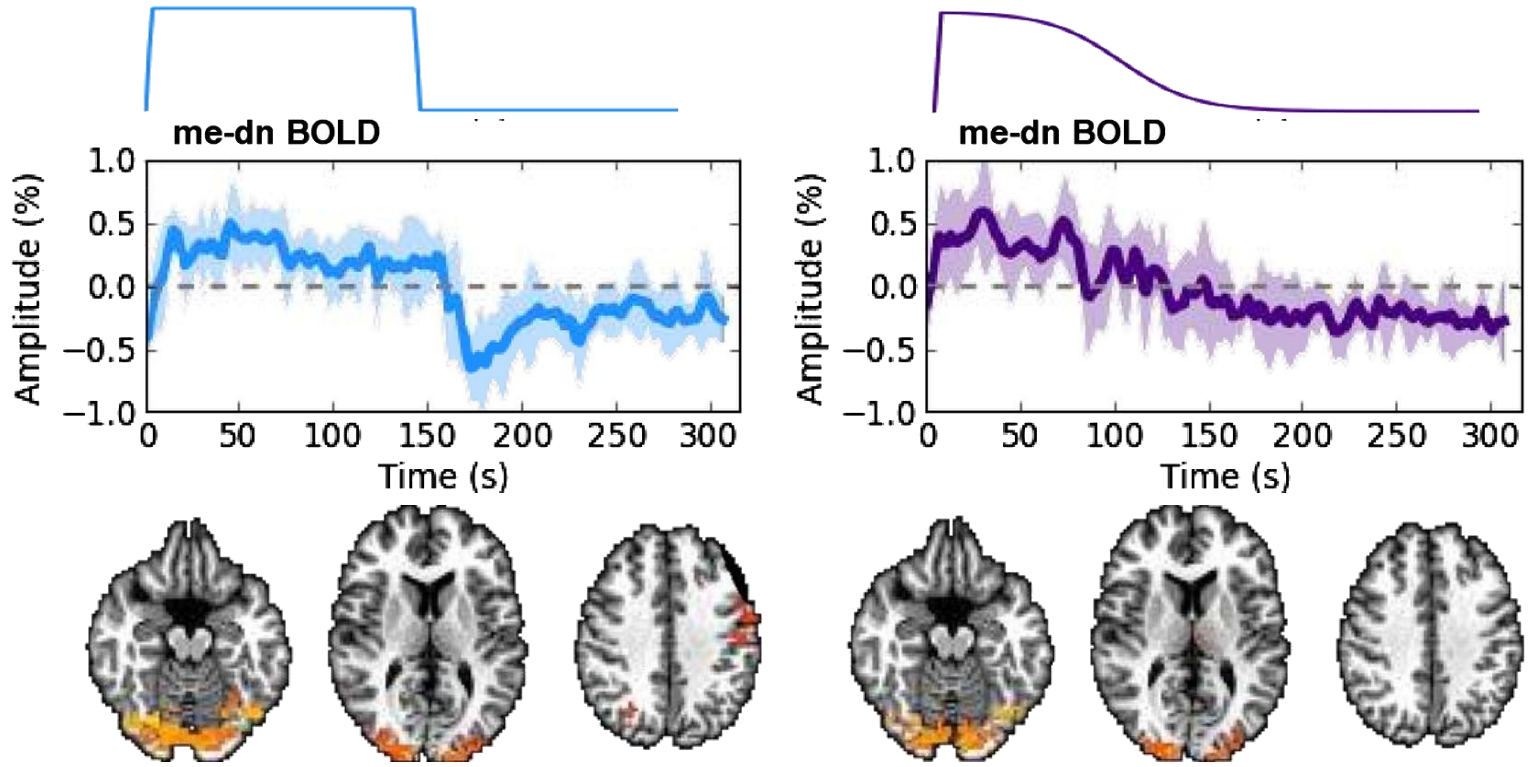
Multi-echo fMRI improves data

Regions with high dropout



Zhao, Raithel et al olfactory fMRI. Imaging Neuro 2024

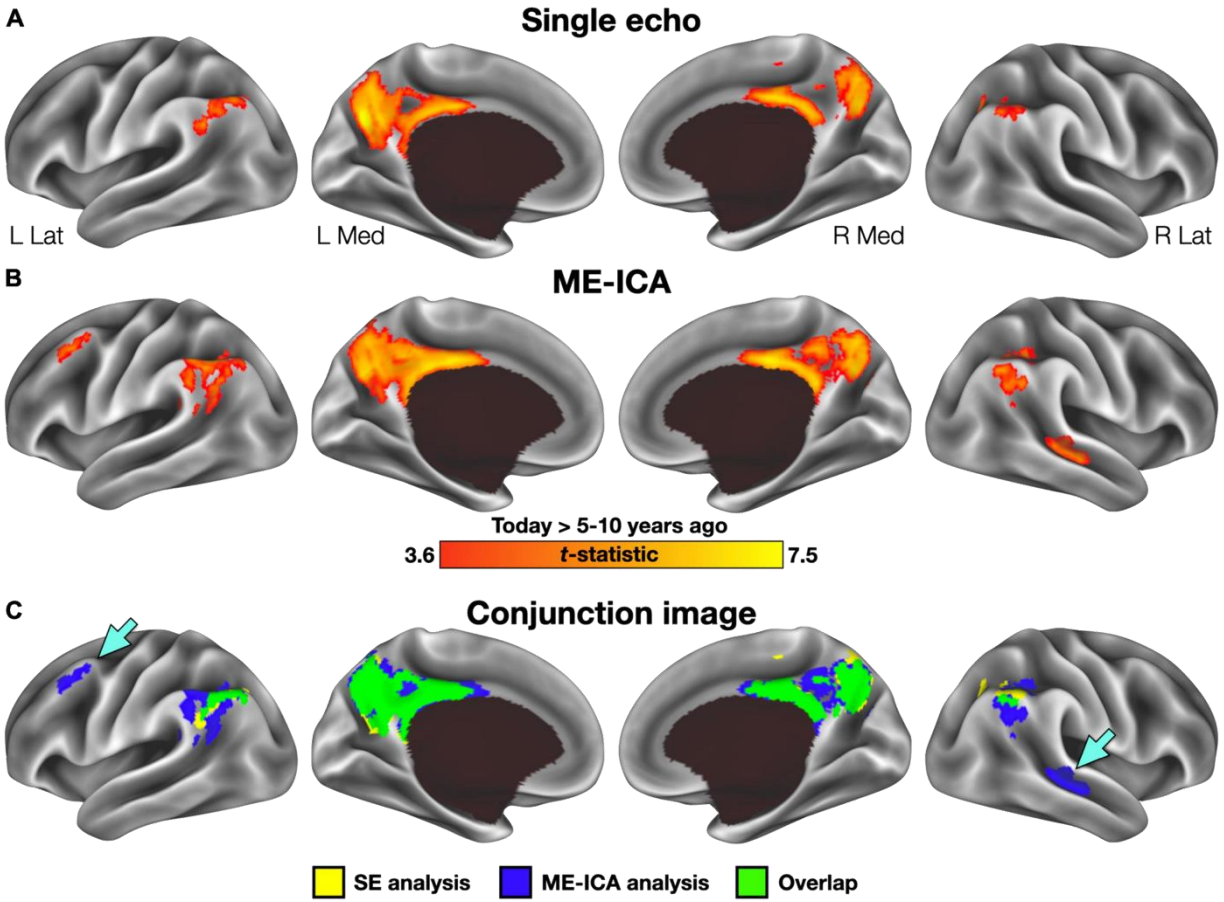
Temporally slow changes



Evans et al. "Separating Slow BOLD from non-BOLD baseline…" NeuroImage 2015

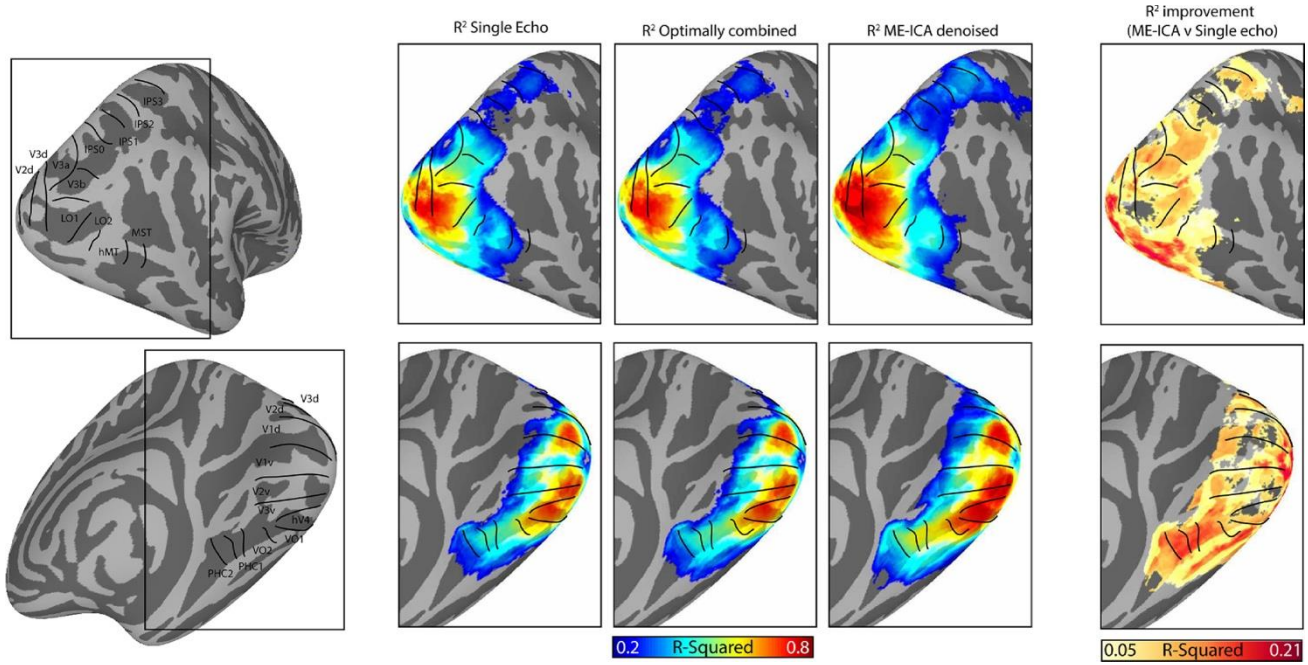
Multi-echo fMRI improves data

Overt Speech



Gilmore et al. "A comparison of single- and multi-echo processing of fMRI Data during autobiographical recall" Front. Neurosc. 2022

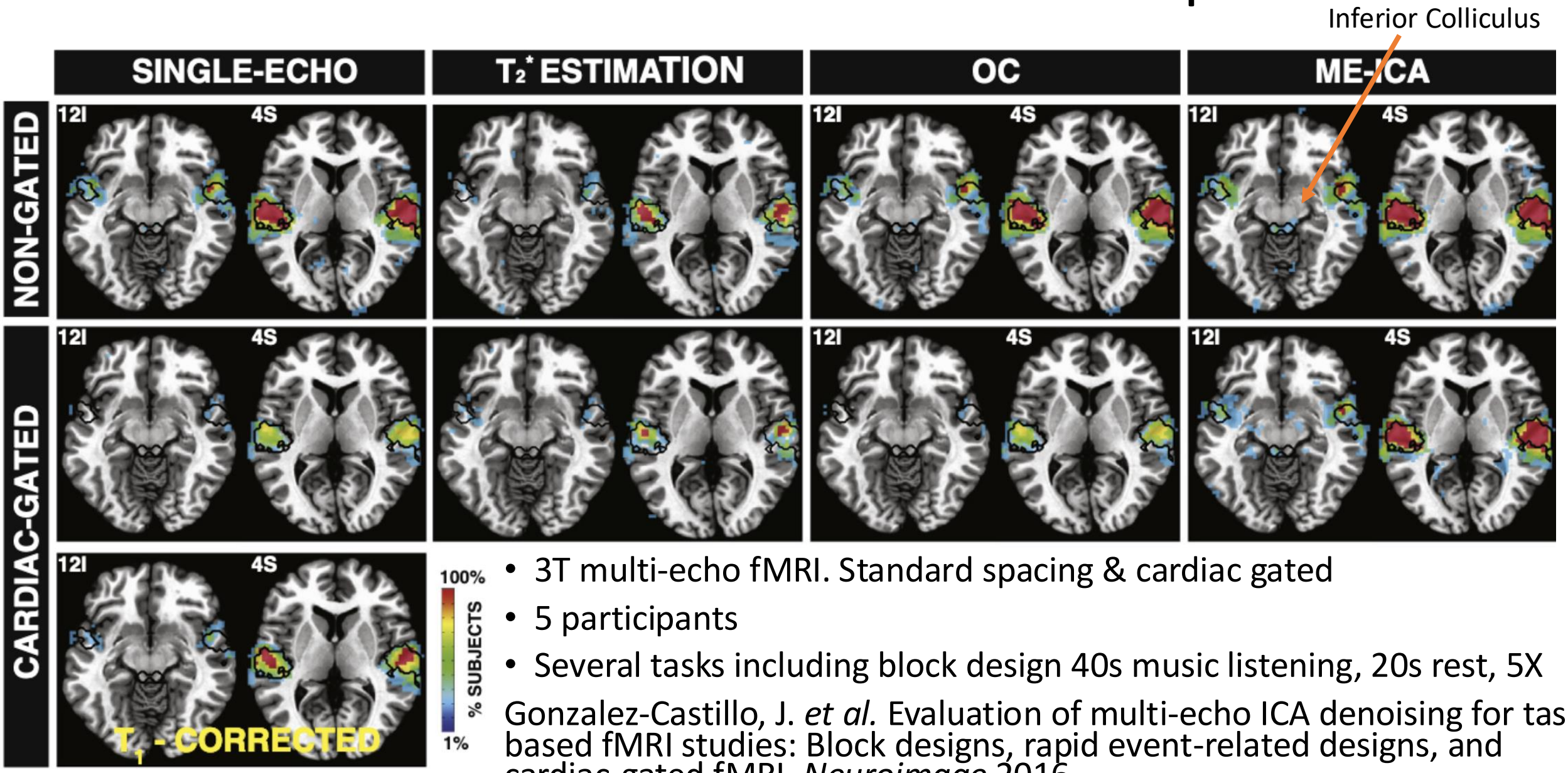
Better retinotopy



Up to 21% Improvement in population receptive field mapping model fit

Steel A. et al. "Evaluating the efficacy of multi-echo ICA denoising on model-based fMRI" NeuroImage 2022

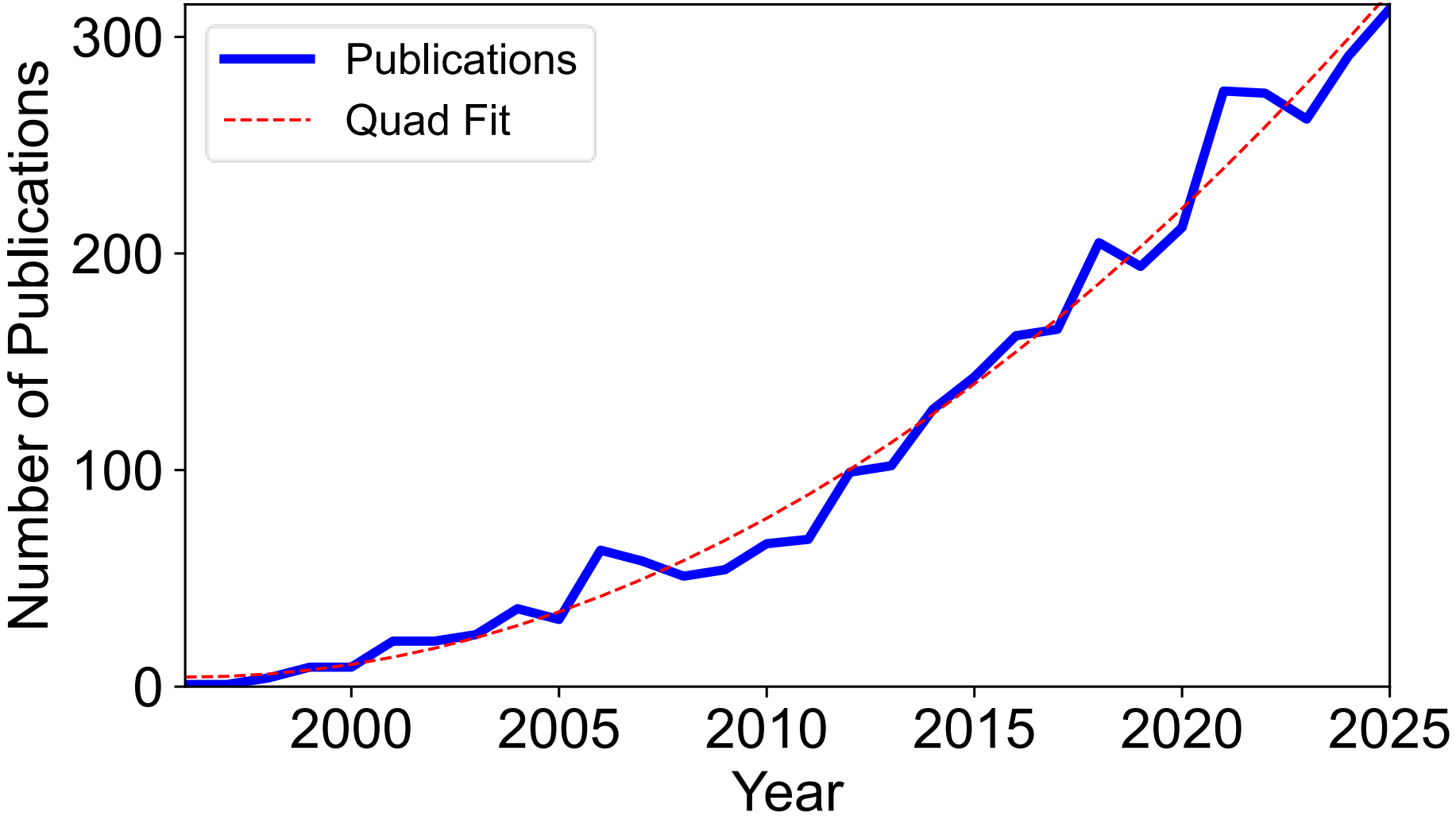
Multi-echo makes other fMRI methods possible



- 3T multi-echo fMRI. Standard spacing & cardiac gated
- 5 participants
- Several tasks including block design 40s music listening, 20s rest, 5X

Gonzalez-Castillo, J. *et al.* Evaluation of multi-echo ICA denoising for task based fMRI studies: Block designs, rapid event-related designs, and cardiac-gated fMRI. *Neuroimage* 2016

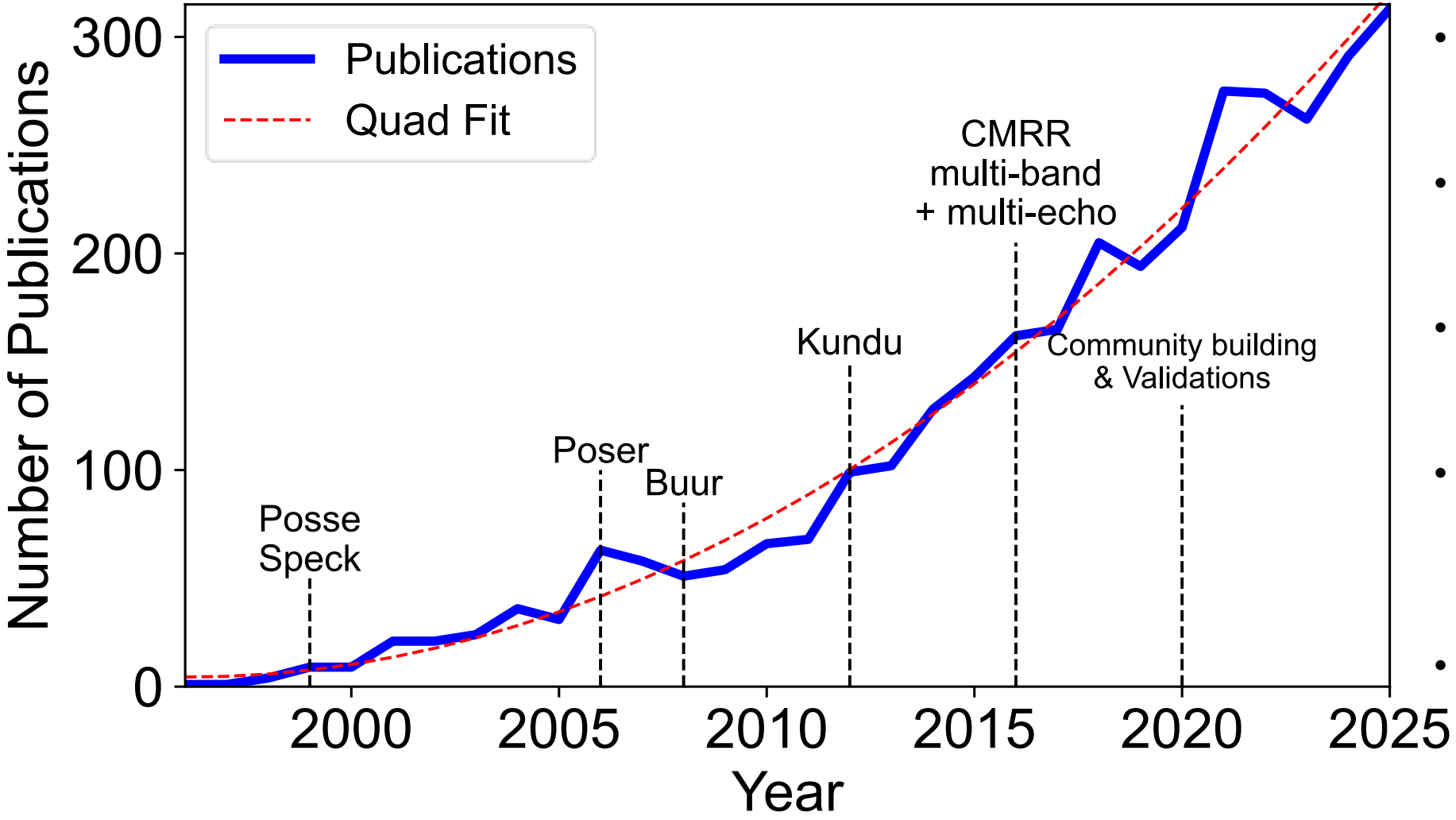
Publication History of Multi-echo fMRI Studies



Reading list & more history

Scopus query: ((ALL(multi-echo) OR ALL(multiecho)) AND ALL(FMRI) AND PUBYEAR > 1991 AND PUBYEAR < 2027)

Publication History of Multi-echo fMRI Studies



- 1999-2008: Development of key theory and noise reduction methods
- 2008-2015: MRI Hardware & pulse sequences limited practical ME usage
- 2012-3: Kundu developed ME-ICA, showing practical benefits that generated wider interest
- 2016: First widely available multi-band + ME sequence made ME possible with minimal compromises
- 2020: Validations of ME benefits start to get published

Reading list & more history

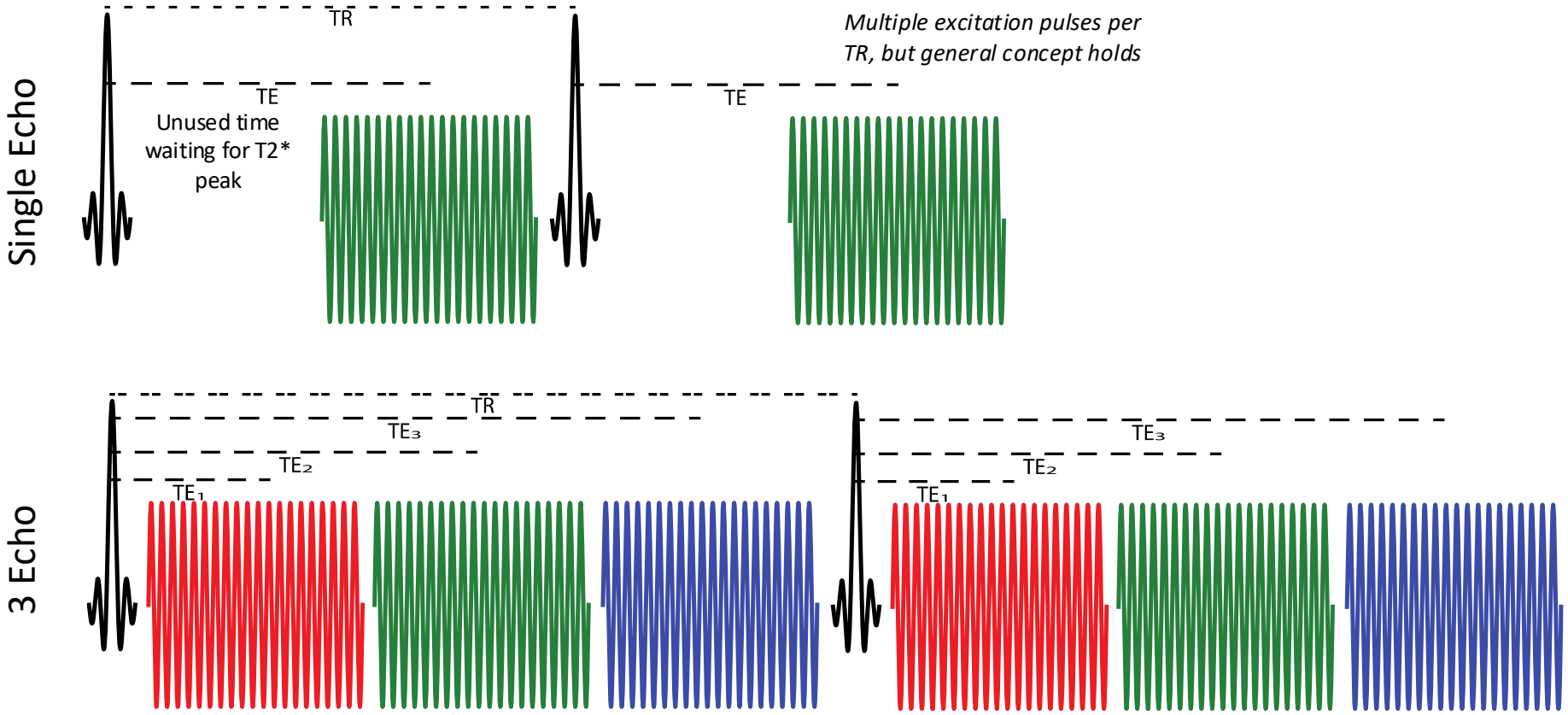
Scopus query: ((ALL(multi-echo) OR ALL(multiecho)) AND ALL(FMRI) AND PUBYEAR > 1991 AND PUBYEAR < 2027)

Multi-echo fMRI shared data

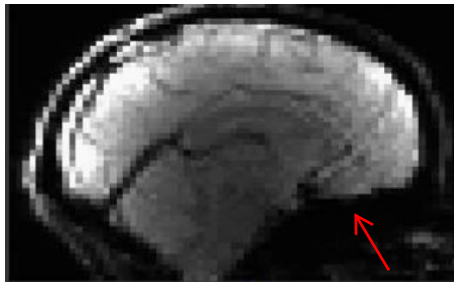
- Neurocognitive aging data release with behavioral, structural, and multi-echo functional MRI measures. N=181 younger, 120 older
- Cambridge Centre for Aging Neuroscience (Cam-CAN). N=649
- Heart rate variability biofeedback training and emotion regulation. N=193
- Le Petit Prince. N=112
- Multi-echo Cambridge. N=89
- Complex multi-echo fMRI, Czech Bioimaging. N=83
- PennLINC Affective Instability. N=49
- Evidence supporting a time-limited hippocampal role in retrieving autobiographical memories. N=40
- Nigh Owls Scan Club (deep sampling). N=5

https://me-ica.github.io/open-multi-echo-data

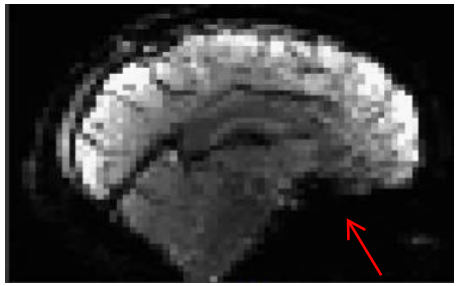
What is multi-echo fMRI?



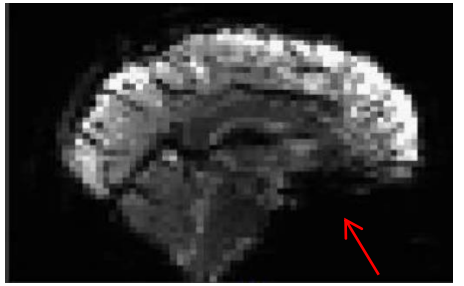
Echo 1



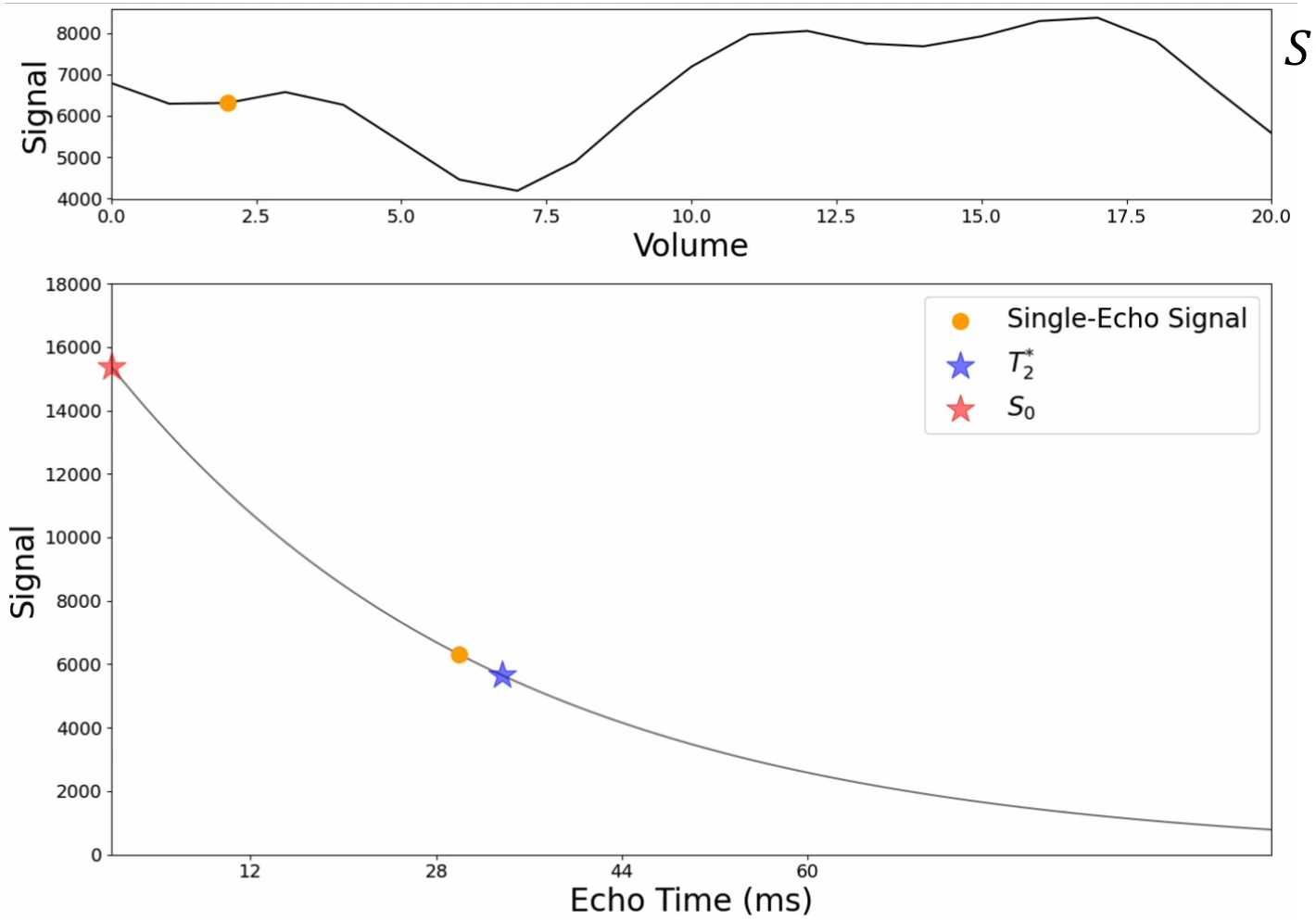
Echo 2



Echo 3



Using multi-echo information



$$S(x,t,TE_k) = \boldsymbol{S_o(x,t)} \cdot e^{-\boldsymbol{R_2^*(x,t)} \cdot TE_k} + n(x,t)$$

The signal decays with echo time

S_0

- The y-intercept at TE=0
- Non-neural signals including head motion & scanner artifacts

$R_2^* = 1/T_2^*$

- The rate of decay
- Altered by several factors including changes in blood oxygenation (BOLD)

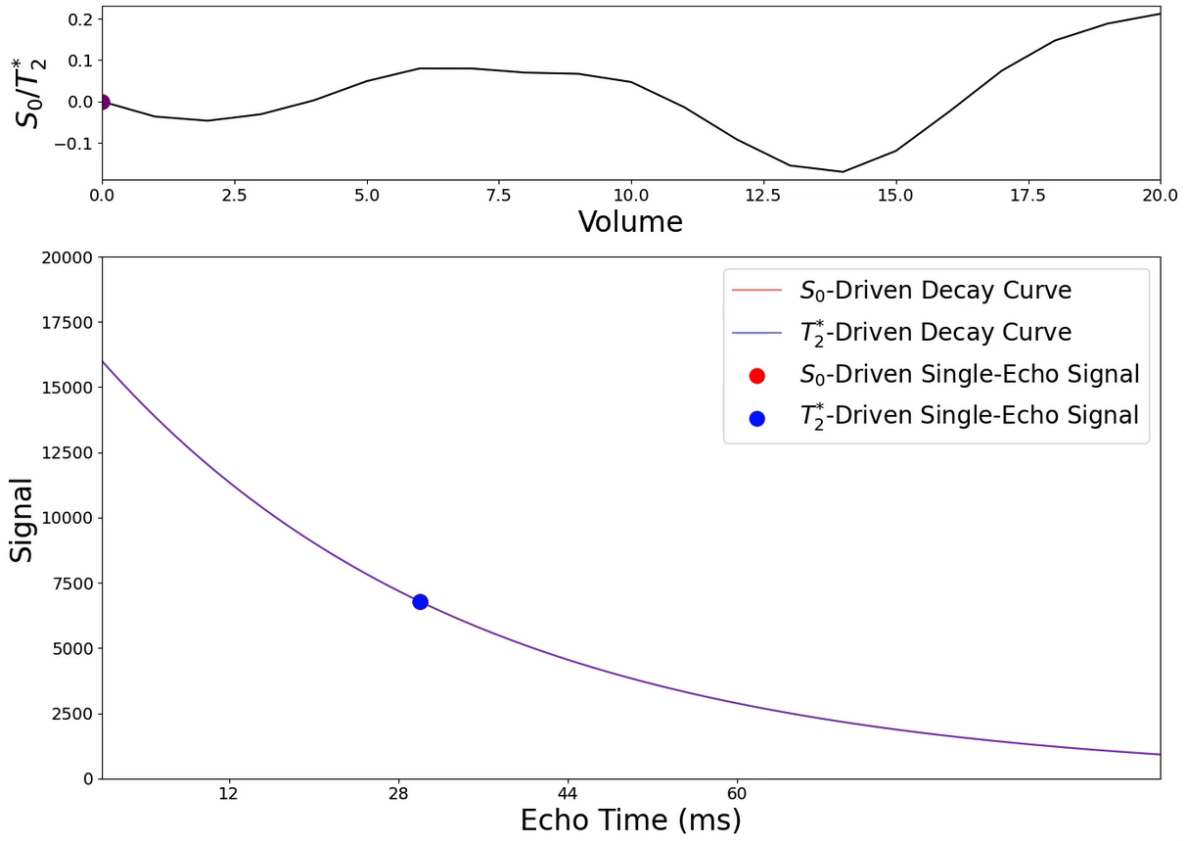
n = thermal noise

- Rician for magnitude only data
- Gaussian for complex data
- Echo time independent

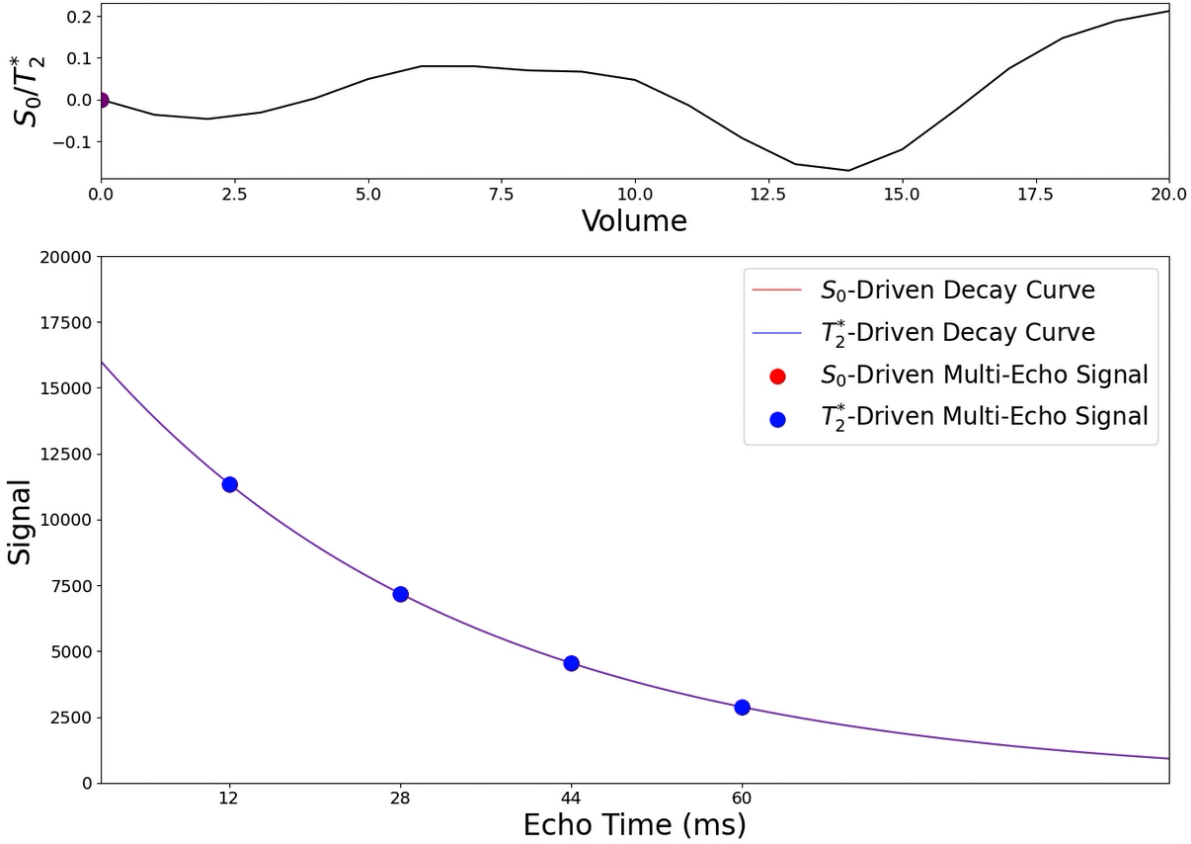
https://me-ica.github.io/multi-echo-data-analysis/content/Signal_Decay.html

Distinguishing T_2^* and S_0

What we measure with single-echo fMRI



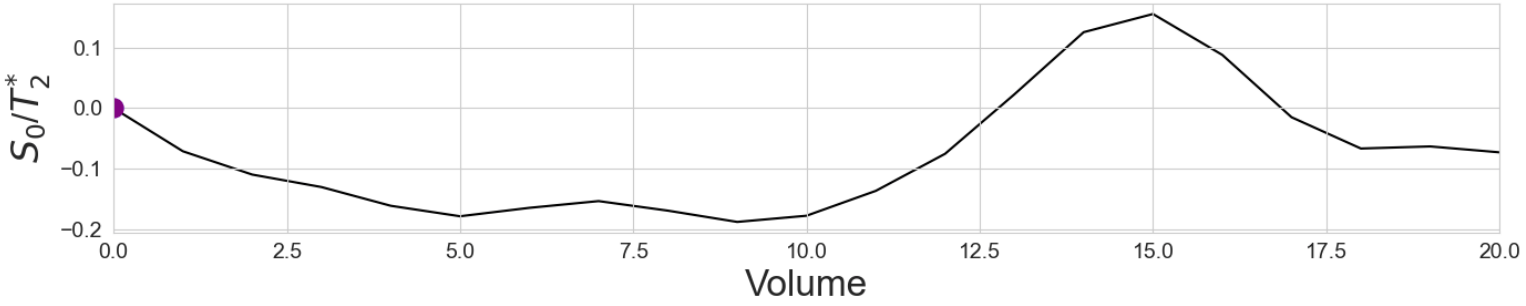
What we measure with multi-echo fMRI

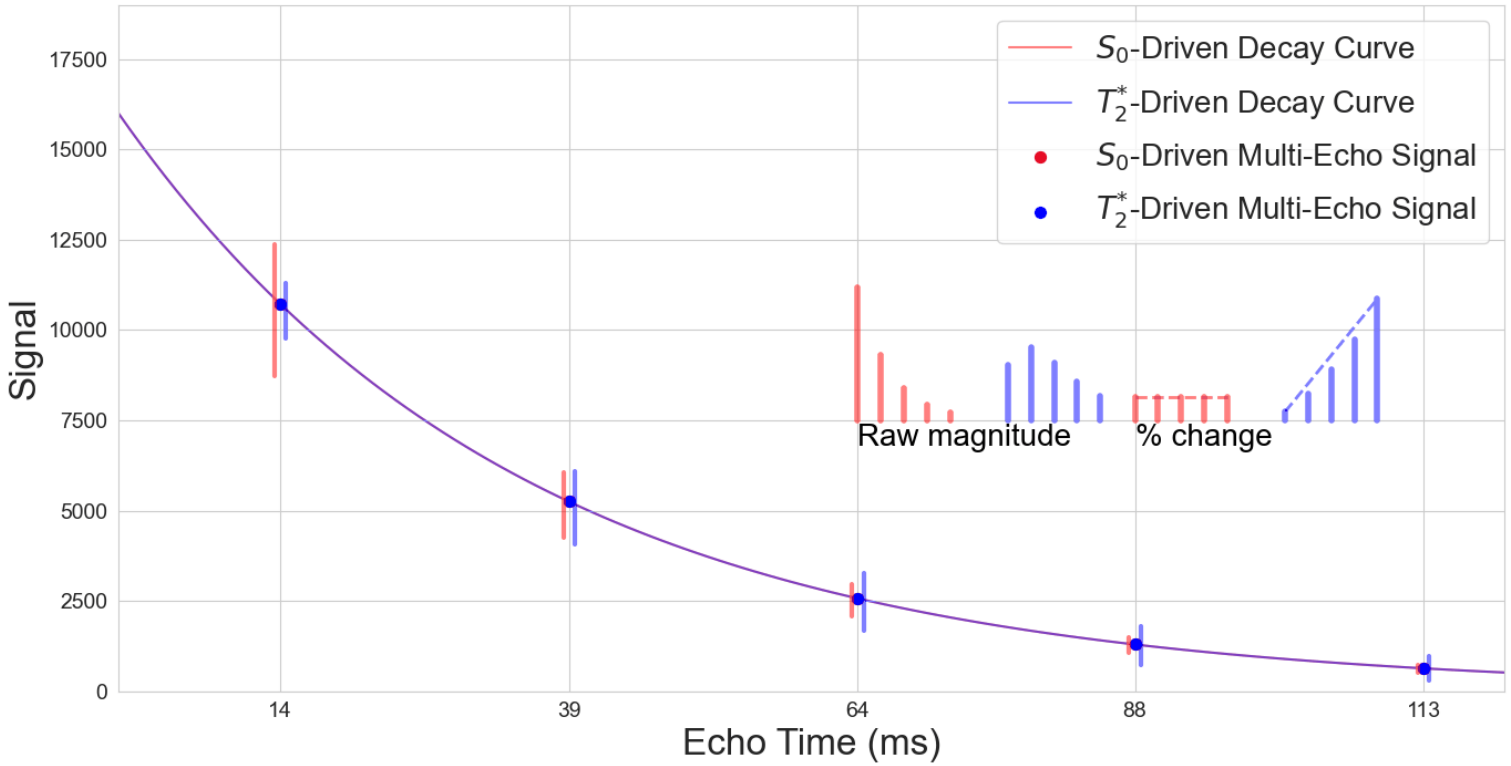


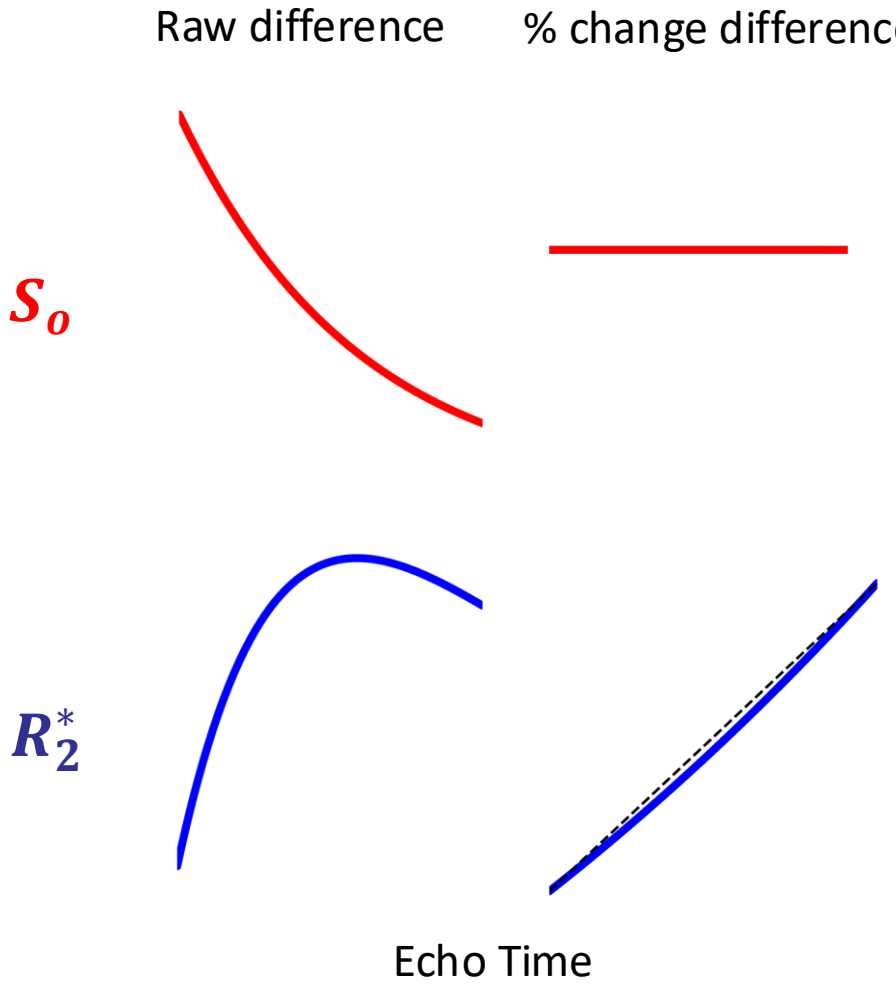
$$S(x,t,TE_k) = \boldsymbol{S_o(x,t)} \cdot e^{-\boldsymbol{R_2^*(x,t)} \cdot TE_k} + n(x,t)$$

https://me-ica.github.io/multi-echo-data-analysis/content/Signal_Decay.html

Distinguishing T_2^* and S_0







$$S(x,t,TE_k) = \boldsymbol{S_0(x,t)} \cdot e^{-\boldsymbol{R_2^*(x,t)} \cdot TE_k} + n(x,t)$$

Multi-echo Math

$$S(x,t,TE_k) = \boldsymbol{S_o(x,t)} \cdot e^{-TE_k \cdot \boldsymbol{R_2^*(x,t)}} + n(x,t)$$

Assuming $n(x,t)$ *is negligible*

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

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

$$S_{\%change} = \frac{S(x,t,TE_k) - \overline{S(x,TE_k)}}{\overline{S(x,TE_k)}} = \left(1 + \frac{\Delta S_o(x,t)}{\overline{S_o(x)}}\right) \cdot e^{-TE_k \cdot \Delta R_2^*(x,t)} - 1$$

First order Taylor Approximation of: $e^{-TE_k \cdot \Delta R_2^*(x,t)}$

$$S_{\%change} = \frac{\Delta S_o(x,t)}{\overline{S_o(x)}} - TE_k \cdot \Delta R_2^*(x,t) \boxed{- \frac{TE_k . \Delta R_2^*(x,t) \cdot \Delta S_o(x,t)}{\overline{S_o(x)}}}$$

Assuming this this negligible

Multi-echo Math

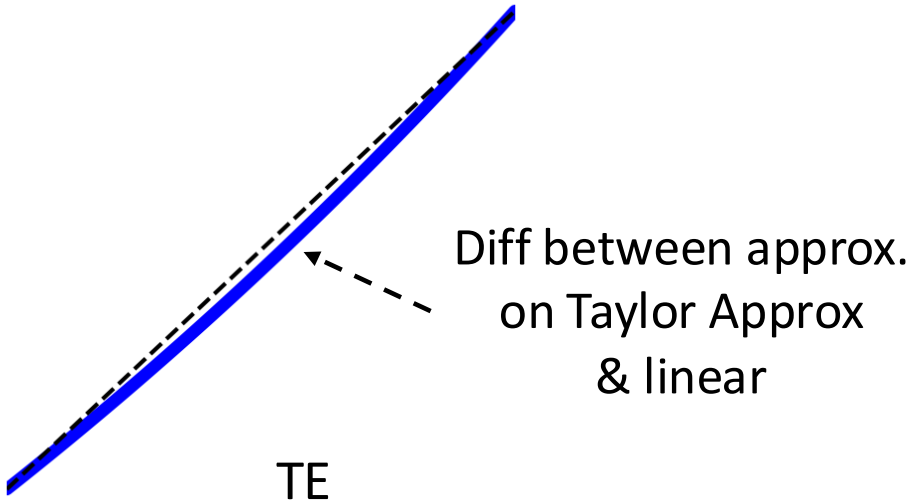
$$S_{\%change} \approx \frac{\Delta S_o(x,t)}{\overline{S_o(x)}} - TE_k \cdot \Delta R_2^*(x,t)$$

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

TE

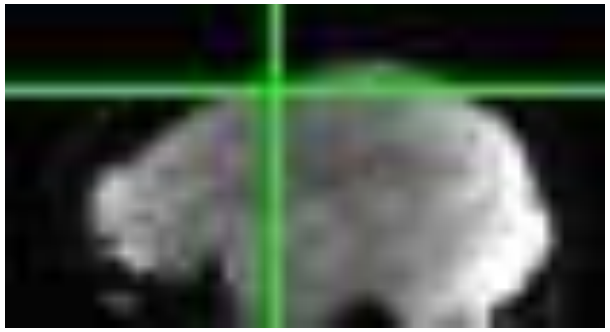
Net Magnet. Fluctuations in at location 'x', time 't'

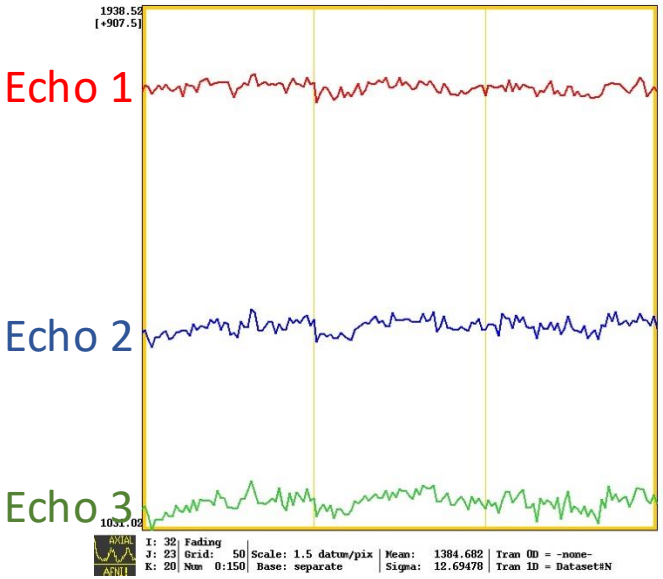
$\Delta R_2^*(x,t)$



BOLD Fluctuations at location 'x', time 't'

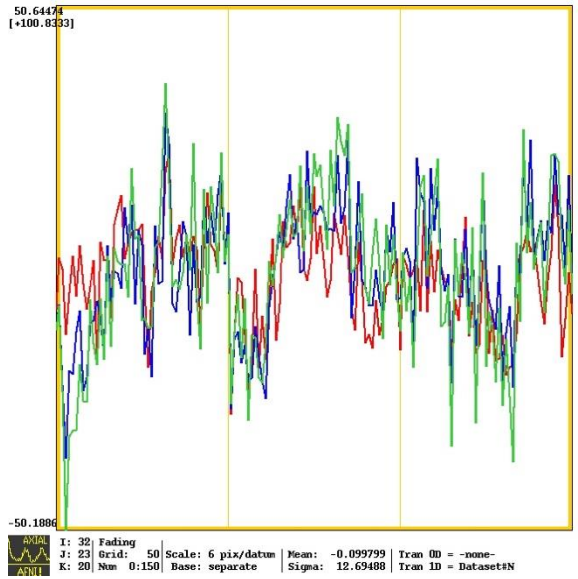
Response magnitudes by echo time

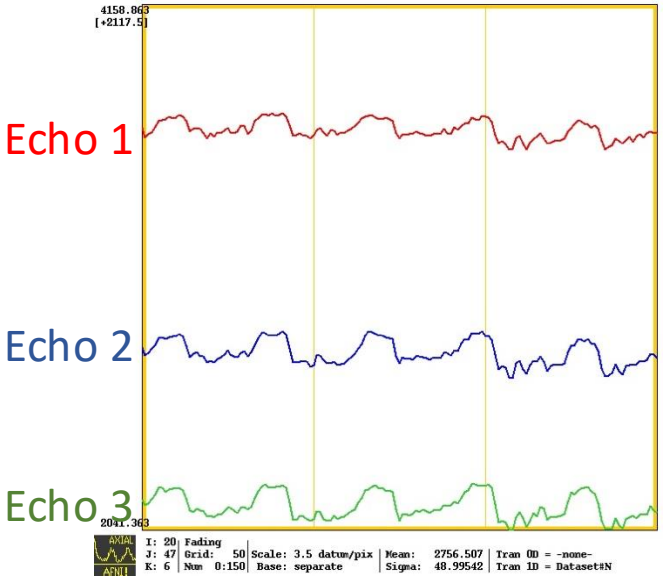




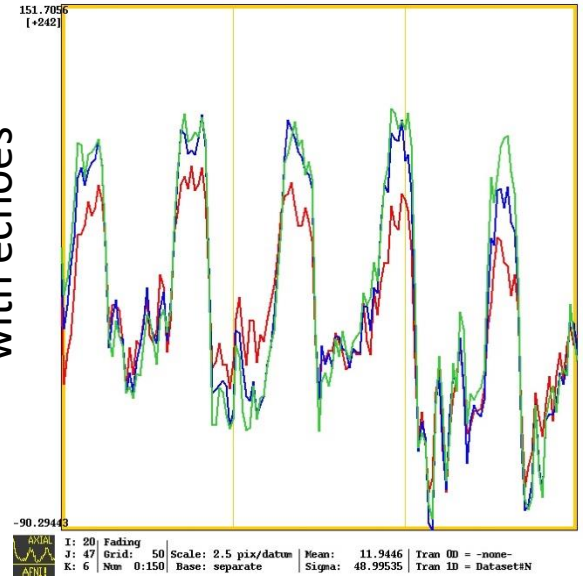
Demeaned Time Series

Fluctuations similar across echoes



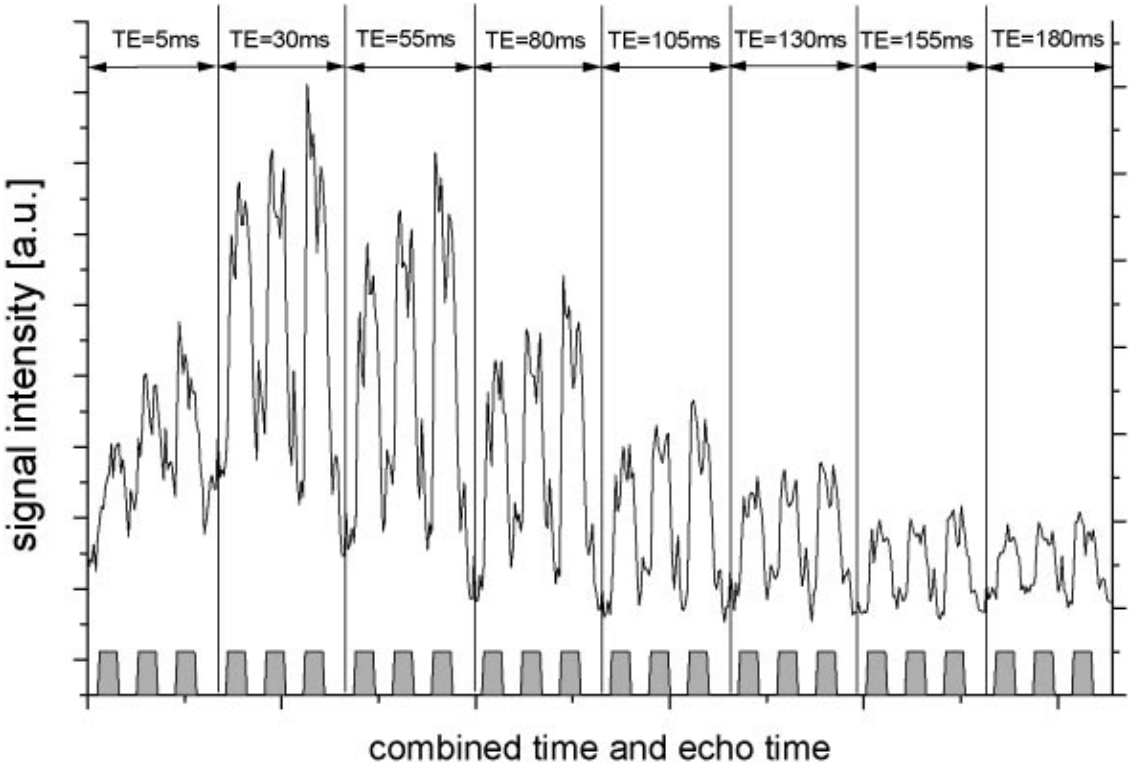


Fluctuations scale with echoes



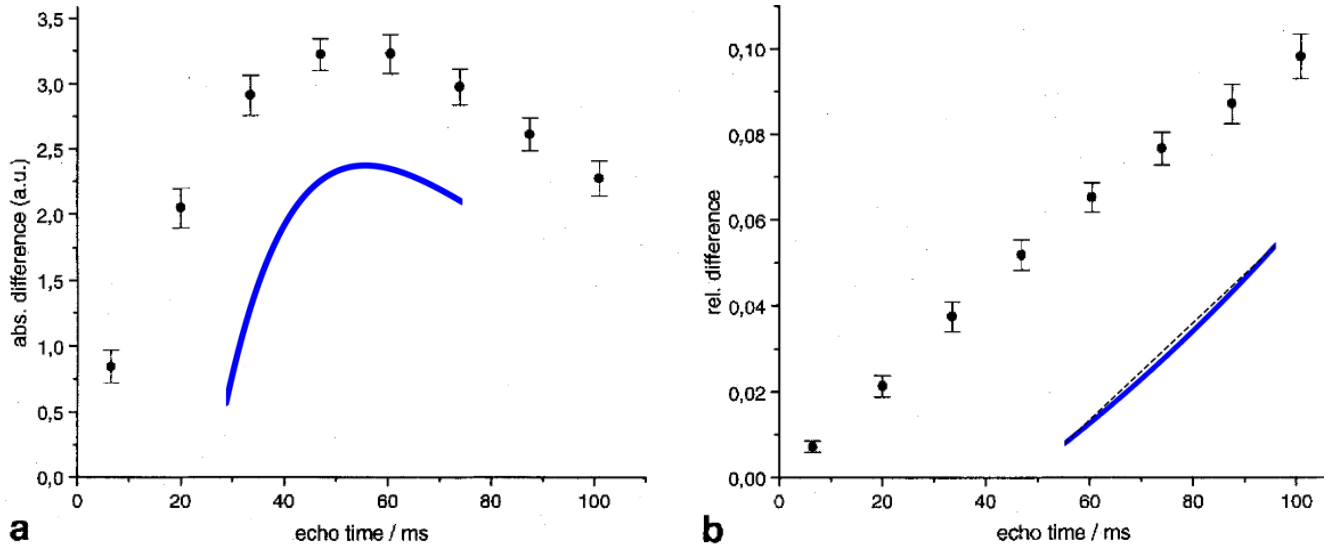
Response magnitudes by echo time

Finger tapping task at 3T



Barth et al NMR Biomed 2001

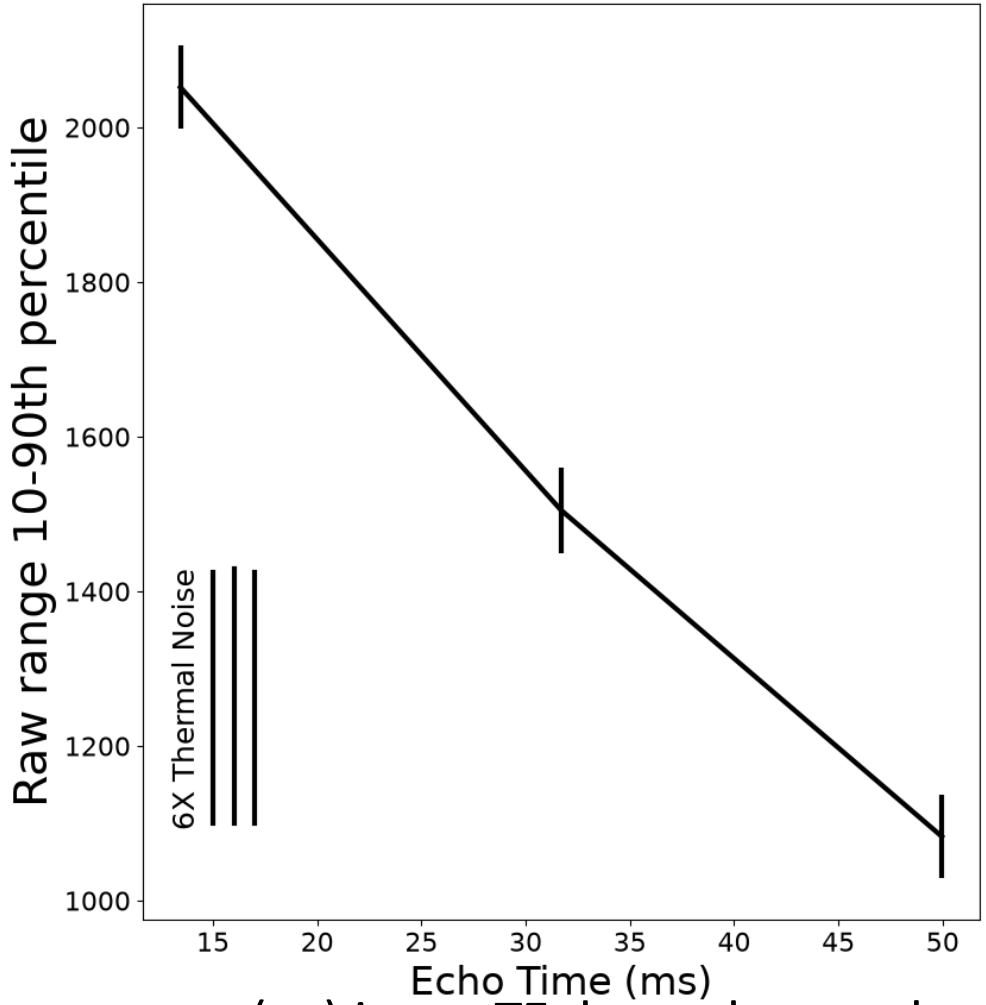
8Hz flashing checkerboard at 2T

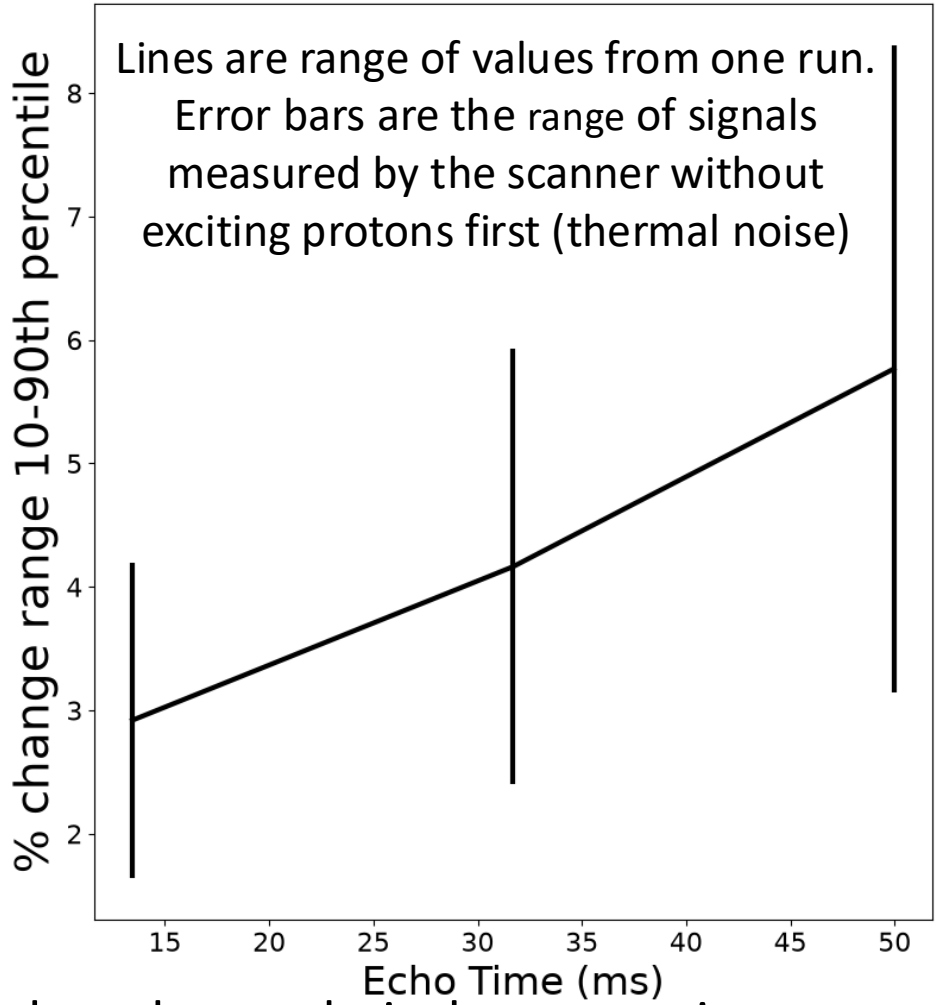


Speck & Hennig 1998
Building off work on functional spectroscopy

Without ignoring thermal noise

$$S(x,t,TE_k) = \boldsymbol{S_o(x,t)} \cdot e^{-TE_k \cdot \boldsymbol{R_2^*(x,t)}} + n(x,t)$$





n(x,t) is not TE dependent, so later echoes have relatively more noise

A linear fit across ≧3 noisy data points is… challenging

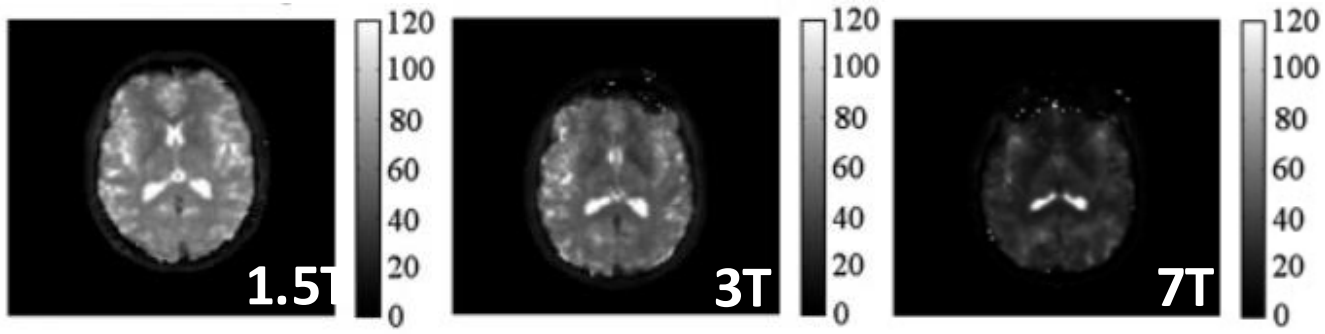
Optimal echo time (TE)

The optimal echo time (TE) = T2* of tissue

- T2* varies by MRI field strength, tissue type, MRI field inhomogeneity

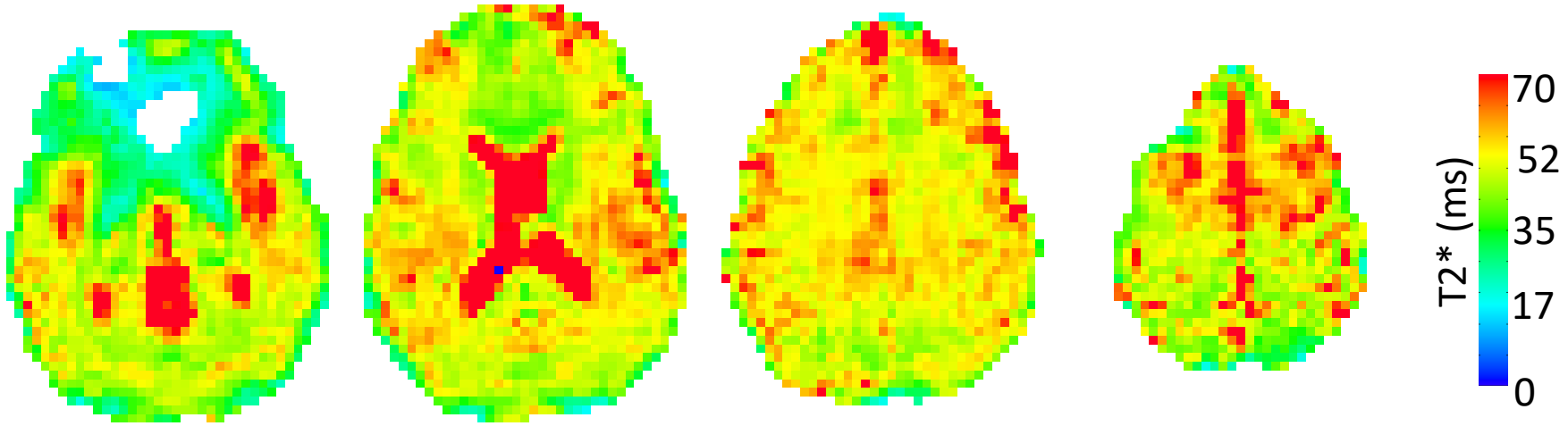
Table 1. Mean corrected T_2^* values for all regions and field strengths

Field strength (T)	Grey matter (ms)	White matter (ms)	Caudate (ms)	Putamen (ms)
1.5	84.0±0.8	66.2±1.9	58.8±2.4	55.5±2.3
3	66.0±1.4	53.2±1.2	41.3±2.3	31.5±2.5
7	33.2±1.3	26.8±1.2	19.9±2.0	16.1±1.6



Peters, Brooks et al. MRM (2007)

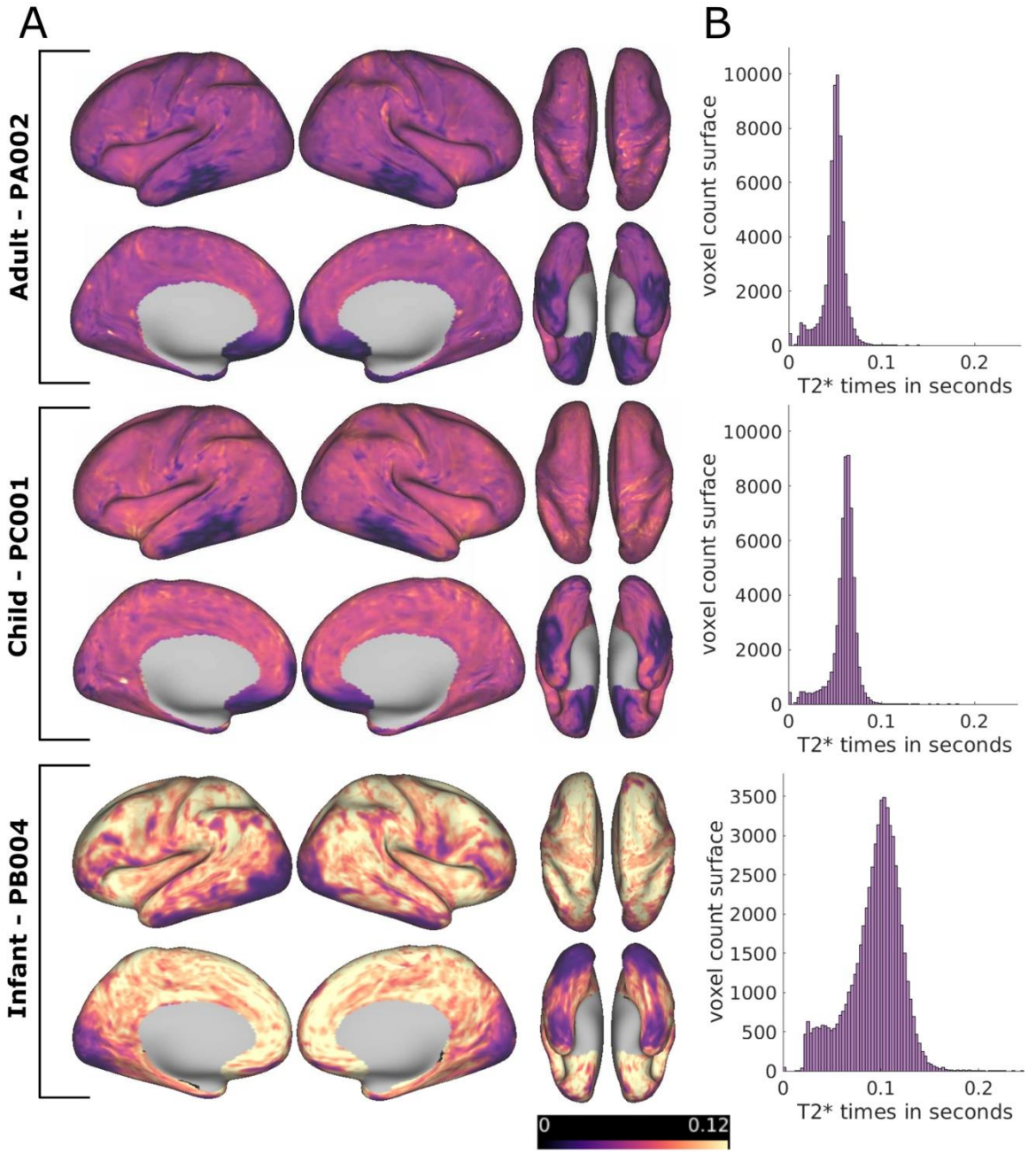
- Since T2* varies, the optimal TE varies. We pick a TE with "good enough" contrast in most of the brain without losing signal in areas of interest
- A longer TE with single echo is also dead time + slower acquisition



Optimal echo time (TE)

T2* also varies by age

Multi-echo acquisition means we collect data that covers a range of optimal TEs



Moser et al. Multi-echo acquisition and thermal denoising advances precision functional imaging. *Imaging Neuroscience* 2025

Using multi-echo to reduce noise

Weighted average of echoes

Method	Weights	Requires T2* estimates	Weights vary by voxel	Weights vary with time
Simple Summation (Posse 1999)	$w_n = 1/N$	No	No	No
TE-Combined	$w_n = \frac{TE_n}{\sum_{i=1}^{N} TE_i}$	No	No	No
T_2^*-Combined (OC‡/BOLD‡‡) (Posse 1999)	$w_n = \frac{TE_n \cdot e^{-TE_n/T_2^*}}{\sum_{i=1}^{N} TE_i \cdot e^{-TE_i/T_2^*}}$	Yes	Yes	No
tSNR-Combined (Poser 2006)	$w_n = \frac{tSNR_n \cdot TE_n}{\sum_{i=1}^{N} tSNR_i \cdot TE_i}$	No	Yes	No
T_2^*-FIT Combined (Heunis 2021)	$w_n(t) = \frac{TE_n \cdot e^{-TE_n/T_2^*-FIT(t)}}{\sum_{i=1}^{N} TE_i \cdot e^{-TE_i/T_2^*-FIT(t)}}$	Yes	Yes	Yes

Adding thermal noise across X independent measurements $\approx \sqrt{X}$ reduction in thermal noise

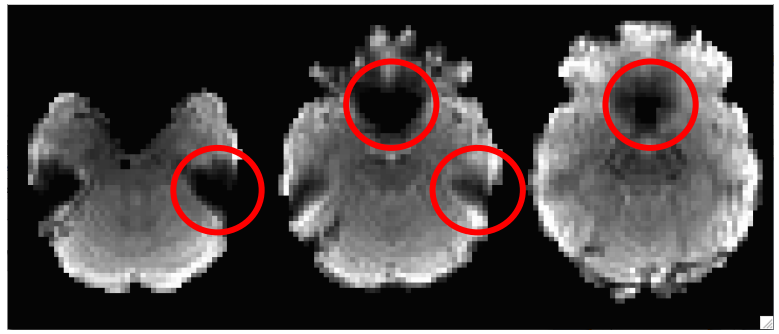
‡ a.k.a. Optimally Combined (OC) in Kundu et al. 2012

‡‡ a.k.a. BOLD weighting in Poser et al. 2006

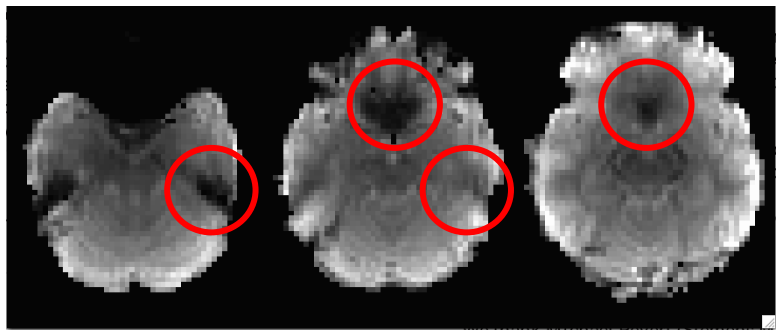
Weighted average of the echoes

T_2^*-Combined Method

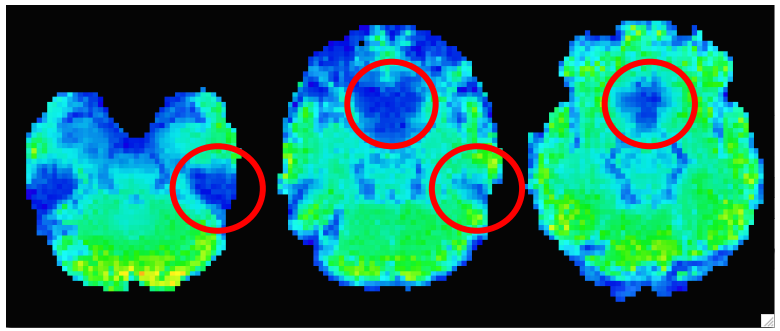
$$w_n = \frac{TE_n \cdot e^{-TE_n / T_2^*}}{\sum_{i=1}^{N} TE_i \cdot e^{-TE_i / T_2^*}}$$



SINGLE ECHO



"OPTIMALLY" COMBINED



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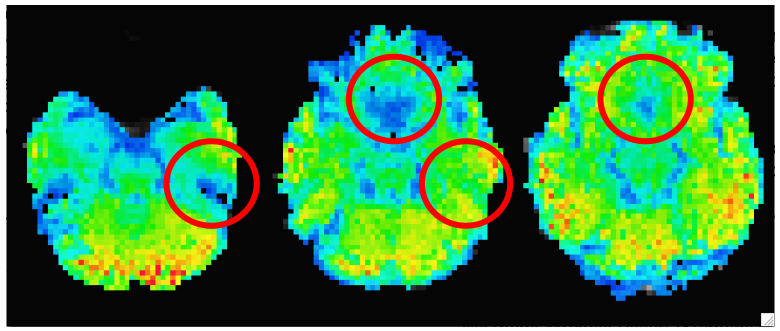


"OPTIMALLY" COMBINED

- Average of echoes weights towards voxelwise mean T_2^*
- Recovers signal in *some* dropout regions
- Straightforward math
- T_2^* fit is on a lower-noise average across time
- Automatically calculated in AFNI, fMRIPrep, tedana, +
- Reliable improvements
  - Improvement should be equal or better than SNR loss from a small increase in acquisition acceleration to acquire multi-echo

Optimize for T_2^* vs trying to remove S_0

- S_0 changes over time
  - Head motion (Power, PNAS, 2018)
  - Slow signal drift (Evans, *NeuroImage* 2015)
  - Overt speech (Gilmore, Front in Neuro, 2022)
  - Phase shifts from respiration (looks like head motion)
  - Inflow (blood from outside the imaging area that enters during acquisition)
  - Most scanner artifacts
- T_2^* changes over time
  - Deoxyhemoglobin concentration (BOLD)
    - Neurovascular coupling
    - Respiratory and Cardiac blood volume and blood oxygenation changes
  - Ghosting & signal leakage of MRI artifacts that contain T_2^* changes

It would be VERY useful if we could remove the S_0 fluctuations and just look at T_2^*

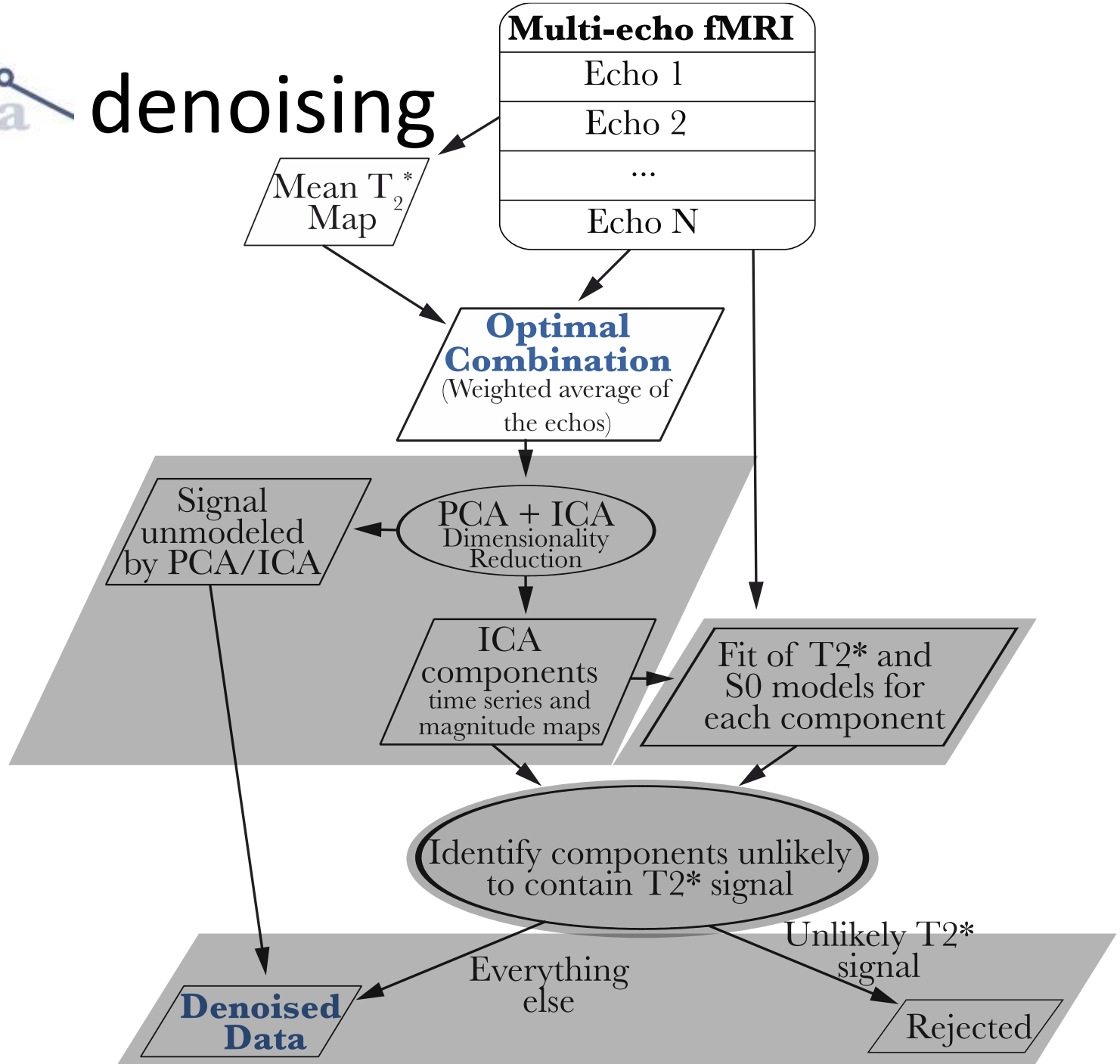
Denoising methods to reduce S_0 fluctuations

- ICA based: MEICA (Kundu 2012 & 2013) →

(DuPre, Salo, et al, *JOSS*, 2021)

- Paradigm Free Mapping (Caballero-Gaudes, *NeuroImage*, 2019)
  - https://me-ica.github.io/multi-echo-data-analysis/content/05_3dMEPFM.html
- Other methods: tedana.readthedocs.io/en/stable/multi-echo.html#other-software-that-uses-multi-echo-fmri

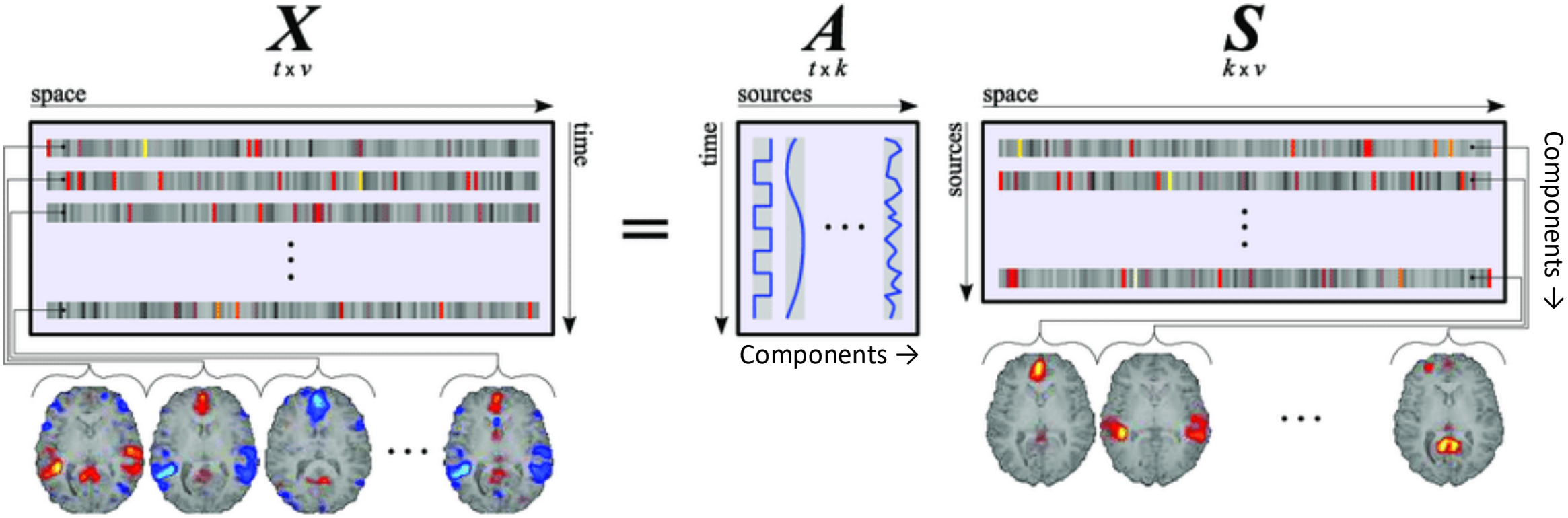
MEICA or tedana denoising



Hand waving explanation of ICA

Weighted average reduces noise in model fit by averaging across time

ICA reduces noise in model fit by averaging across spatio-temporal components

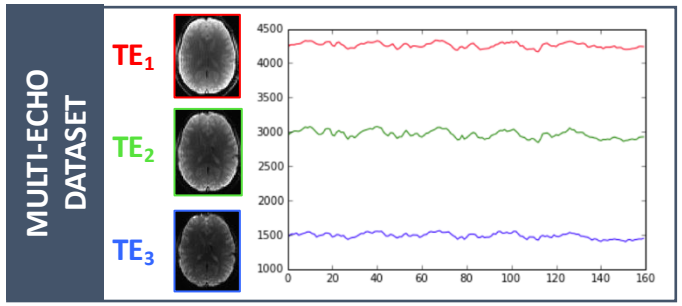


Ylipaavalniemi, *Variability of Independent Components in functional Magnetic Resonance Imaging*

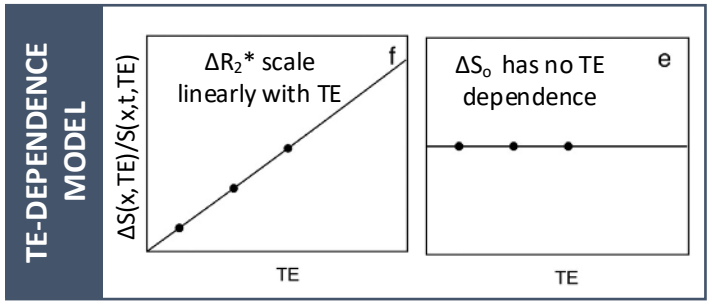
Originally applied to multi-echo denoising by Buur, *IEEE J. Sel. Top. Signal Process* (2008)

Method in ME-ICA and tedana software initially developed in Kundu, *NeuroImage* (2012)

Identifying components unlikely to contain T_2^*



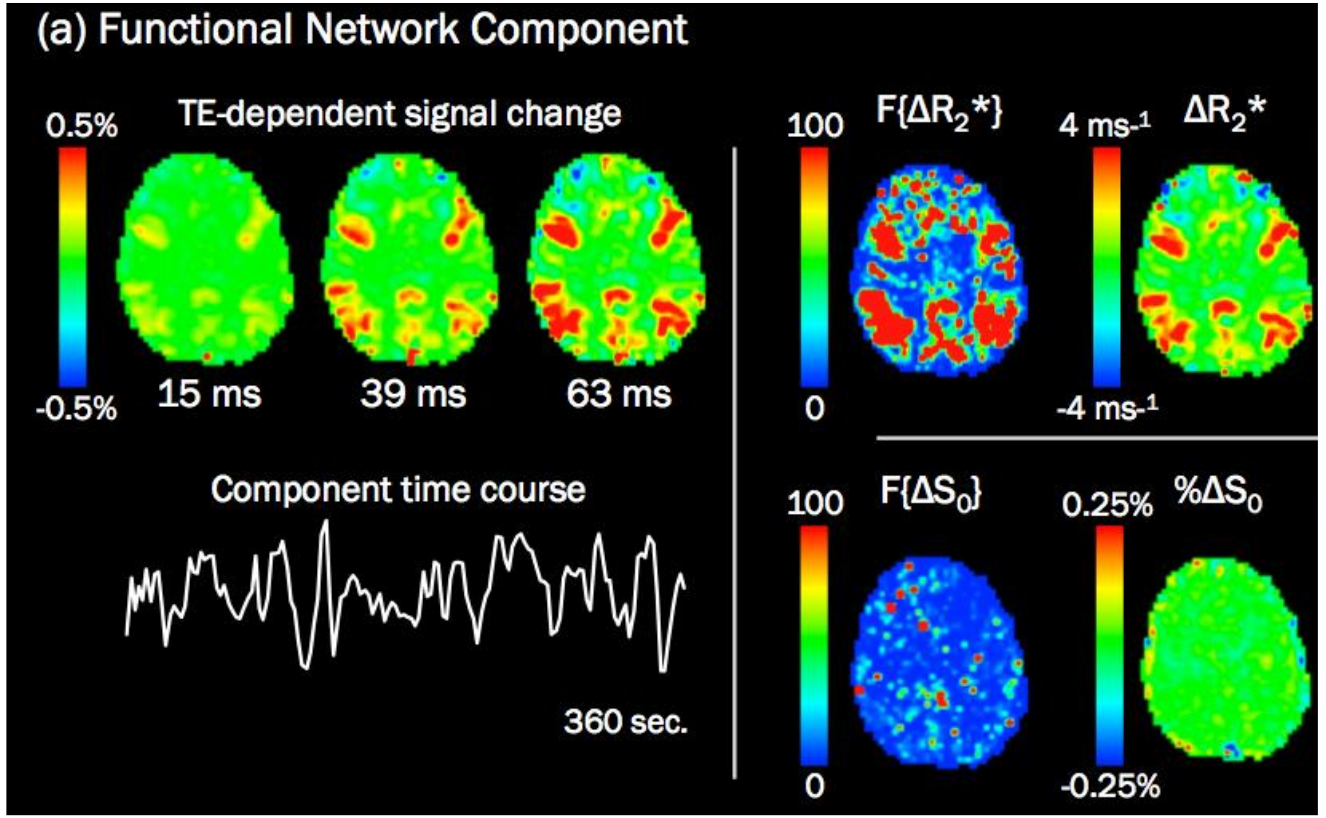
Linear fit of ICA component time series to each voxel and echo



Fit across echoes to

$R_2^* \left(\frac{1}{T_2^*}\right)$

or S_0 models



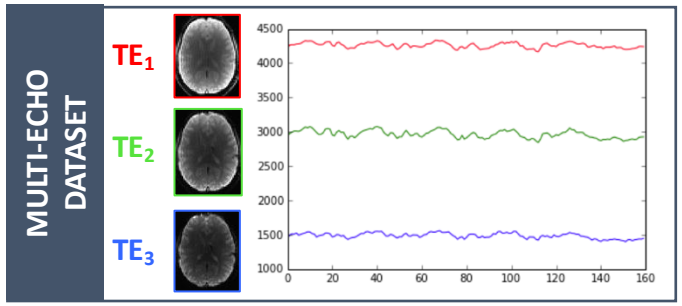
Calculate the weighted sum of the ICA component weight map and the model fit to T2* (Kappa) and S0 (Rho)

Kappa (κ) = 210

Rho (ρ) = 10

Kundu et al., NeuroImage 2012

Identifying components unlikely to contain T_2^*



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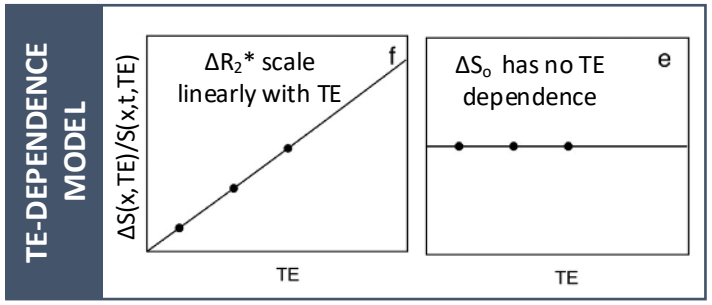

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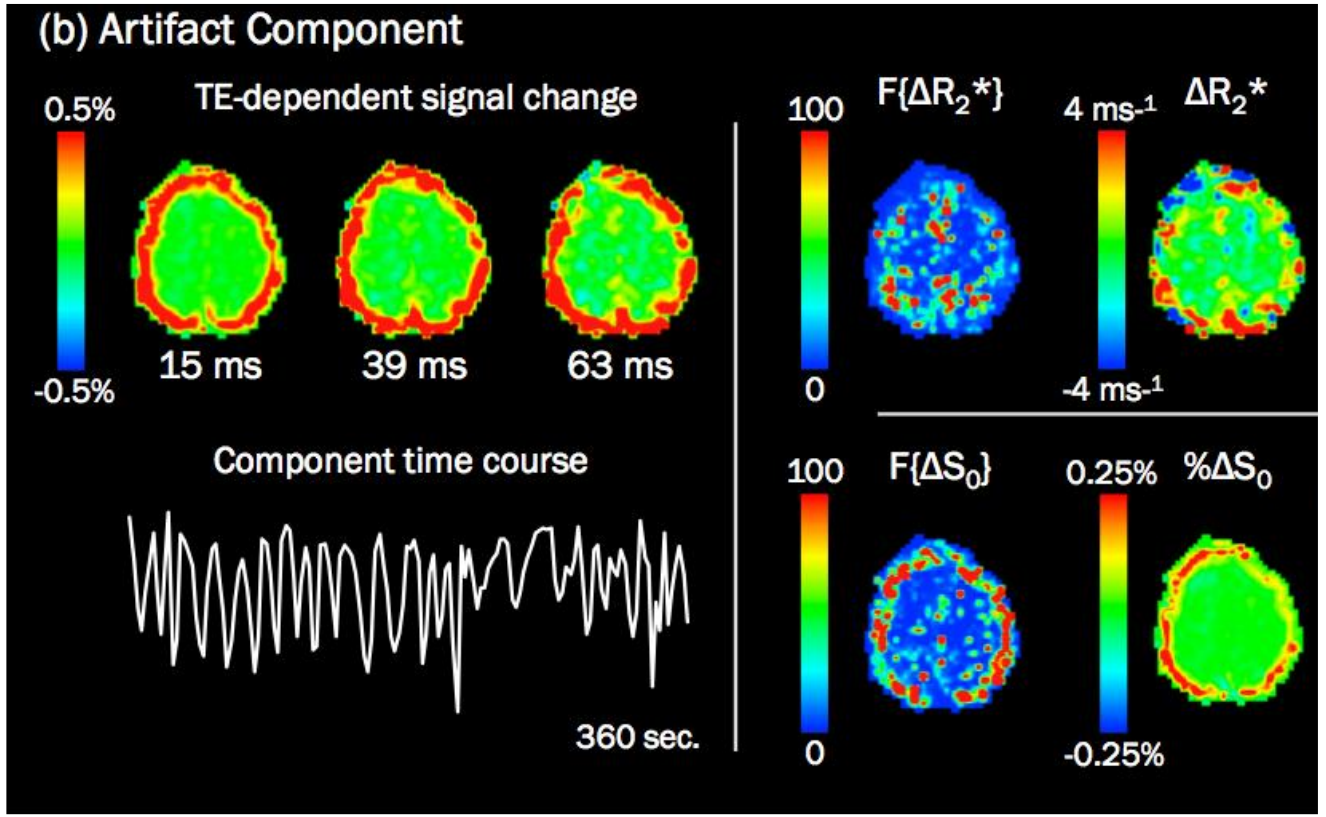


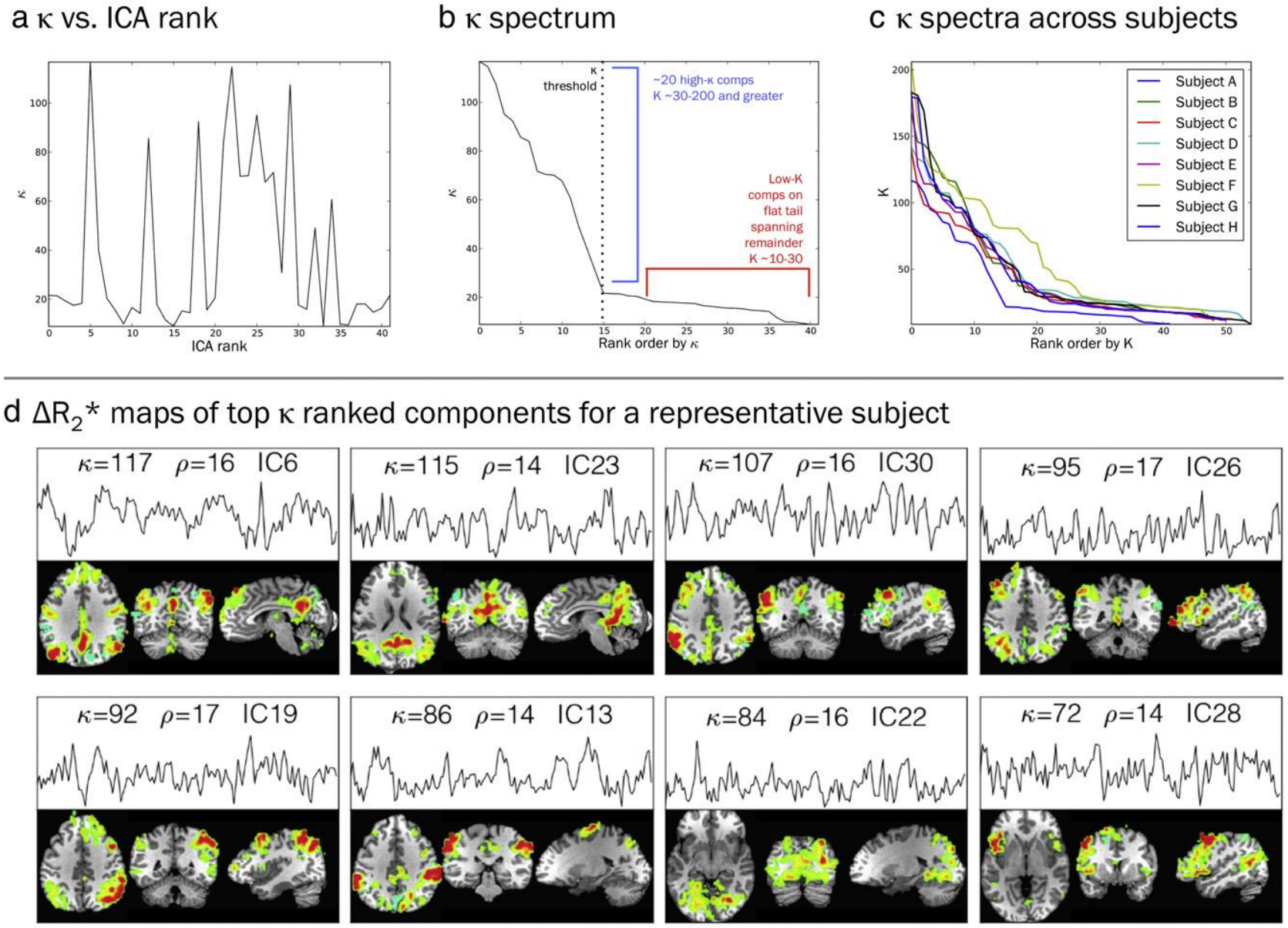
Calculate the weighted sum of the ICA component weight map and the model fit to T2* (Kappa) and S0 (Rho)

Kappa (κ) = 32

Rho (ρ) = 81

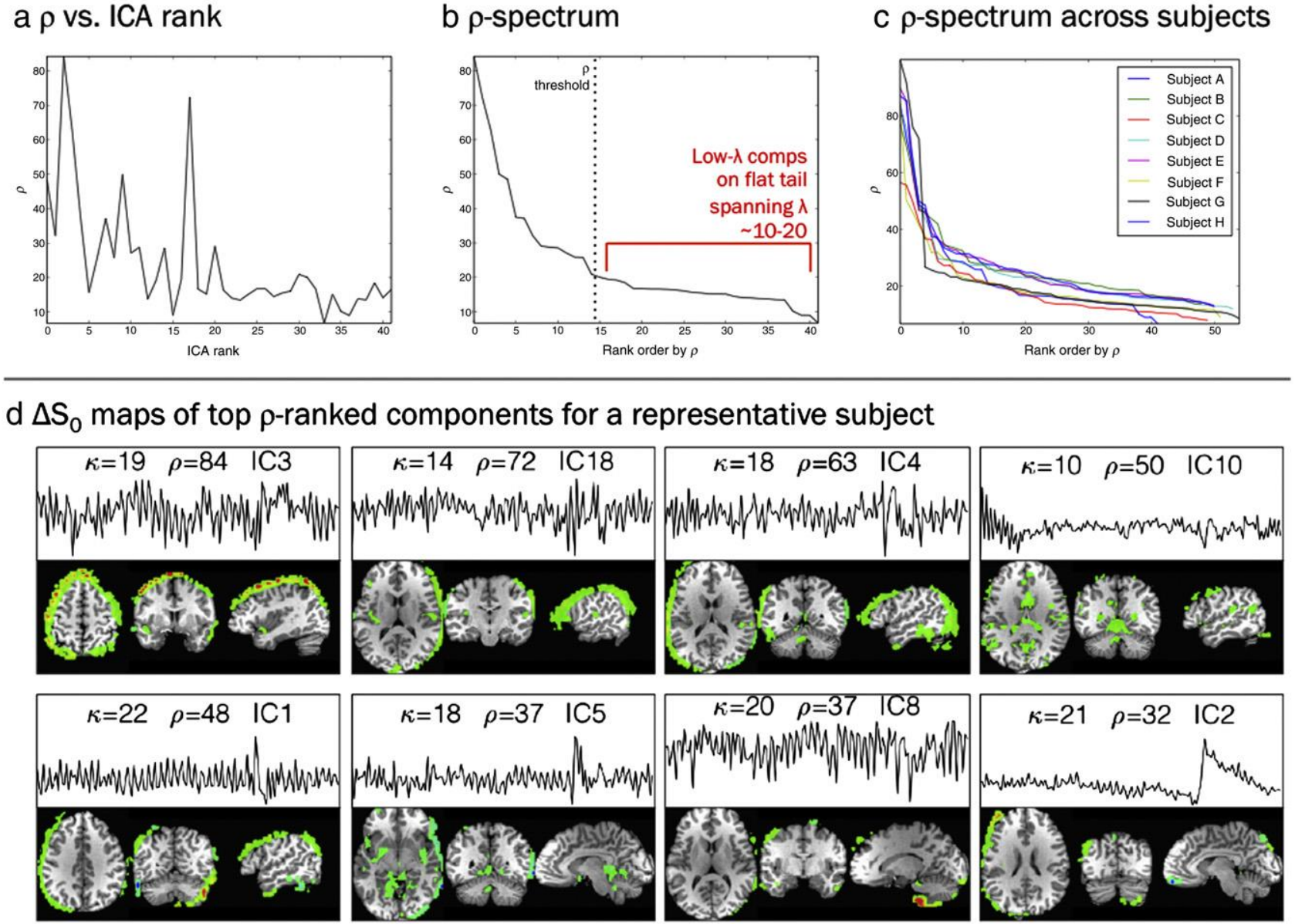
Kundu et al., NeuroImage 2012

Example retained components



Kundu et al., NeuroImage 2012

Example rejected components



Kundu et al., NeuroImage 2012

ICA component report in tedana

Component	Kappa	Rho	Variance %	κ Rank	ρ Rank	Dice FT2	Dice FS0	S/N t	Classification	Tags
ICA 29	105.57	18.36	0.54	7.00	16.00	0.79	0.67	13.35	accepted	Likely BOLD
ICA 30	68.46	17.99	0.37	14.00	18.00	0.75	0.64	17.81	accepted	Likely BOLD
ICA 31	136.49	28.57	9.08	1.00	2.00	0.72	0.63	5.96	accepted	Likely BOLD

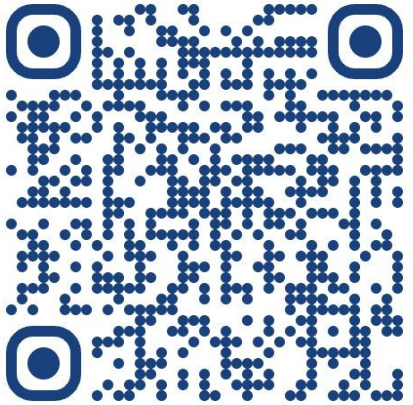
Interactive component browser in RICA

rica-fmri.netlify.app

https://me-ica.github.io/ohbm-2026-multiecho/tedana_processed/tedana_report.html

Running tedana

Code & Interactive Reports



```
pip install tedana
tedana -d data_e1.nii data_e2.nii data_e3.nii \
  -e 15 30 45 \
  -tree minimal \
  --mask mask_file.nii \
  --convention bids
```

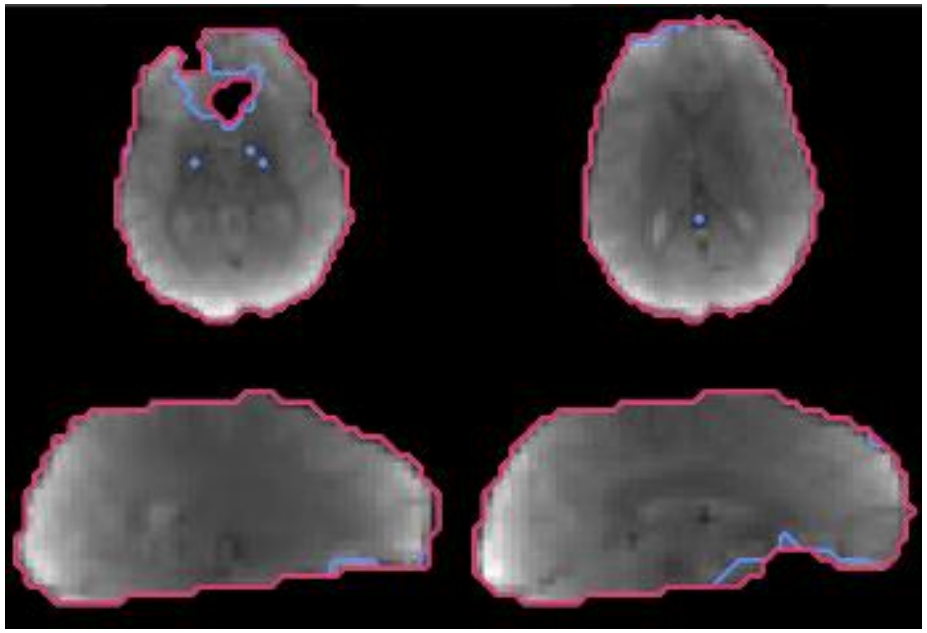
Built into AFNI & fMRIPrep pipelines

tedana.readthedocs.io includes:

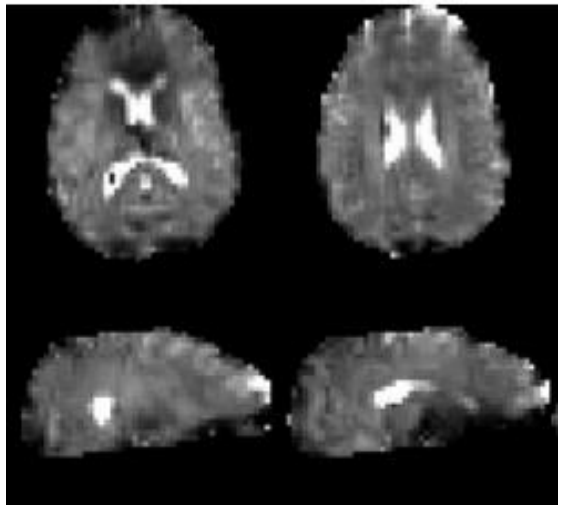
- Instructions on expected preprocessing steps
- Descriptions of options, output files, and visualizations
- Can also run from within python

Tedana quality check report

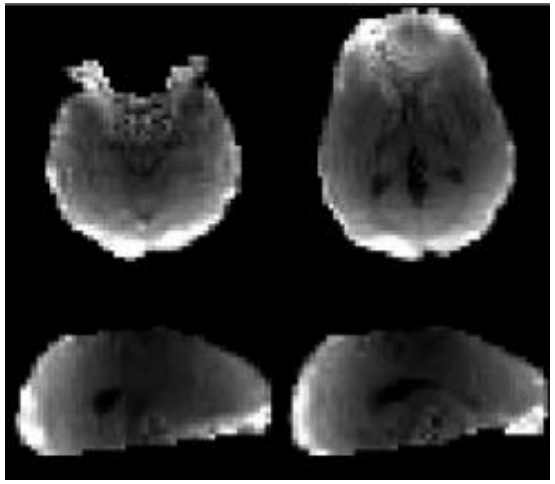
Initial & mask with 3 good echoes



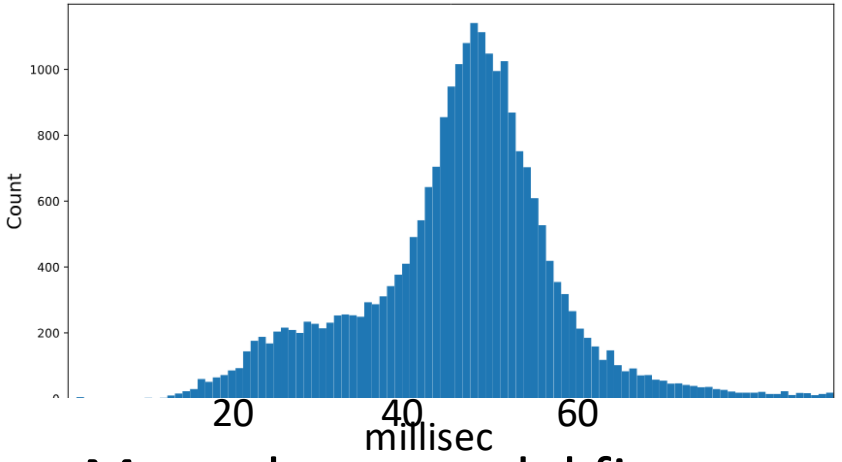
Mean T_2^*



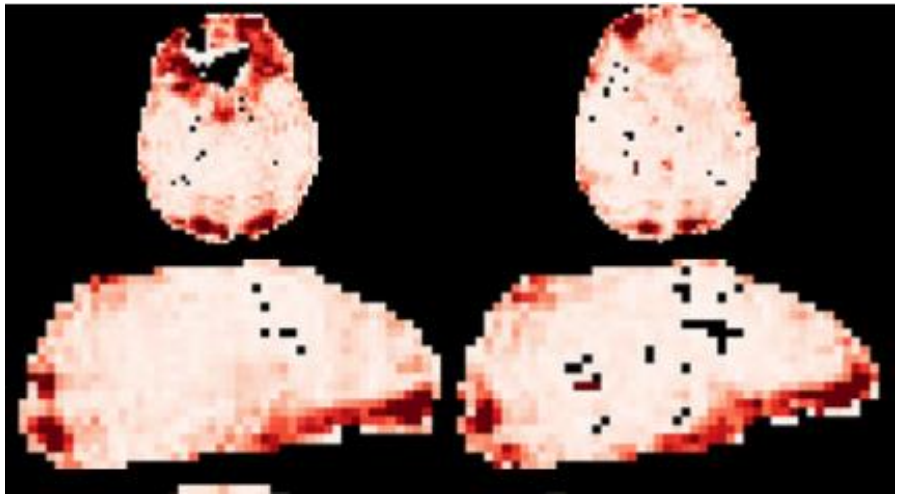
Mean S_0



T_2^* Distribution

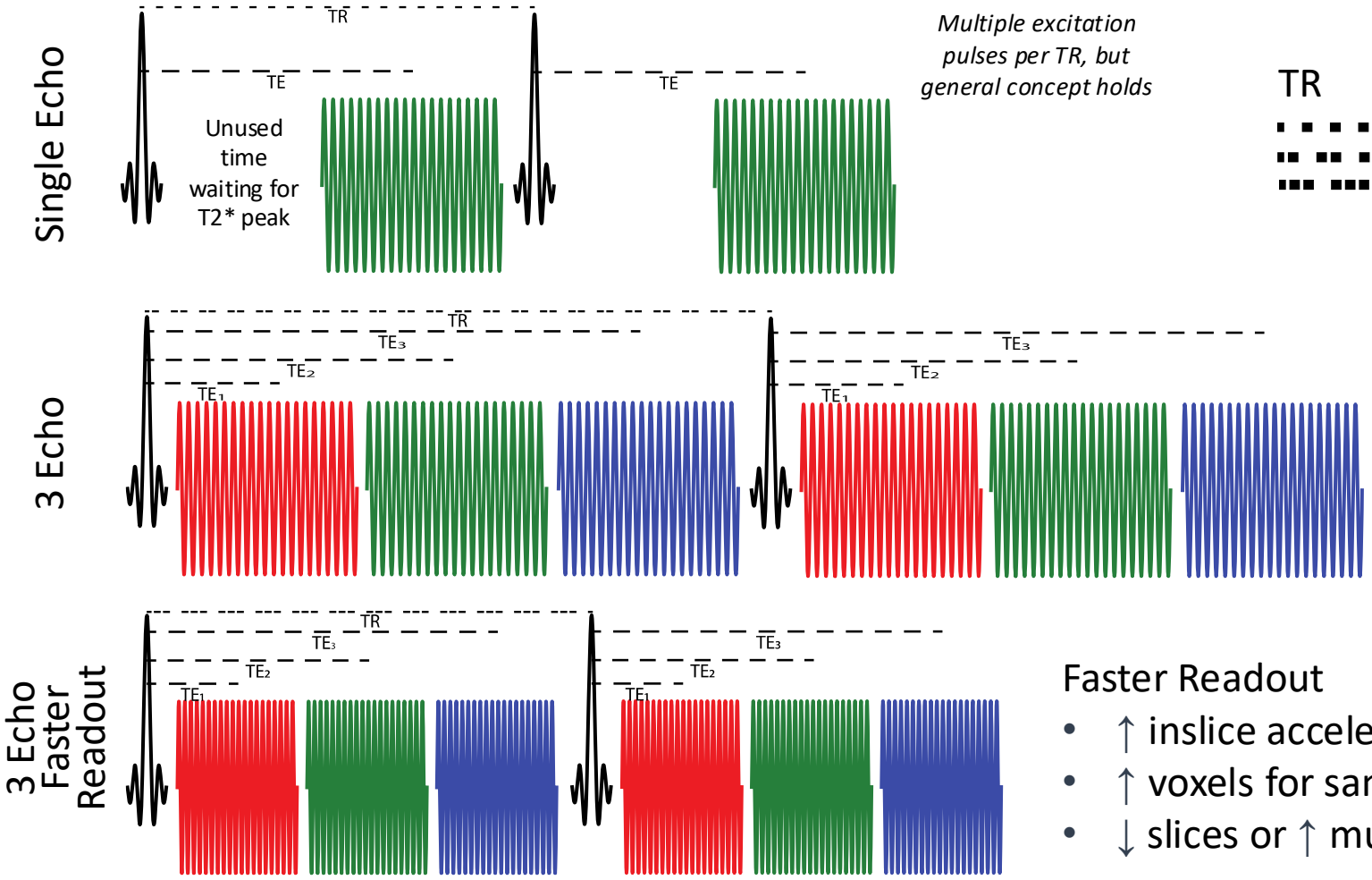


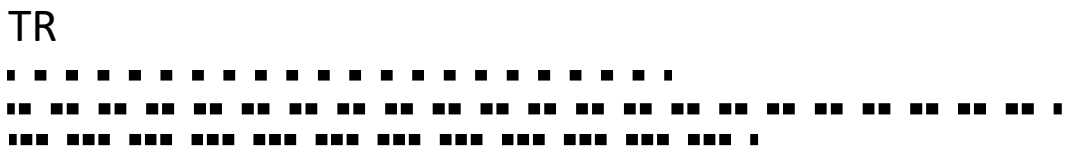
Mean decay model fit error



Acquisition Considerations

- Common question: Multi-echo fMRI or a short TR?
- Better question: How many echoes for how short a TR?



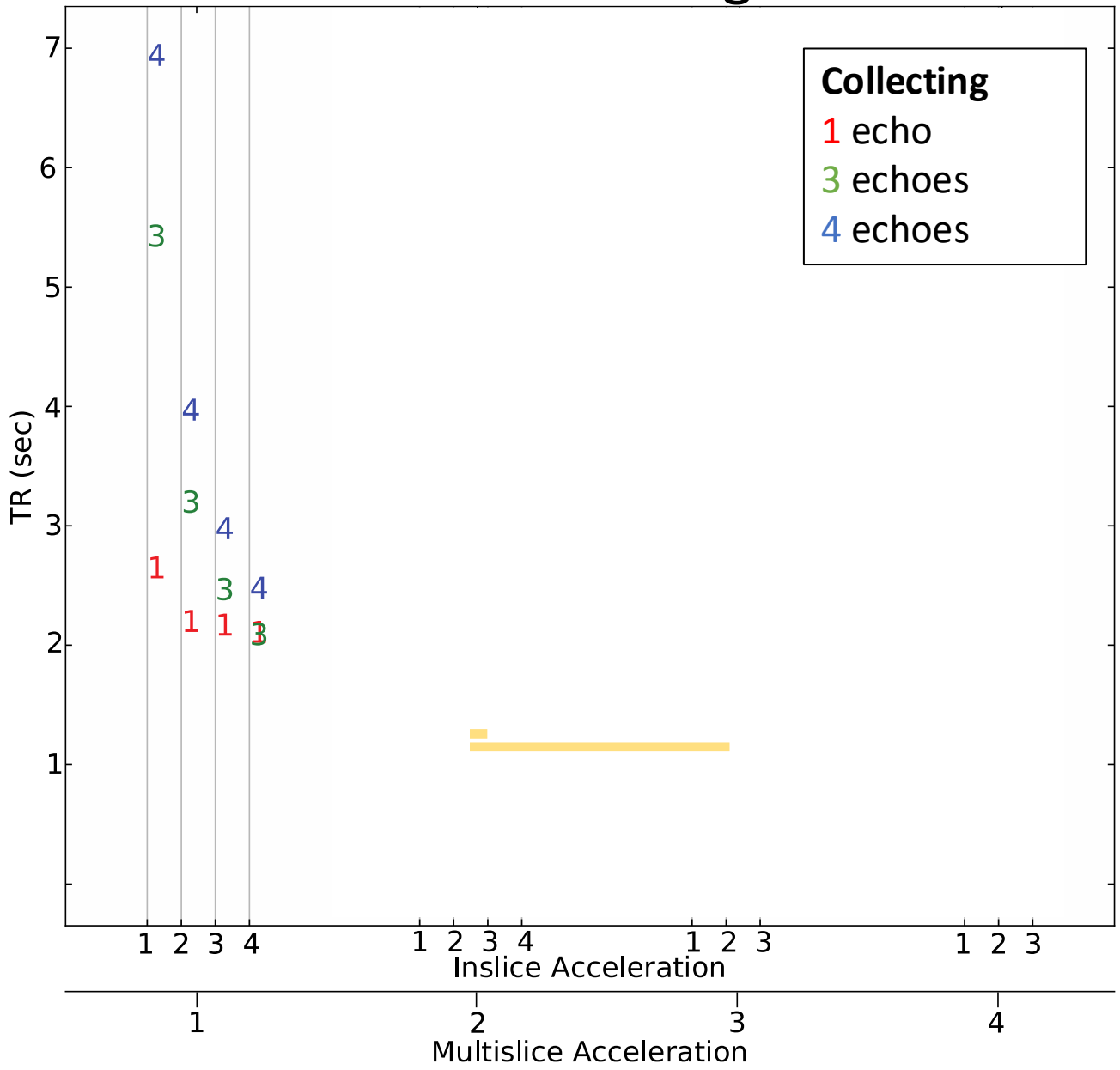


Optimize many acquisition parameters based on study goals, just like any other fMRI study

Faster Readout

- ↑ inslice acceleration (GRAPPA, ASSET, etc)
- ↑ voxels for same field-of-view
- ↓ slices or ↑ multislice or multiband acceleration

TR variation for multi-echo vs single-echo



Collected on a Siemens Prisma 3T MRI
Siemens OS VD11

CMRR Multiband pulse sequence
64 channel head coil

3mm^3 voxels 42-44 slices
cortex & cerebellum coverage

3 vs 1 echo for:

Inslice Acceleration = 2: 40-50% TR cost

Inslice Acceleration = 3: ~14% TR cost

Inslice Acceleration = 4: ~-1% TR cost

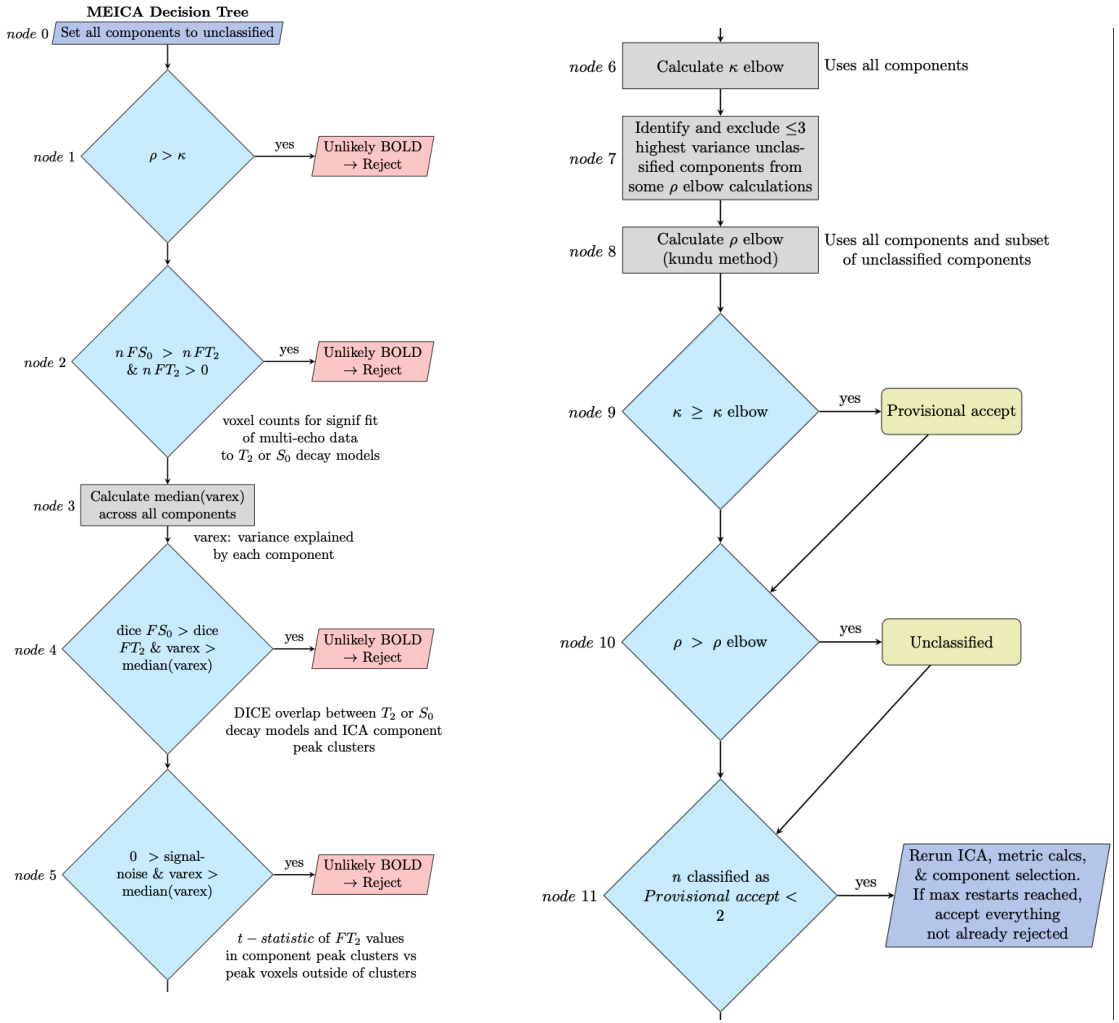
Thinking through an acquisition plan

- Cost of acquiring multi-echo can be balanced with a combination of:
  acceleration↑, voxel size ↑, slices↓, & TR ↑
- More CNR from "optimal combination" of echoes **should** balance lower SNR from acceleration↑
- https://me-ica.github.io/multi-echo-data-analysis/content/Acquiring_Multi_Echo_Data.html

Recommendations

- If a scientific Q requires pushing the limits of small voxels or short TRs, multi-echo might not be practical
- Planning a single-use data set: Consider multi-echo
  - You should see modest benefits with optimal combination
  - Denoising to remove S_0 will help, but might require more effort
- Planning a longer-term project with goals of data re-use: Strongly consider multi-echo
  - Immediate benefits, and larger longer-term benefits are likely
  - Development of additional ways to use multi-echo fMRI are likely

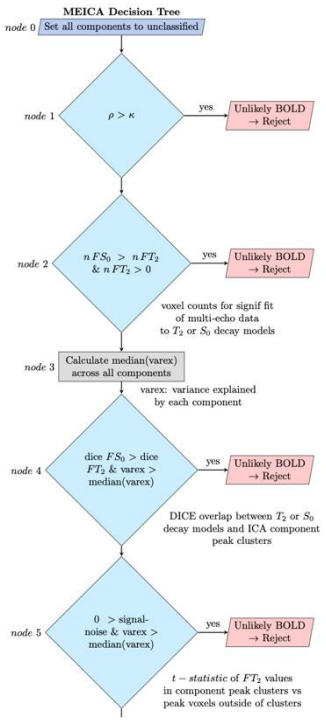
Deciding what to reject is not solved

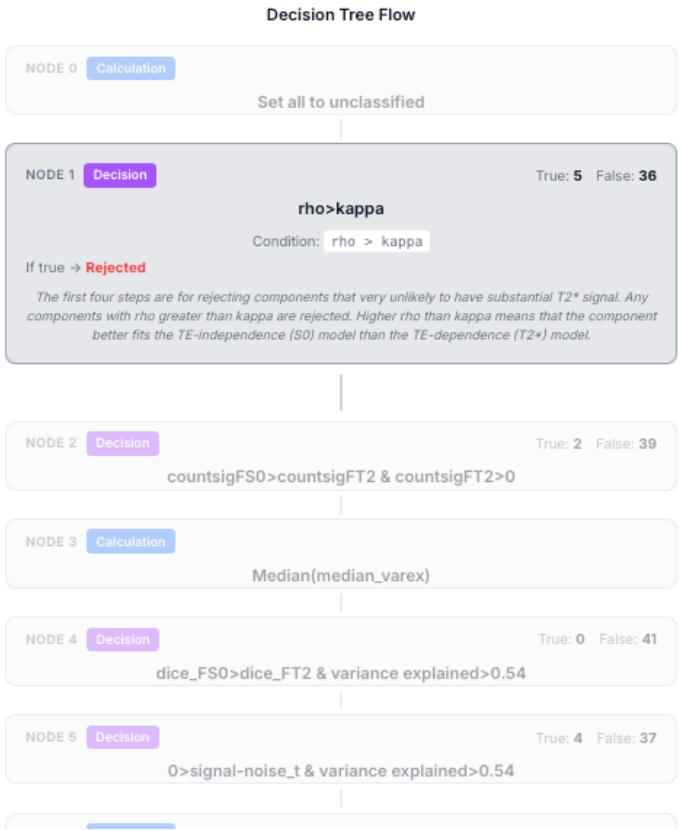


https://tedana.readthedocs.io/en/stable/included_decision_trees.html

Deciding what to reject is not solved

- Tedana is designed to allow for multiple decision tree options
  - Supports continued innovation
  - Supports dataset-specific changes (more/less aggressive, infants, patients)

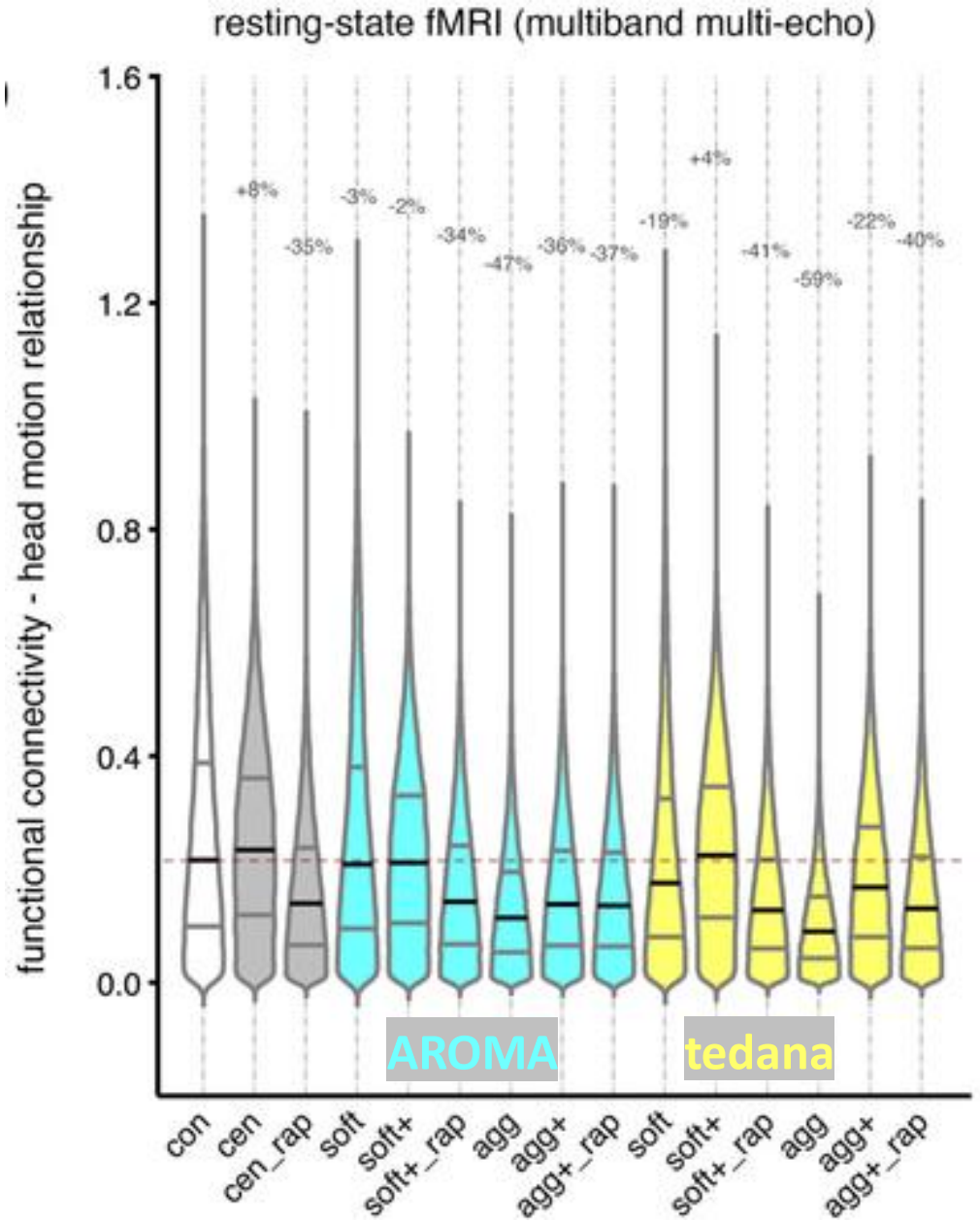




Interactive view of the accept vs reject decision tree

Open in Rica

Continuing work and comparisions

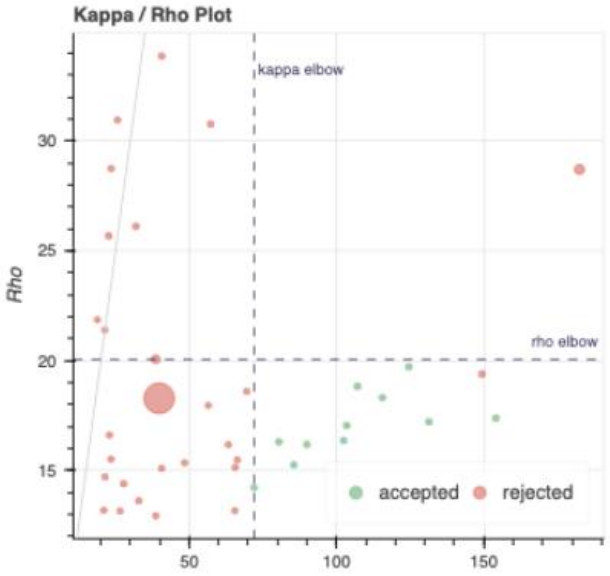


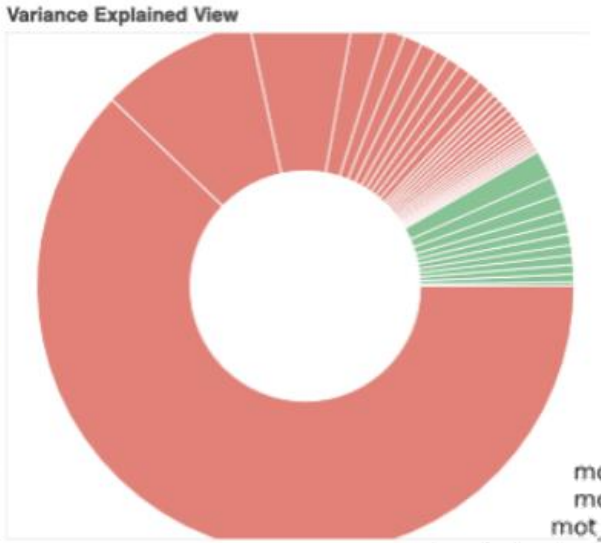
- Comparisons between & combining many denoising methods
- Default tedana seems to be better than others and removing relationship between head motion & task
- Other metrics in the paper showed benefits of combining ICA-based methods with other methods

Agg → tedana default
\+ → head motion & aCompCorr
_rap → RapidTide

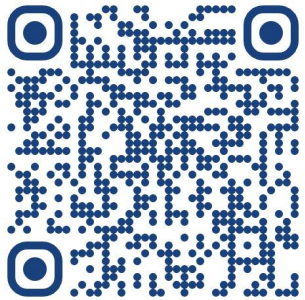
Zhai, et al. 2026. " Benchmarking fMRI Denoising Pipelines." *Human Brain Mapping*

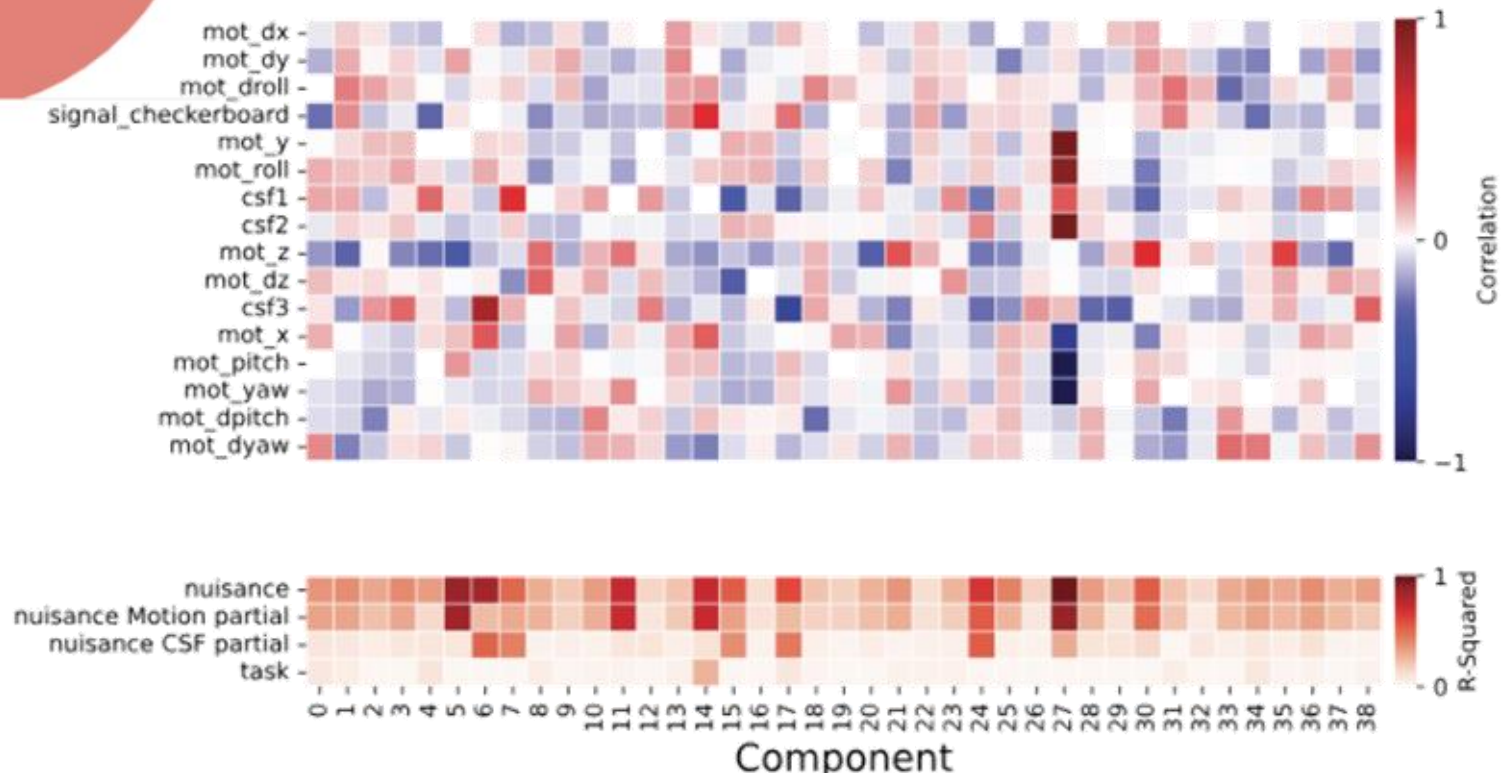
Mapping external regressors to components in tedana





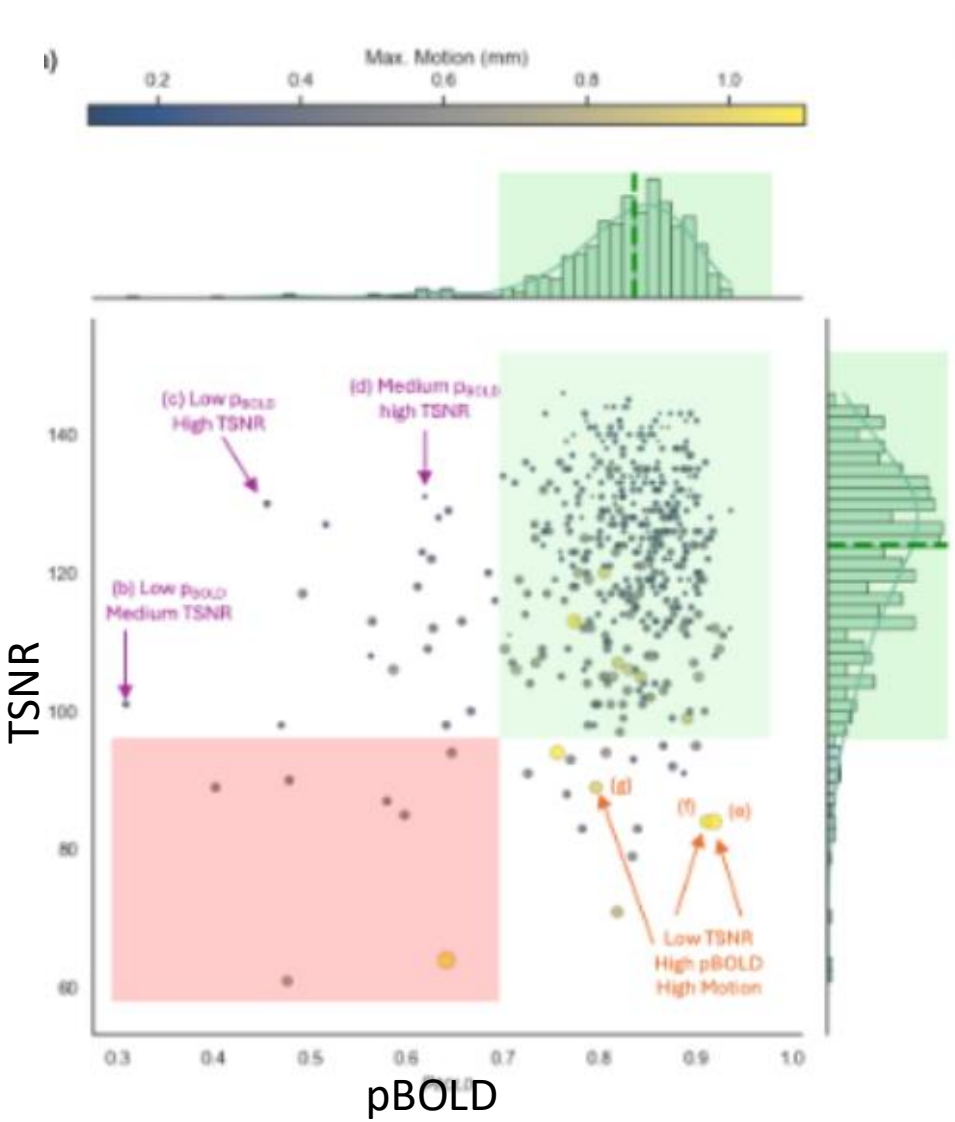
Code & Interactive Reports

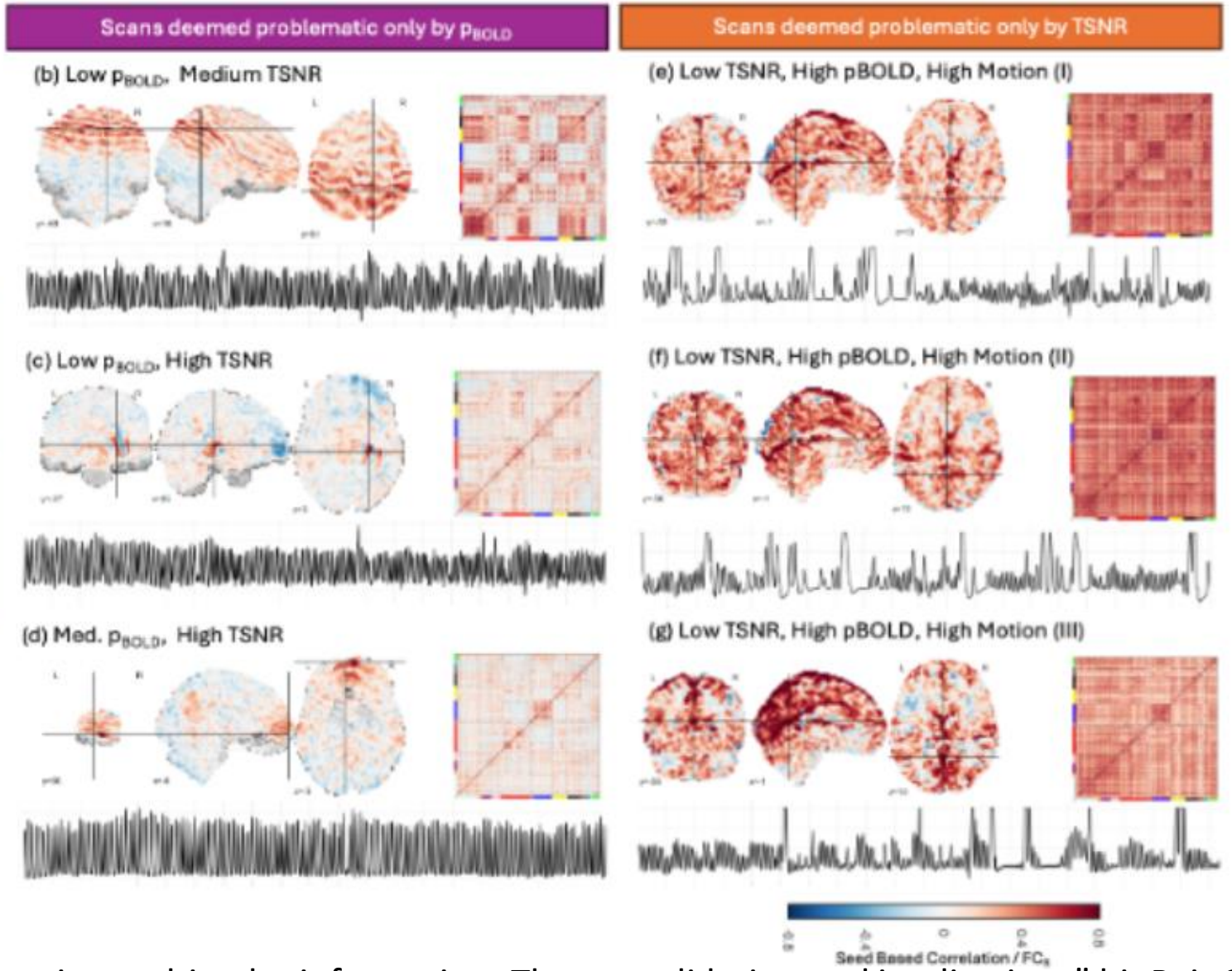




Multi-echo is more info about what we measure

The scope of what we can do with this info is wide open





Gonzalez-Castillo, et al, "A new fMRI quality metric using multi-echo information: Theory, validation and implications" bioRxiv 2026

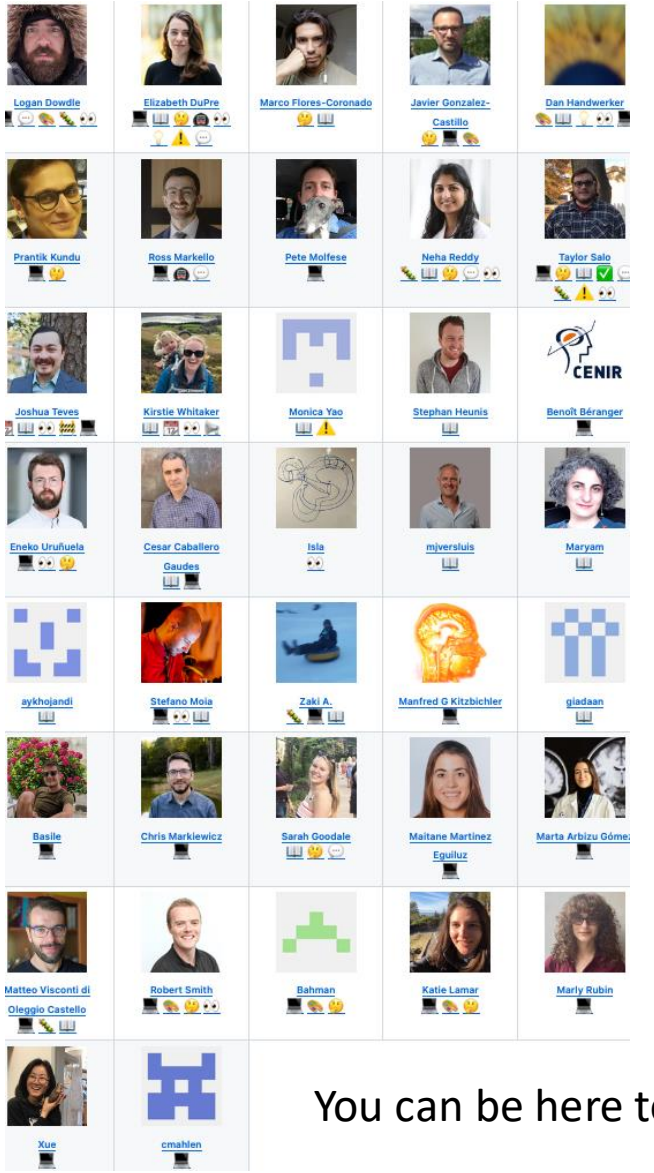
Open questions

- ICA helps, but nothing says it's the optimal information averaging method.
- Better ways to decide what to remove
- Interactions with non-neural T_2^* (respiration+)
- Combining information across runs, days, and people
- Censoring volumes & detrending
- Better validation methods and more comparisions with other methods
- Acquisition improvements: More/faster echoes? EPTI? ZeroTE+multi-echo

Software & Community

- Tedana started in May 2018 by Elizabeth DuPre to advance MEICA by Prantik Kundu
- Processing code
- Multi-echo education
- Approx 37 contributors and counting
- Monthly developer calls, a periodic newsletter, active issue board & code updates

Code:
https://github.com/me-ica/tedana
Documentation:
https://tedana.readthedocs.io



You can be here too!

Discussions are open

github.com/ME-ICA/tedana/pulls?q=is%3Apr+is%3Aopen+sort%3Acomments-desc

16 Open ✓ 751 Closed Author Label Projects Milestones Reviews

Parallelize component figure creation ✓ refactoring reports
#1356 opened on Feb 9 by tsalo Member • Review required

Refer to unstandardized PEs as PEs and standardized PEs as betas ✓ breaking-change documentation refactoring 1
#1338 opened on Jan 29 by tsalo Member • Review required

Use standardized parameter estimates for metrics instead of unstandardized ones ✓ breaking-change TE-dependence 1
#1337 opened on Jan 29 by tsalo Member • Approved

Allow simultaneous estimation of TE-(in)dependence metrics ✓ enhancement TE-dependence 1
#1357 opened on Feb 9 by tsalo Member • Draft

Calculate dependence metrics for modified mixing matrices and confounds ✓ enhancement 2
#1350 opened on Feb 6 by tsalo Member • Review required

Add tree argument to ica_reclassify ✗ enhancement 1
#1360 opened on Feb 11 by tsalo Member • Draft

Expand interpolation option to perform two-stage interpolation+fitting ✓ enhancement T2*/S0 estimation
#1459 opened last week by tsalo Member • Approved

ENH: Modularize tedana.py workflow into pipeline stages ✓ refactoring
#1280 opened on Dec 18, 2025 by eurunuela Member • Draft 4 of 6 tasks

Refactor workflows with shared module architecture ✓ refactoring
#1281 opened on Dec 18, 2025 by eurunuela Member • Draft 1 of 5 tasks

Support for new contributors

https://github.com/ME-ICA/tedana/blob/main/CONTRIBUTING.md 80%

ines (288 sloc) | 18.9 KB Raw Blame

Welcome to the `tedana` repository! We're excited you're here and want to contribute.

These guidelines are designed to make it as easy as possible to get involved. If you have any questions that aren't discussed below, please let us know by opening an issue!

Before you start you'll need to set up a free GitHub account and sign in. Here are some instructions.

Already know what you're looking for in this guide? Jump to the following sections:

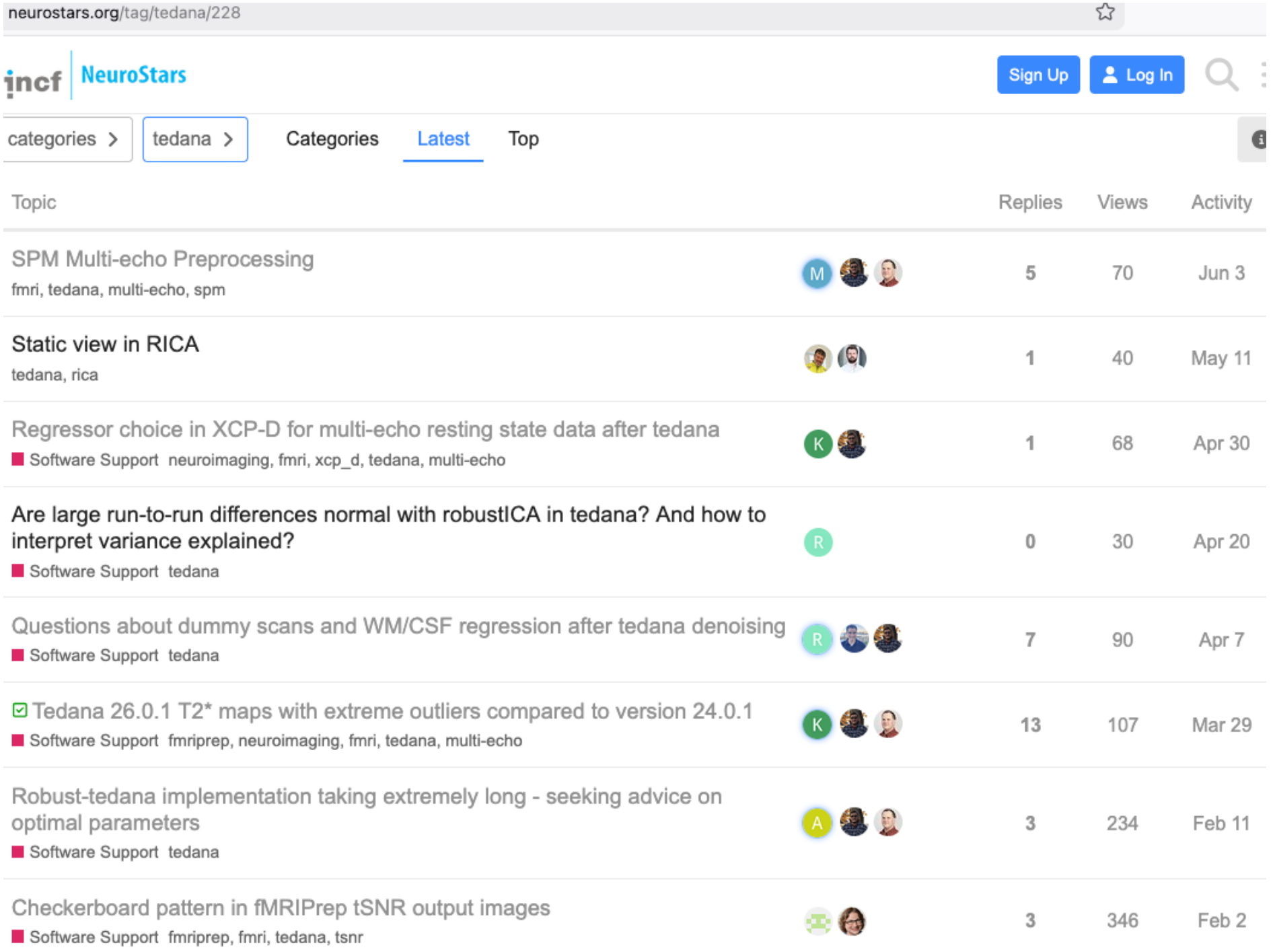
Don't know where to get started? Read Joining the conversation and pop into Mattermost to introduce yourself! Let us know what your interests are and we will help you find an issue to contribute to. Thanks so much!

Joining the conversation

`tedana` is a young project maintained by a growing group of enthusiastic developers— and we're excited to have you join! Most of our discussions will take place on open issues. We also maintain a Mattermost chat room for more informal conversations and general project updates.

There is significant cross-talk between these two spaces, and we look forward to hearing from you in either venue! As a reminder, we expect all contributions to `tedana` to adhere to our code of conduct.

neurostars message board for users



More contributors are welcome!

- Code contributions
- New ideas for data processing and visualization
- Documentation & education
- Questions that can help us identify gaps in the code or documentation
- Shared datasets to help with validation
- Processing your datasets to help validate methods & potential improvements

Acknowledgements

- Javier Gonzalez-Castillo
- Taylor Salo
- Eneko Uruñuela

- Xue Davis
- Logan Dowdle
- Elizabeth DuPre
- Katie Lamar
- Stefano Moia
- Neha Reddy
- Marly Rubin
- Marlene Smith
- Robert Smith
- Bahman Tahayori