Progress and open questions with multi-echo fMRI denoising

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Section on Functional Imaging Methods
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About me

I am the grandchild of child refugees
& the child of an immigrant

Grew up: Long Island, NY

Johns Hopkins
Biomedical Engineering, Computer Science
Psych minor

- **Michael Steinmetz**: Spatial encoding, primate Electrophysiology (and fMRI!) (John Port, Christos Constantinidis)
- **Steven Yantis**: Attention, human psychophysics and fMRI (Susan Courtney, Trisha Van Zandt)

NIMH Summer student with Karen Berman
Room 4C101

- MRI voxel-based morphometry & schizophrenic patients (precollected data)
- Piloting PET study with Williams Syndrome patients

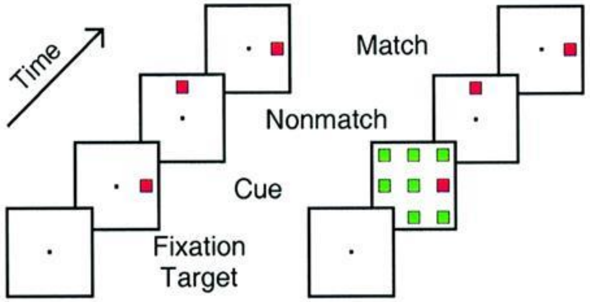
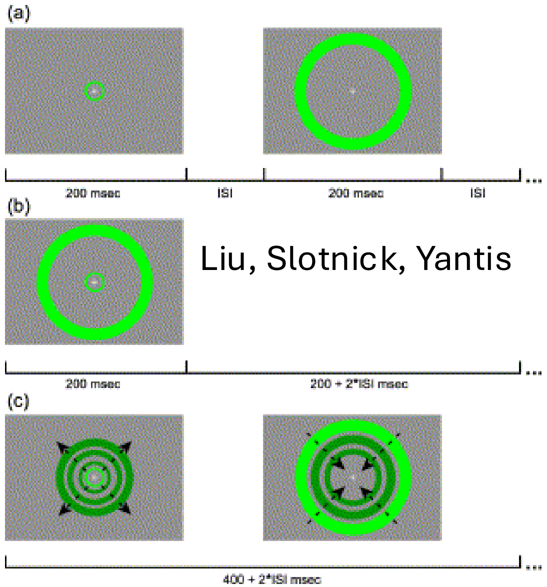
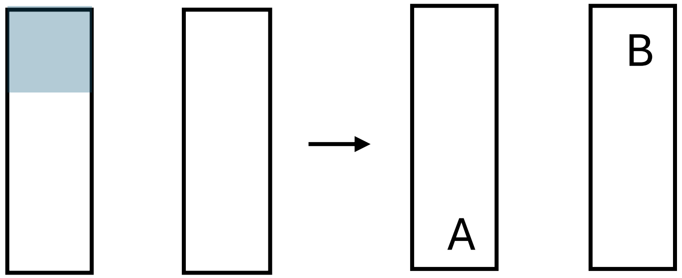
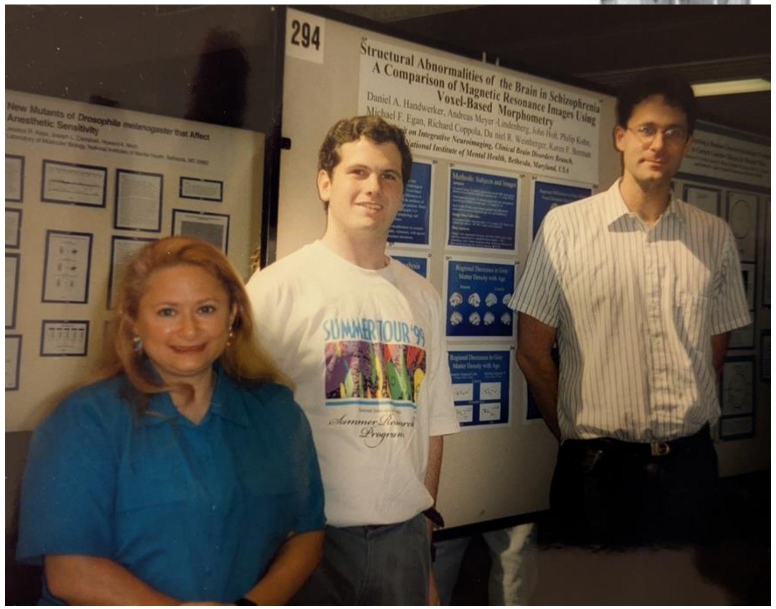


Figure 2
Constantinidis & Steinmetz



Liu, Slotnick, Yantis





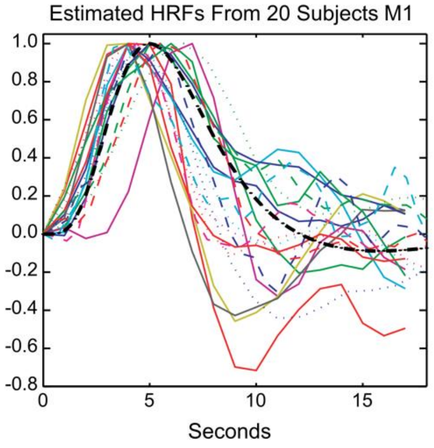
About me

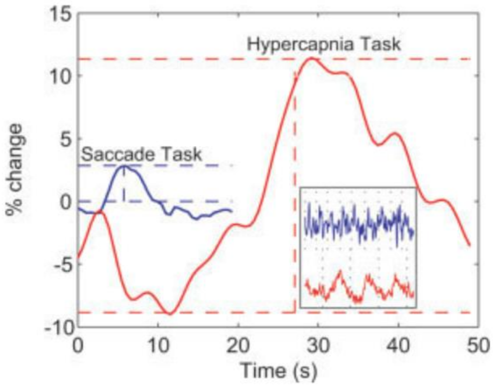
Grad school application:
Many researchers who study the brain are neuroscientists or psychologists who have developed engineering skills, or are engineers interested the brain. The field has a growing number of people who received their primary education in multiple disciplines. I hope to continue my studies **in both fields**.

My current interests are in the uses of fMRI to study the brain. I believe fMRI has **barely begun to reach its full potential** and I hope that in my future research, I can both use and improve on existing technology.

Personal photos removed

UC Berkeley, UCSF Joint grad group in Bioengineering
PhD mentor Mark D'Esposito





Personal photo removed

UCSF Postdoc
Roland Henry
DTI + fMRI + ECoG

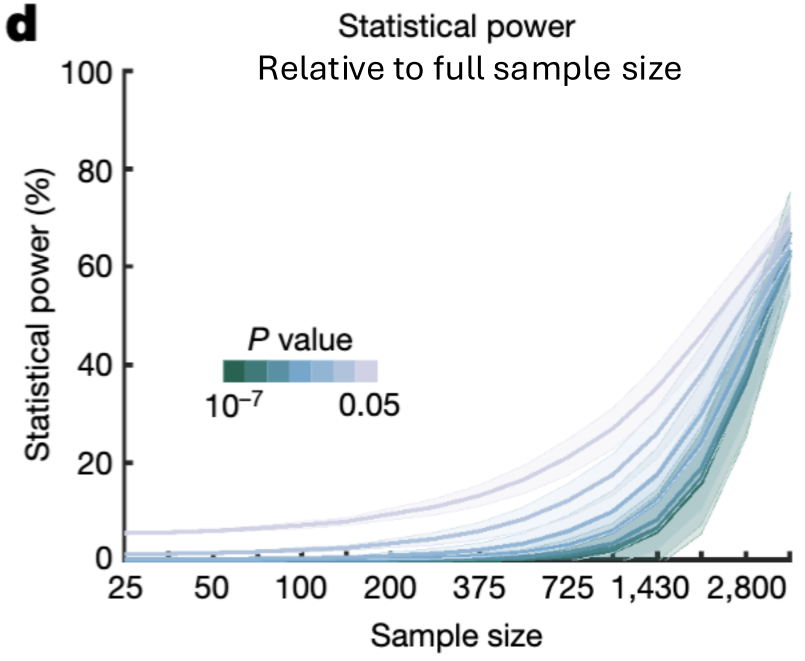
Personal photo removed

NIMH Postdoc then Staff Scientist

Personal photo removed

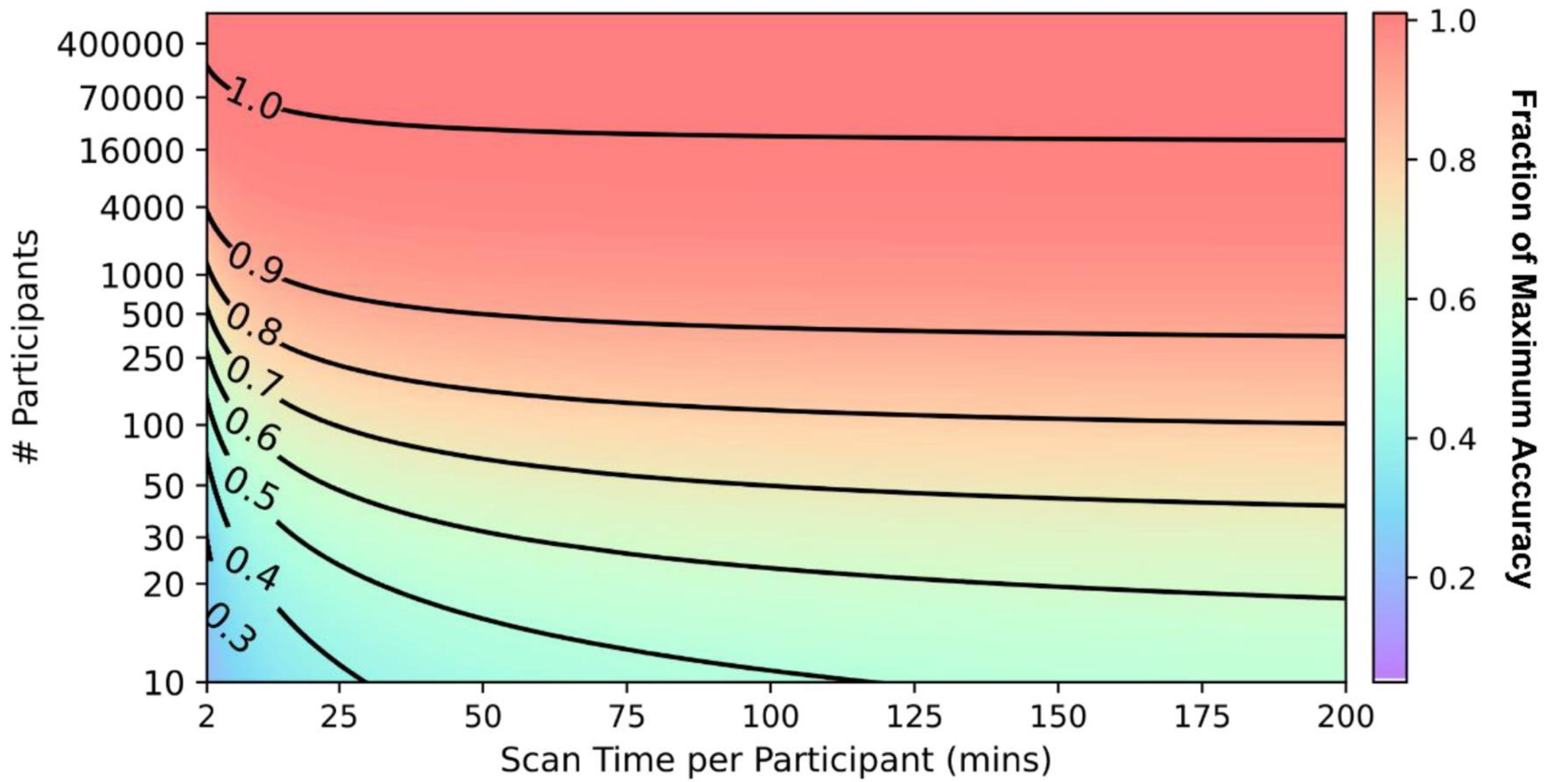
Reaching fMRI's full potential

Many participants?



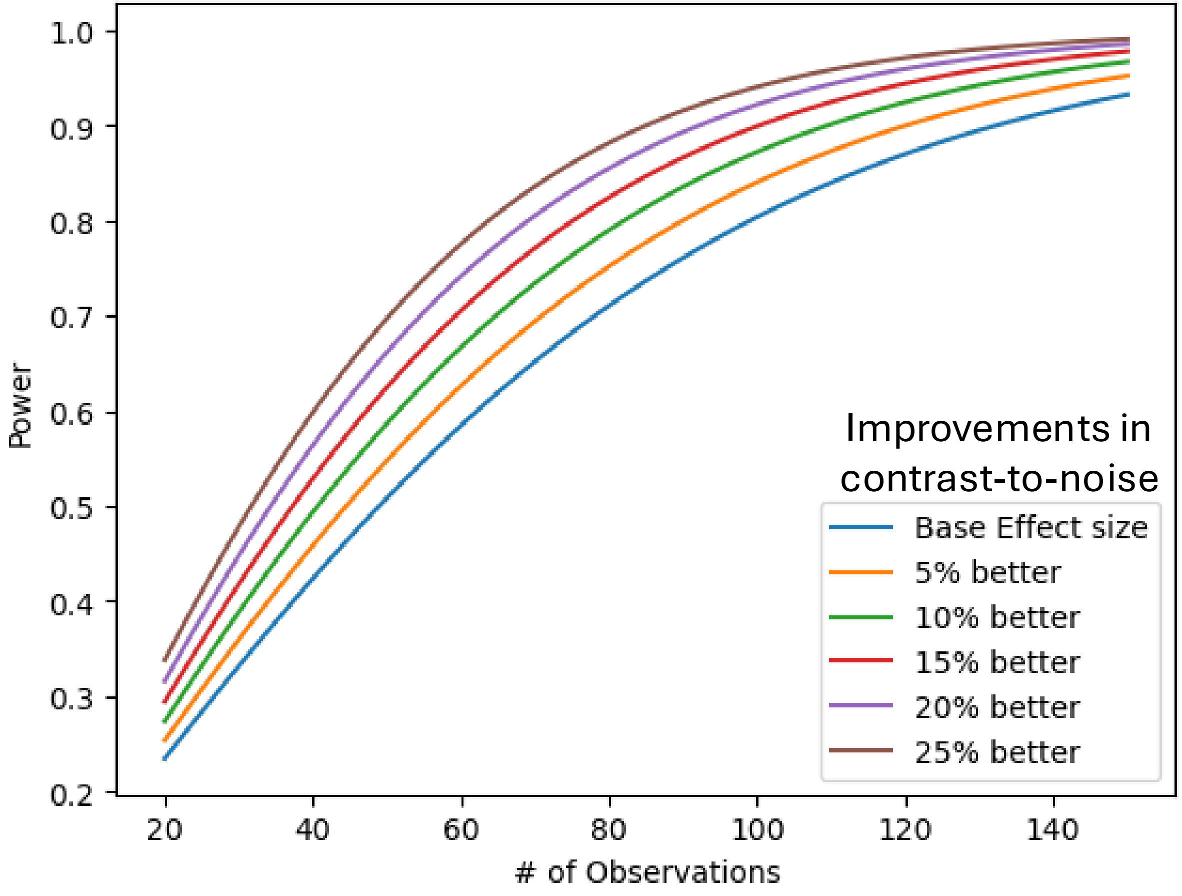
Marek, Tervo-Clemmens, et. al. 2022
Reproducible brain-wide association studies require thousands of individuals https://doi.org/10.15154/1503209

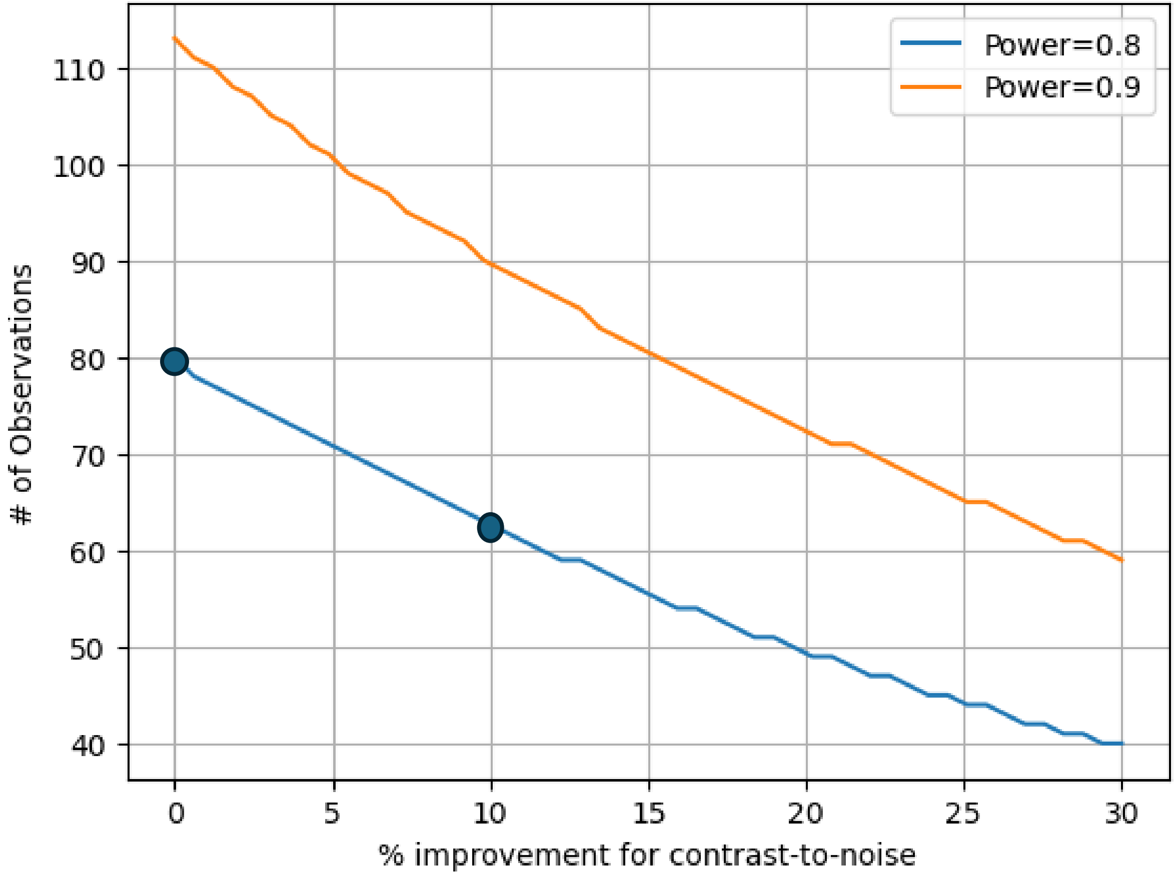
Scan time per participant?



Ooi, Orban, et. al. 2024
MRI economics: Balancing sample size & scan duration in BWAS
https://www.biorxiv.org/content/10.1101/2024.02.16.580448v2

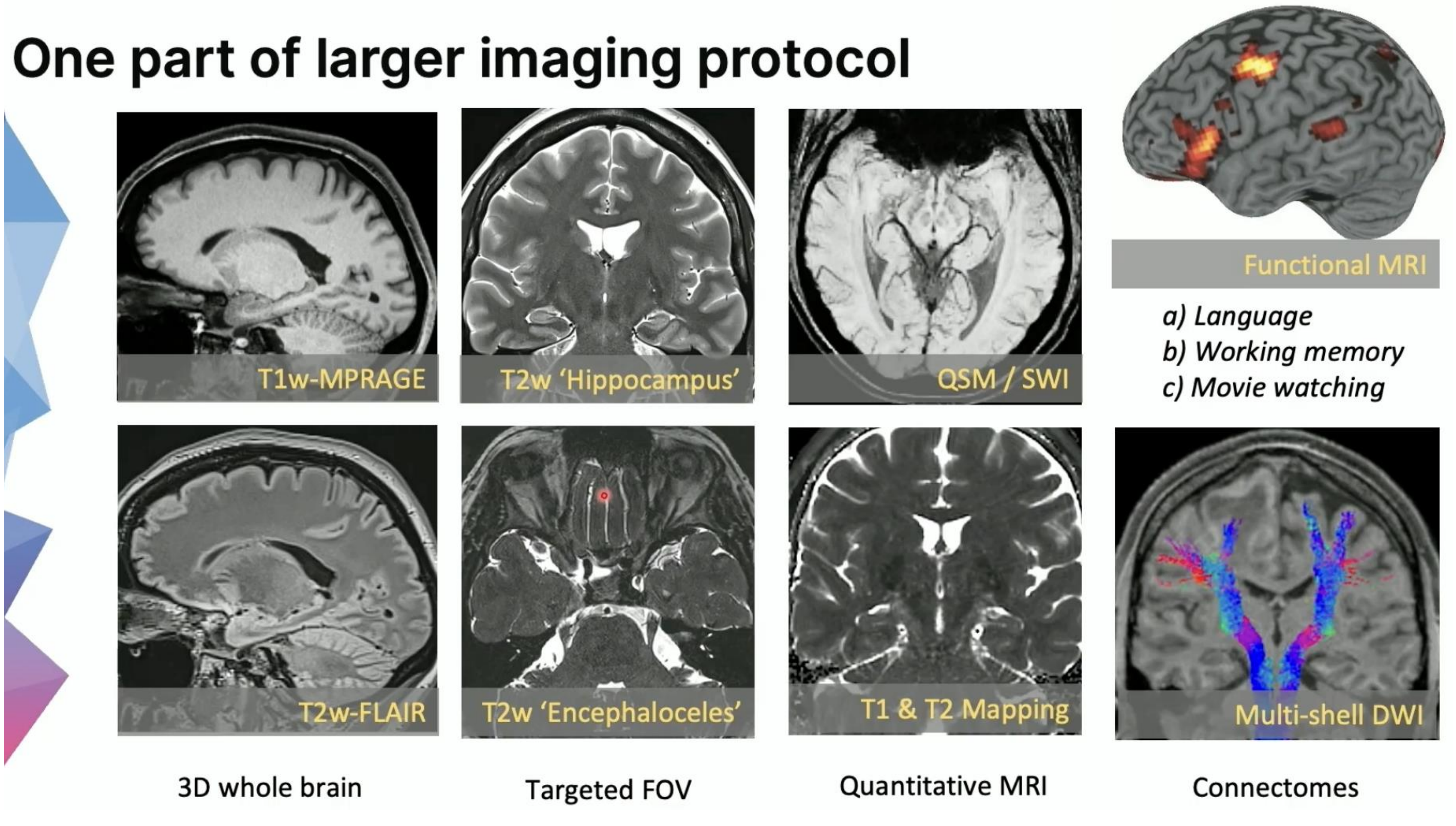
Data quality also matters!





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

Example: Australian Epilepsy Study



Patient MRI time is very limited.

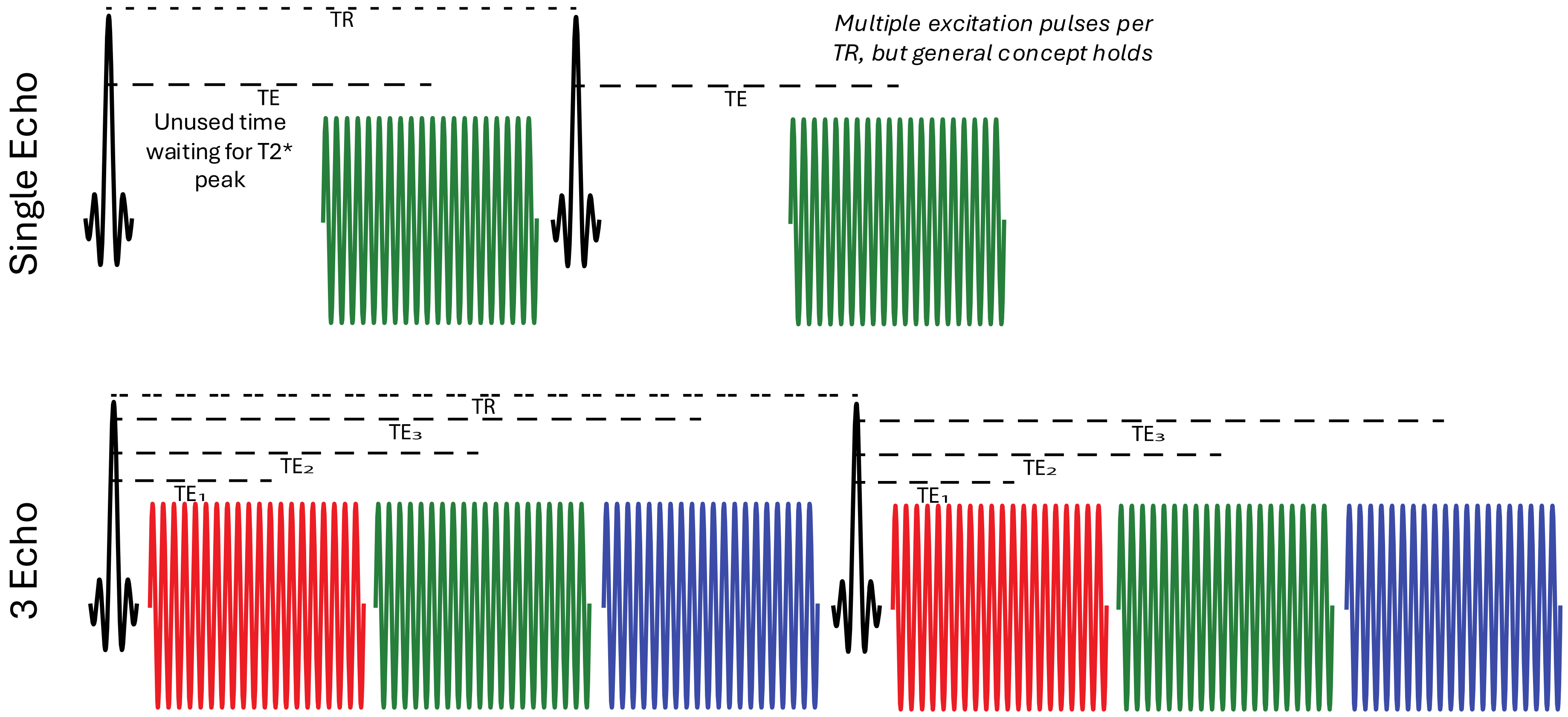
Protocol has 3 min for fMRI with the goal of identifying language lateralization

TR=0.9s, MB=4
Multi-echo=3
3mm^3 voxels
Uses tedana denoising

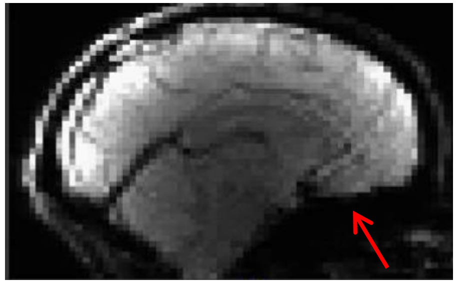
Of 271 patients scanned only 2% of fMRI scans were unsuccessful

Chris Tailby, OHBM 2025 https://youtu.be/sNc0Icn2Gps?si=TOx--M0WrSFSFd6v

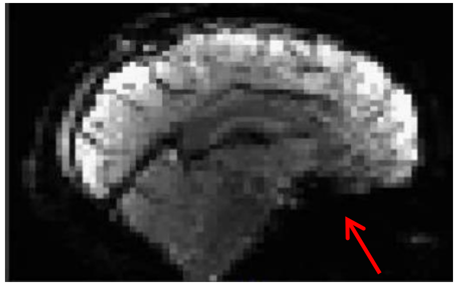
What is multi-echo fMRI?



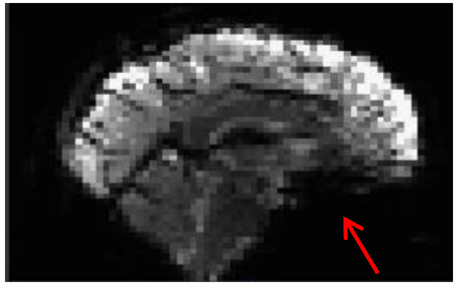
Echo 1



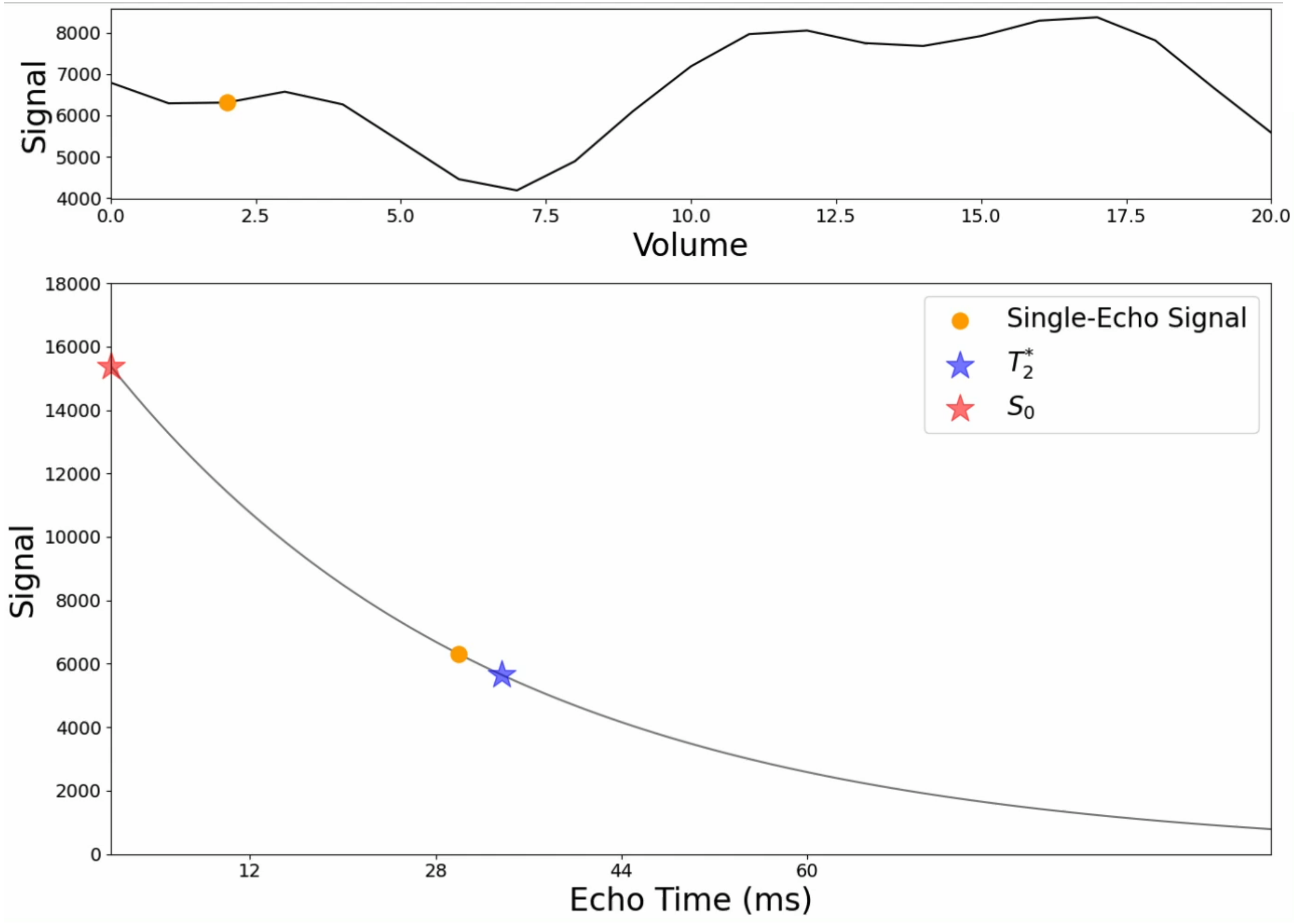
Echo 2



Echo 3



Using Multi-echo information



$$S(t, TE) = S_0(t) \times e^{\frac{-TE}{T_2^*(t)}} + noise$$

The signal decays with echo time

S_0

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

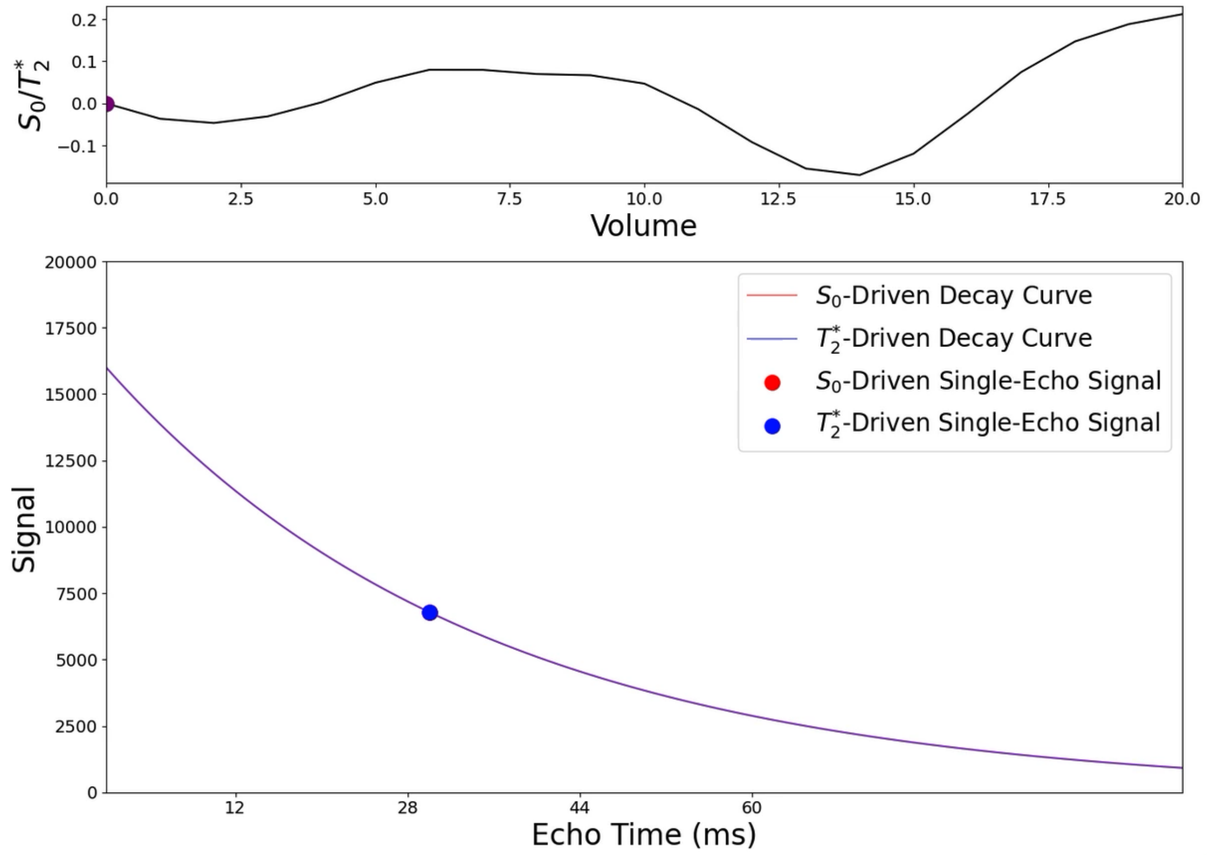
T_2^*

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

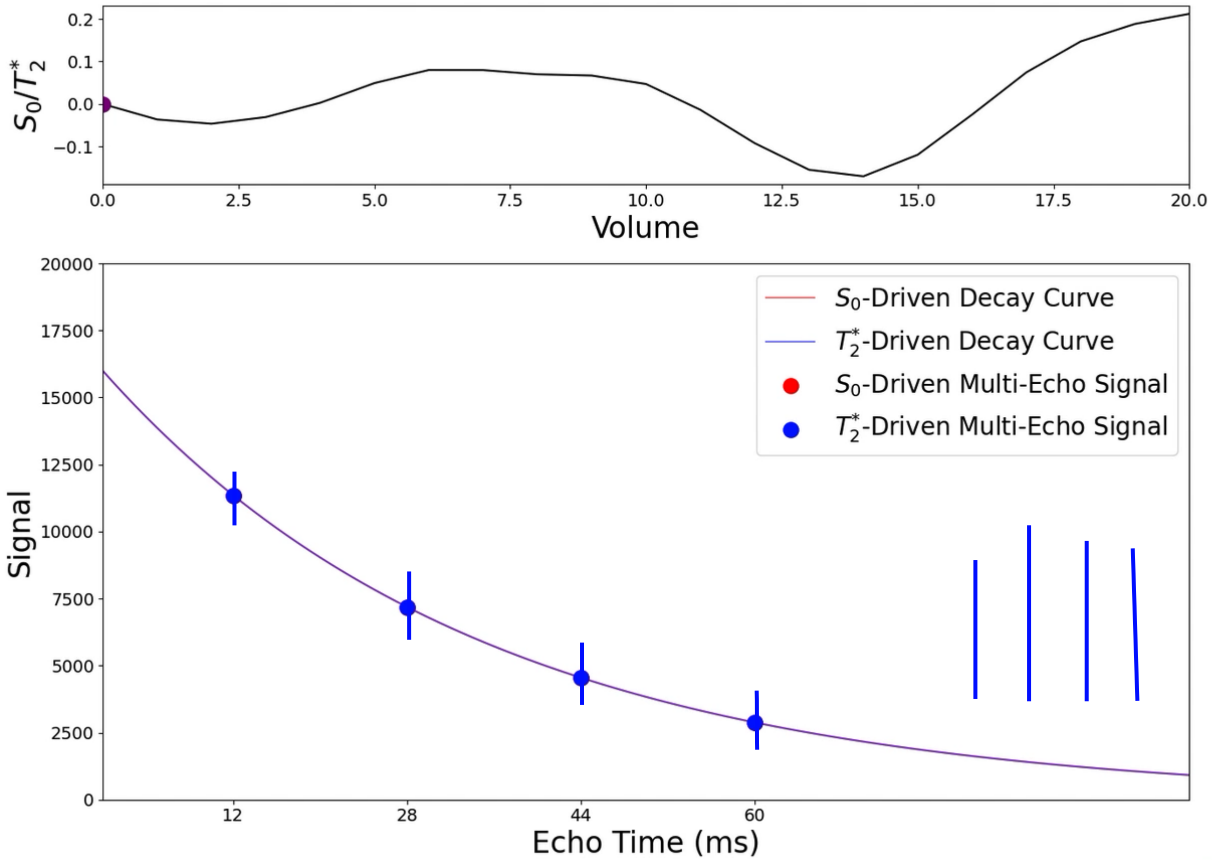
Taylor Salo: https://me-ica.github.io/multi-echo-data-analysis/content/Signal_Decay.html

Multi-echo gives us info to distinguish T_2^* and S_0

What we measure with single-echo fMRI



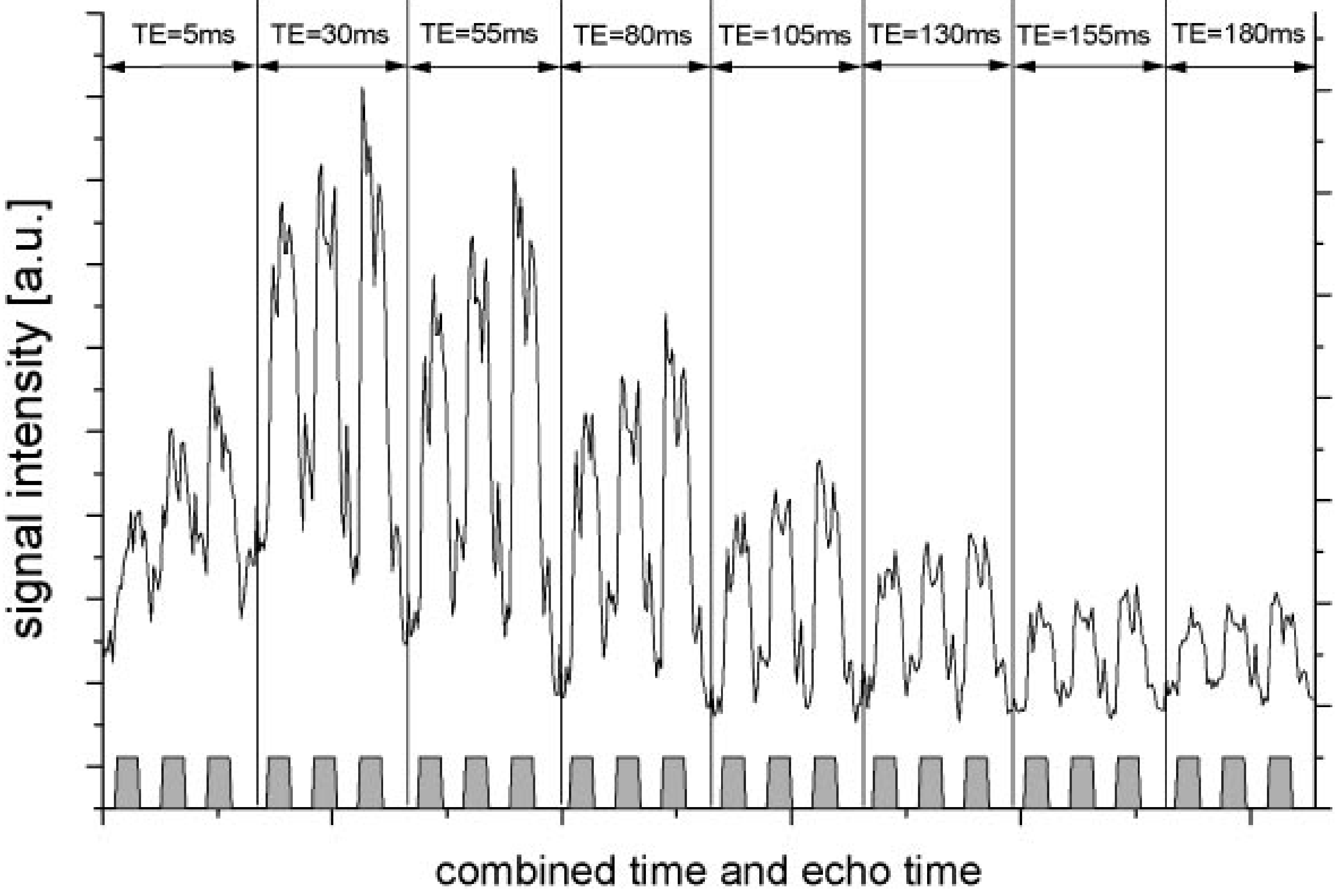
What we measure with multi-echo fMRI



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

fMRI response magnitudes by echo time

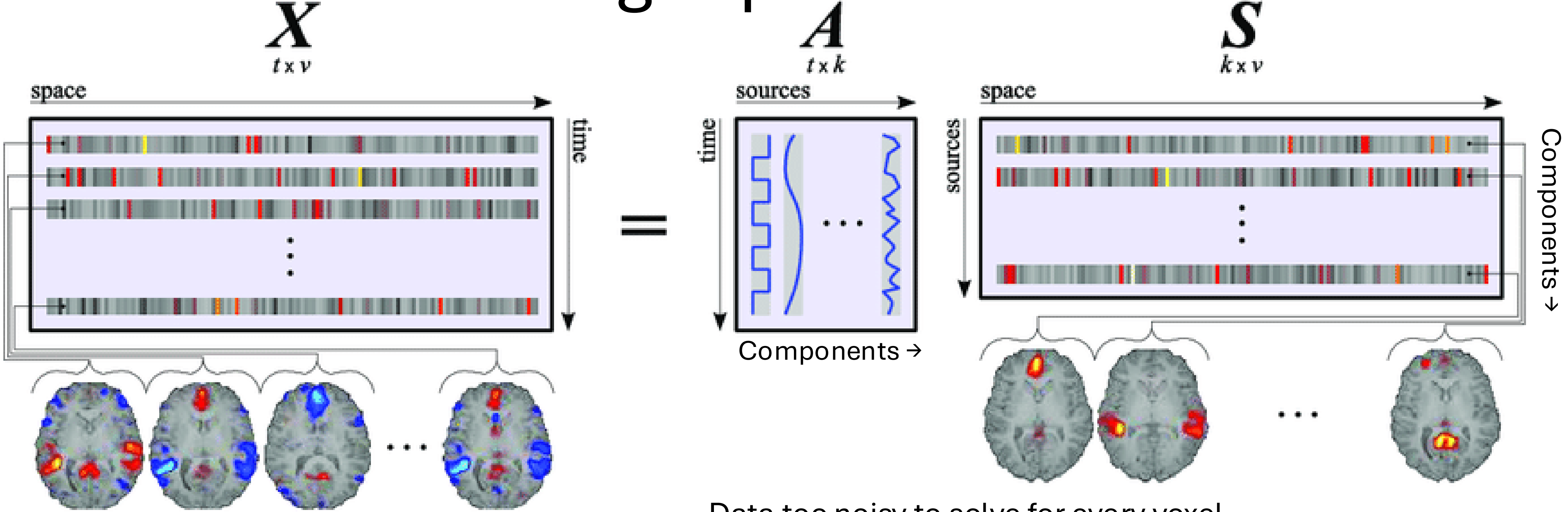
Average across active voxels in a finger tapping task at 3T



Barth et al NMR Biomed 2001, p484

MEICA or tedana denoising

Hand waving explanation of ICA



Ylipaavalniemi, *Variability of Independent Components in functional Magnetic Resonance Imaging*. Available from: https://www.researchgate.net/figure/Spatial-ICA-of-fMRI-data-The-rows-of-the-data-matrix-X-and-sources-matrix-S-are_fig3_267419506

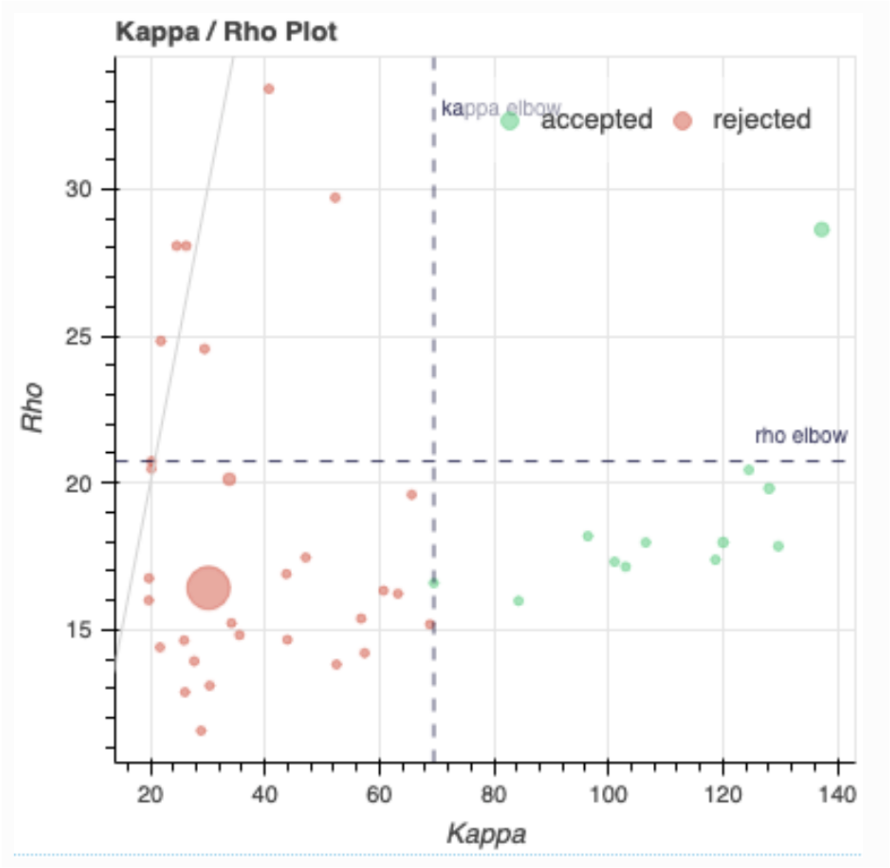
Data too noisy to solve for every voxel and time point separately

$$S(t,TE) = S_0(t) \times e^{\frac{-TE}{T_2^*(t)}} + noise$$

Solving for 2 variables
≥3 measurements

ICA is “intelligent” signal averaging

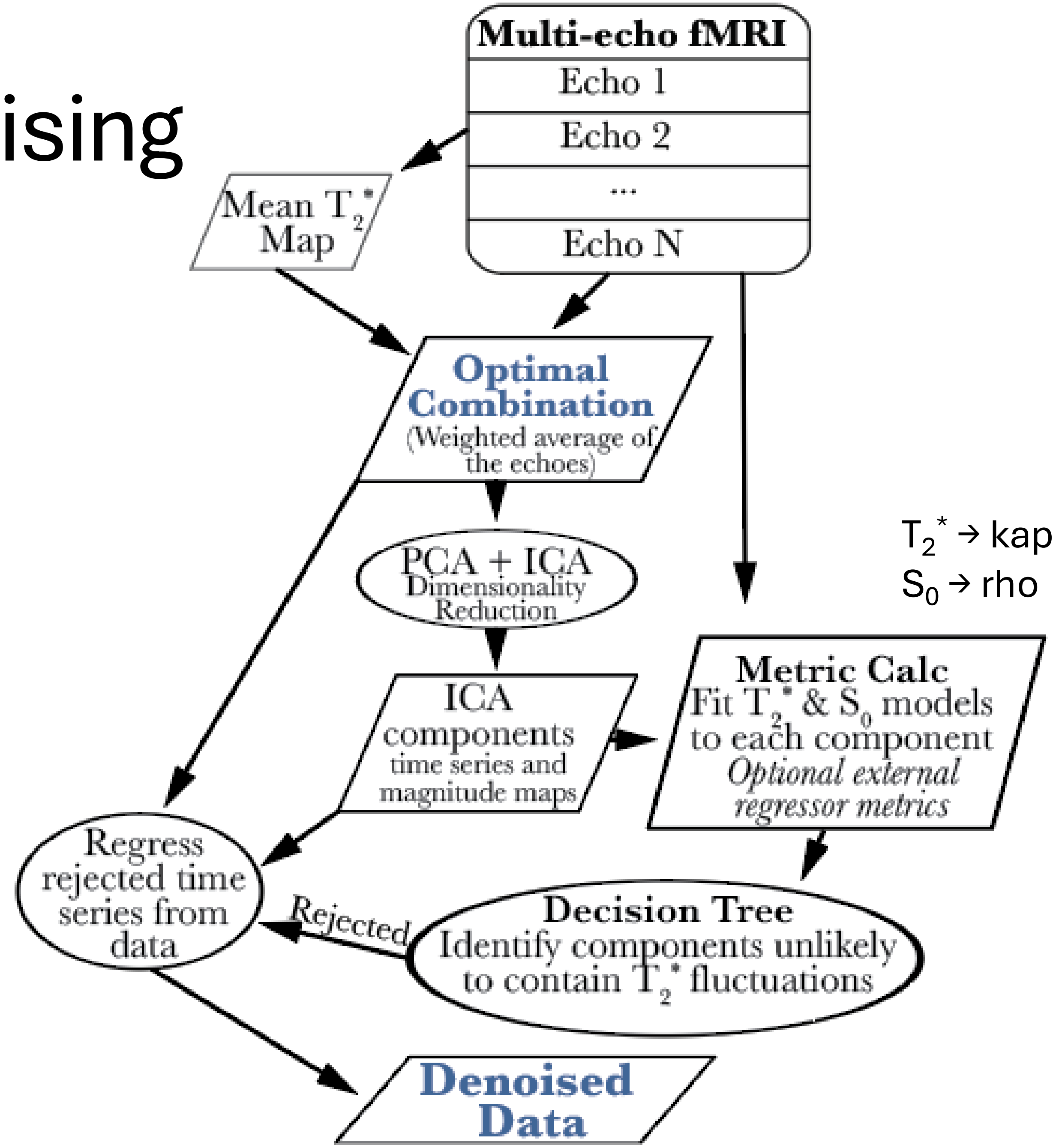
MEICA or tedana denoising



MEICA (Kundu 2012 & 2013)

tedana (DuPre, Salo, et al, *JOSS*, 2011)

tedana.readthedocs.io

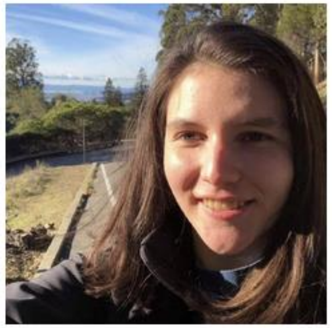


T_2^* → kappa

S_0 → rho

What's new in tedana

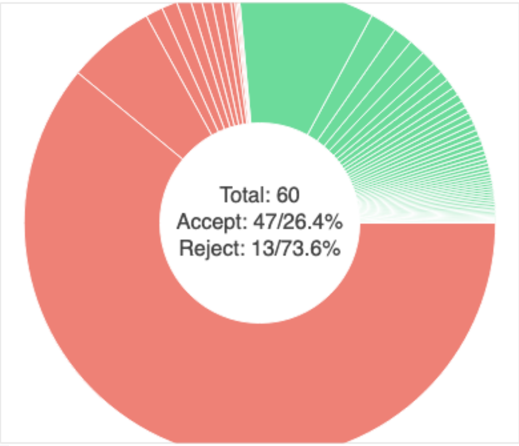
- **Version 26.0.0 released 2 days ago!**
- 11 people added to the code in the past year
- More contributed content and ideas
- Multi-echo users' meetings: https://www.youtube.com/@tedana-devs
- New contributors in the past year

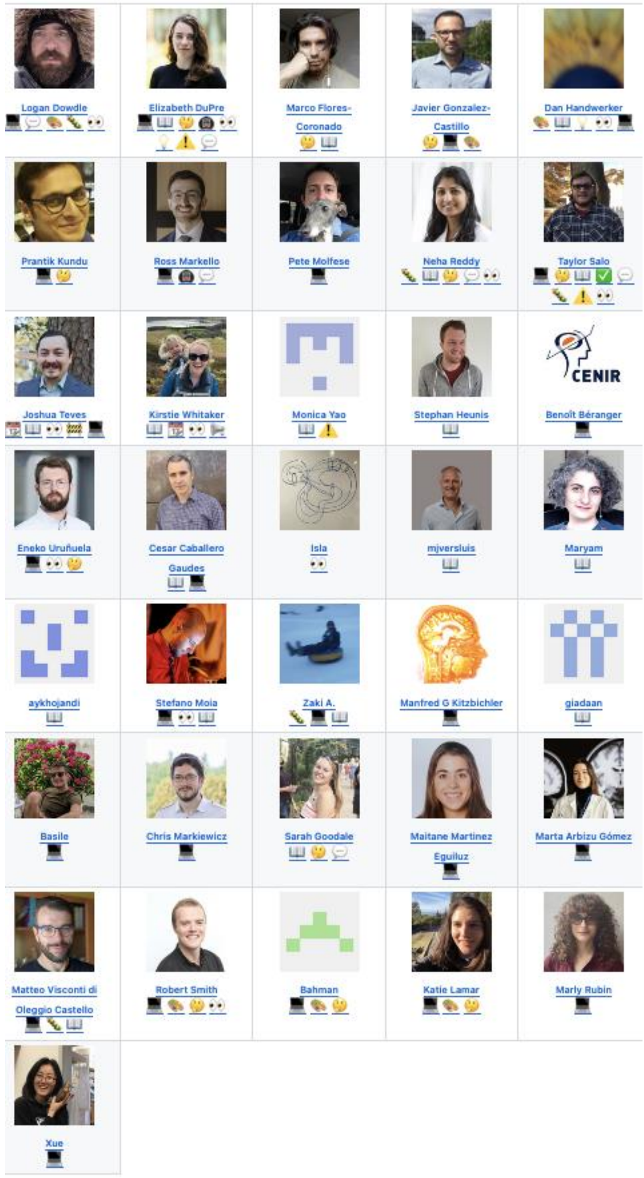


Katie Lamar

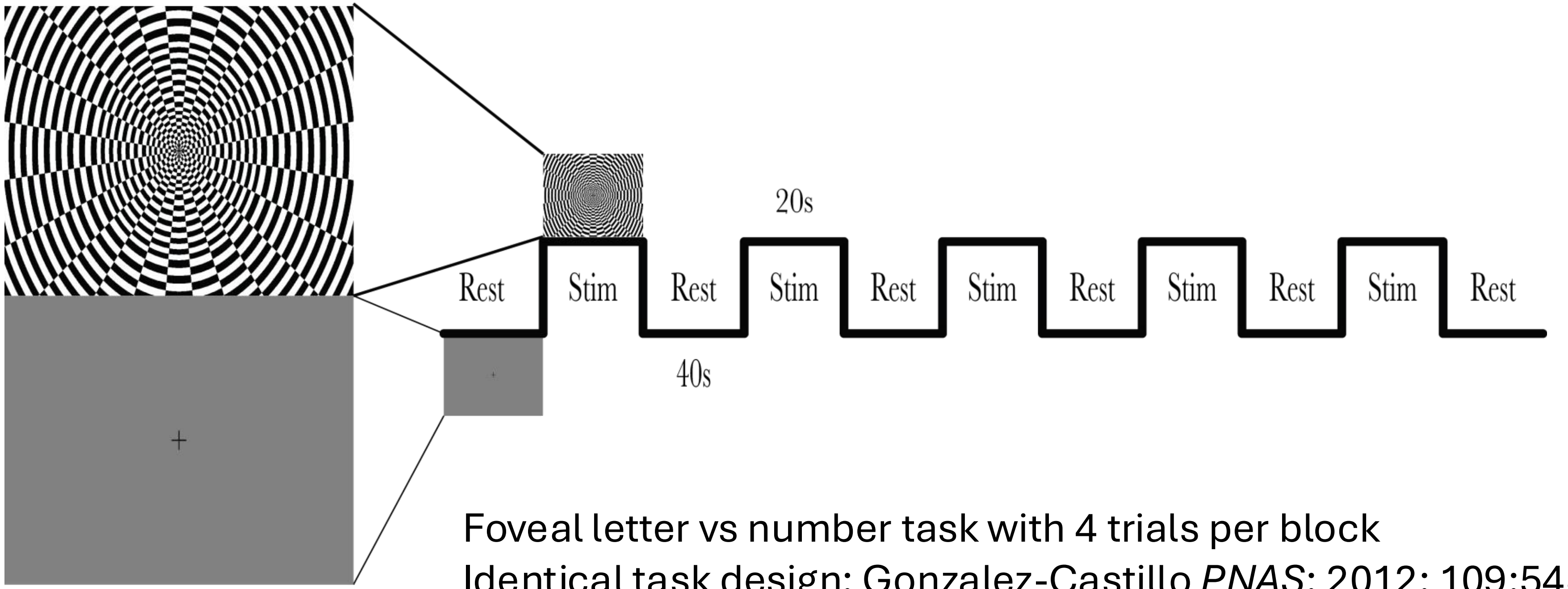
Marly Rubin

Xue





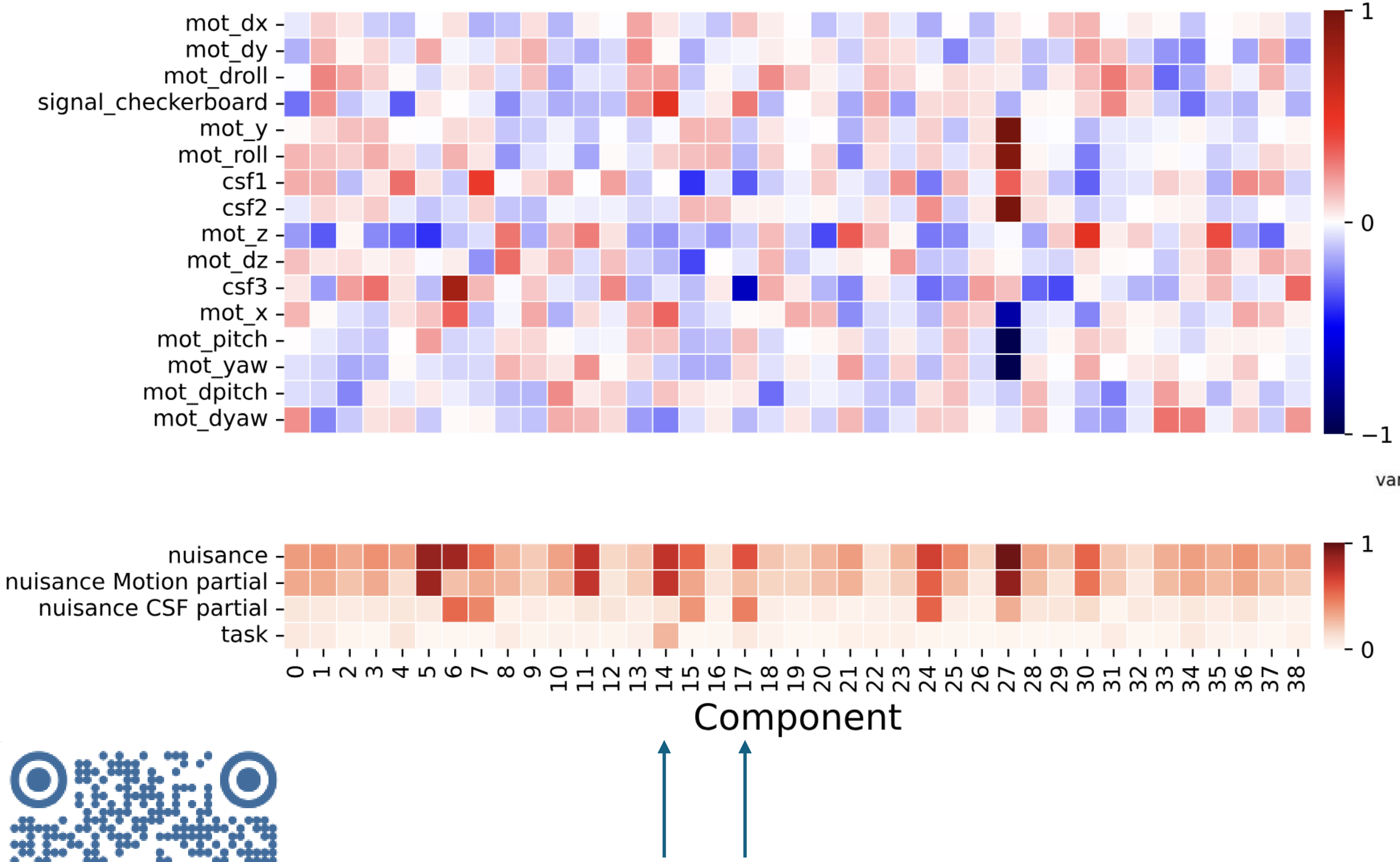
Block design checkboard + attention task

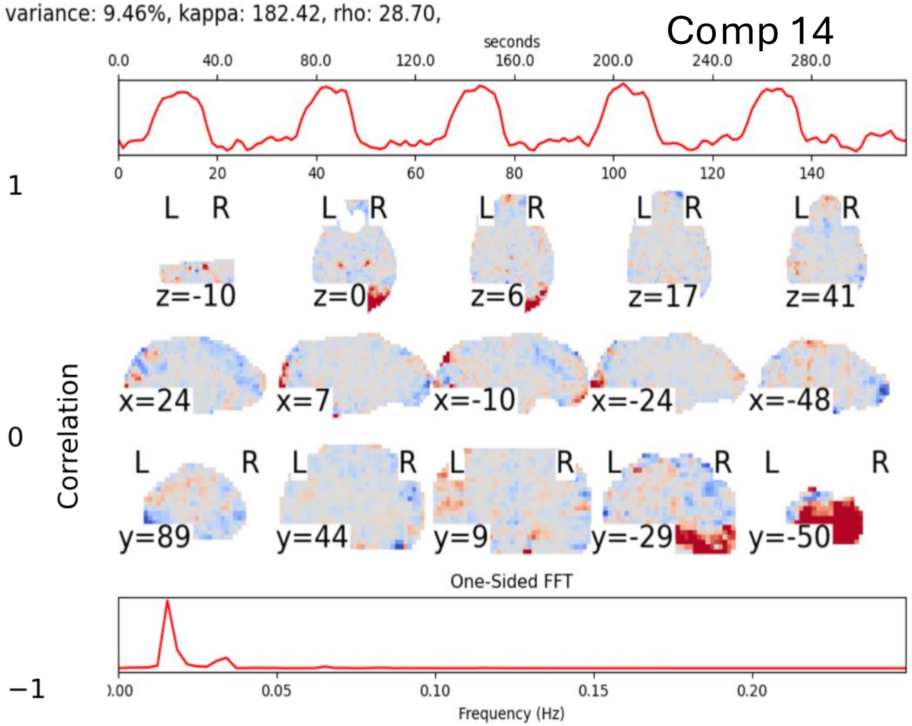


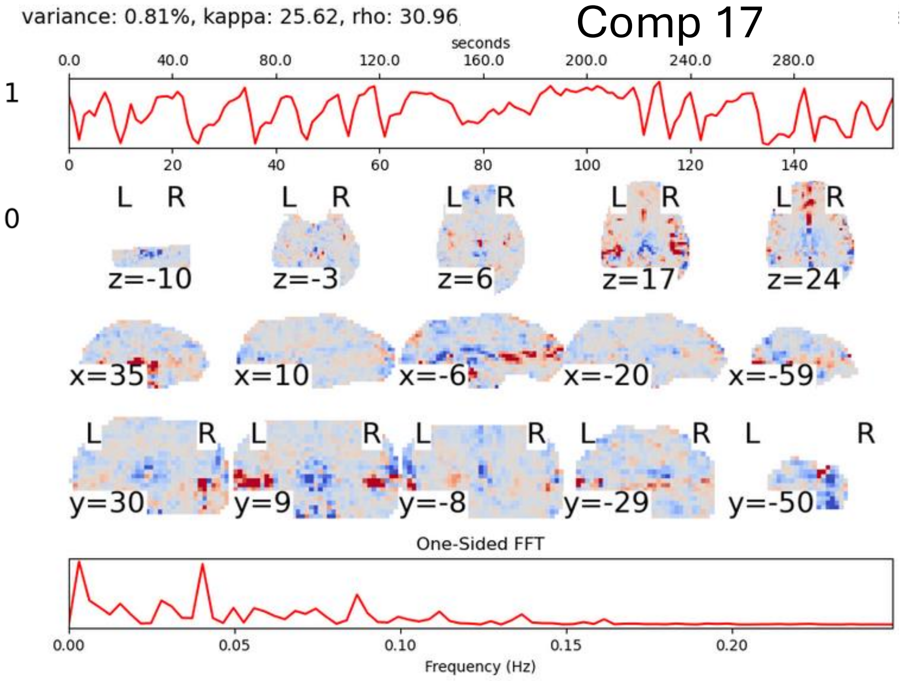
Foveal letter vs number task with 4 trials per block
Identical task design: Gonzalez-Castillo *PNAS*; 2012; 109;5487

- GE MR750, 3T, 32 channel coil
- EPI: 3.5mm^3, **5 echoes, TE=15.4, 29.7, 44.0, 58.3, 72.6ms**
  FA=75°, TR = 2s,
- 5.5 minutes, 161 volumes

External Regressors



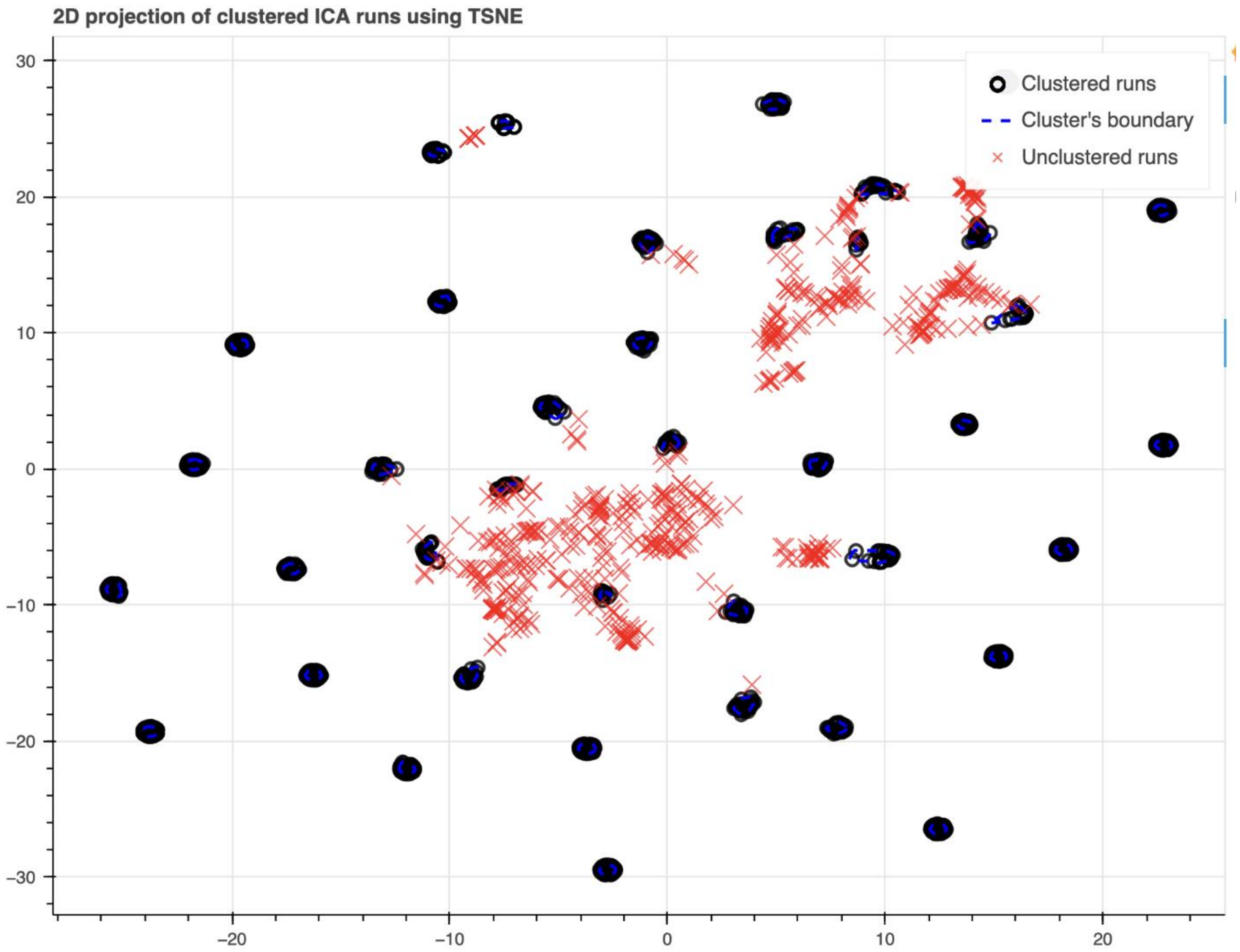




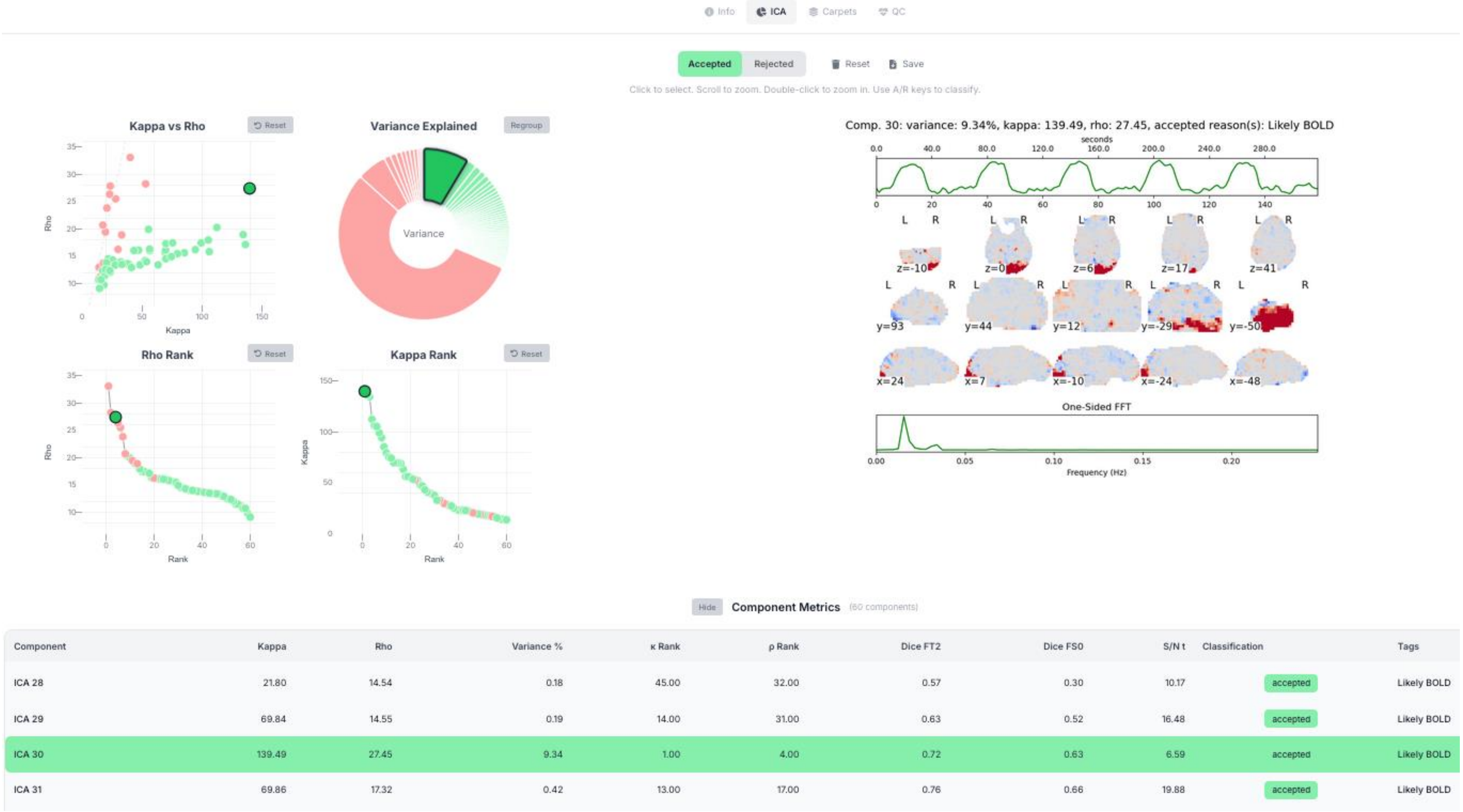
https://me-ica.github.io/ohbm-2025-multiecho/
tedana_external_regress_processed/tedana_report.html

Robust ICA

Added by Australian Epilepsy Project team



Better access to RICA interactive visualization



More tedana additions

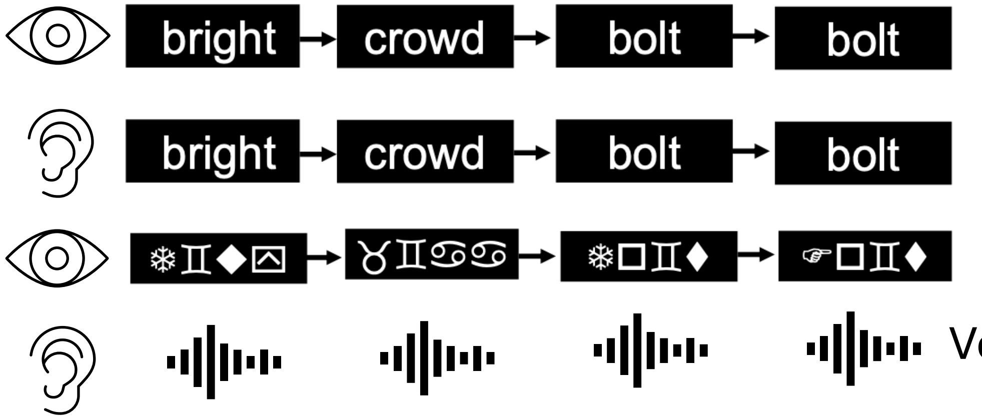
- Better memory management: Only storing voxels within masks
- Better parallelization for some processing steps
- Added more metrics for understanding each component
- Can designate dummy scans within tedana
- Input user-specified degrees of freedom for EPITI data
- Custom decision trees can be updated to figshare and automatically integrated into tedana
- Revived work on interactive book: https://me-ica.github.io/multi-echo-data-analysis
- Tracking openly shared multi-echo data https://me-ica.github.io/open-multi-echo-data
- Everything: https://github.com/ME-ICA/tedana/releases

How many components for ICA?
(Dimensionality estimation)

Marlene Smith

- Tedana has several well-established options for estimating the number of components
- They sometimes fail
  - If you have 200 timepoints, 10 or 199 components are implausible
  - 199 isn't ICA anymore and your brain is doing more than 10 things at once
- Want to understand why and ideally find a method to estimate the "right" number of components
- ICA is supposed to model the number of non-Gaussian statistically independent components + 1
- Many methods assume data are independent and identically distributed (i.i.d.). FMRI data are not, but there are existing methods that are supposed to deal with this… Easy to solve?

Audio vs Visual + Word vs NonWord Task



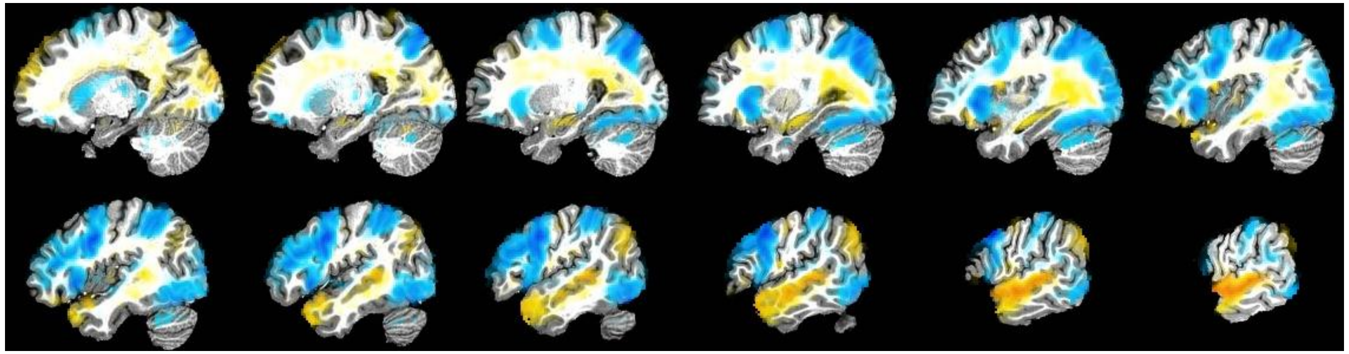
Vocoded words

4 sec trials
Press button if a stim repeats in a trial
Jittered event related design
25 minutes of data over 3 runs
340-345 volumes/run

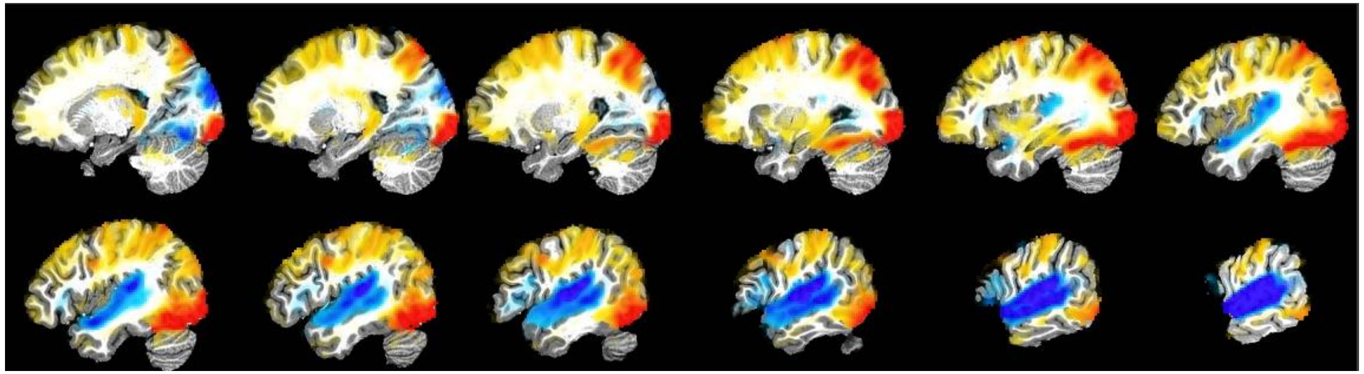
3T Siemens Prisma
TE=13.44, 31.7, & 49.96ms
TR=1.5s, SMS=2 iPAT=2
3.0 mm^3 isotropic voxels.
25 volunteers

Group contrasts

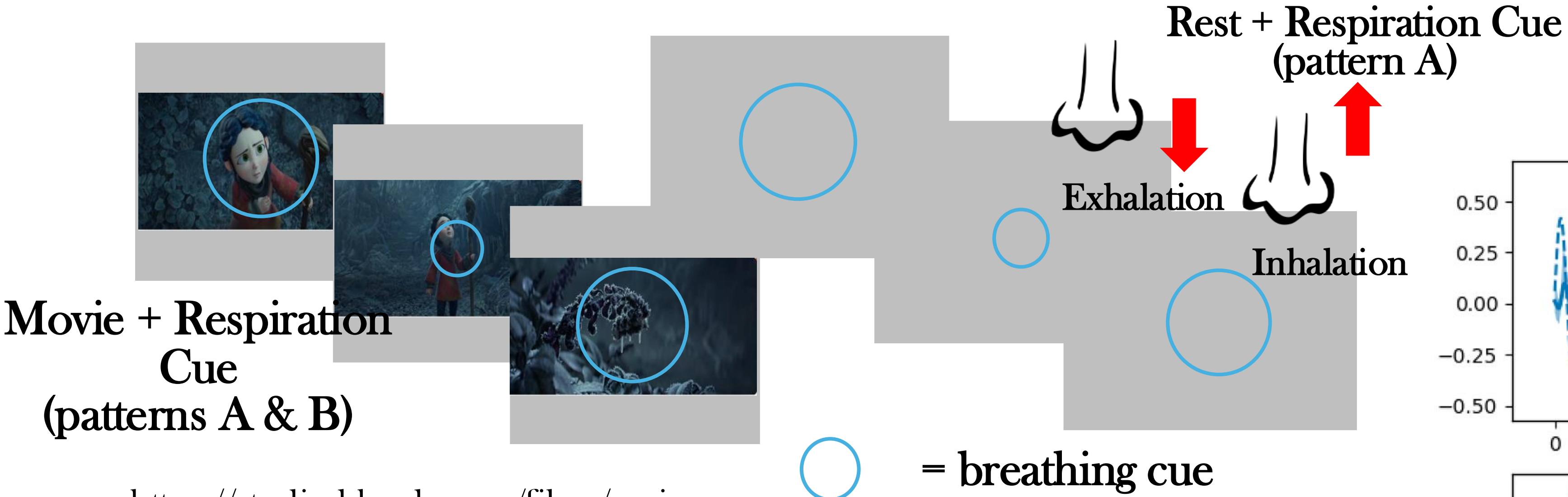
Word - Nonword



Visual - Audio



Paced Breathing and Movie Task

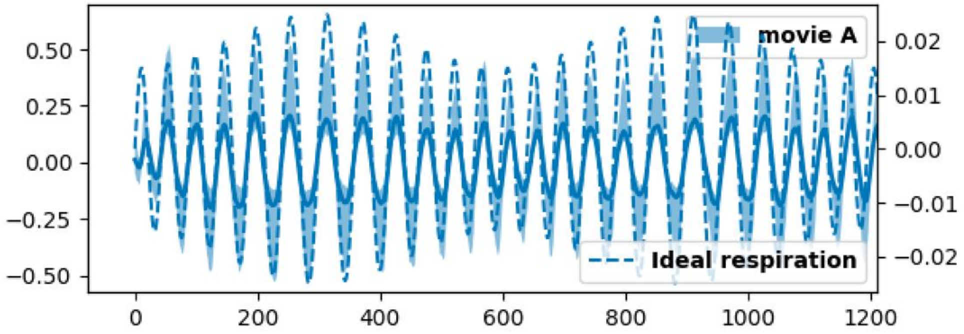


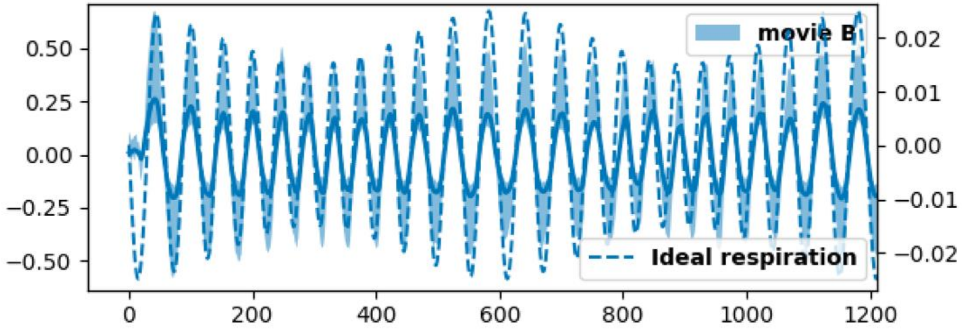
https://studio.blender.org/films/spring

3T Siemens Prisma
TR=1.5s
TE=13.44, 31.7, & 49.96ms
SMS=2 iPAT=2
3.0 mm^3 isotropic voxels.
25 volunteers

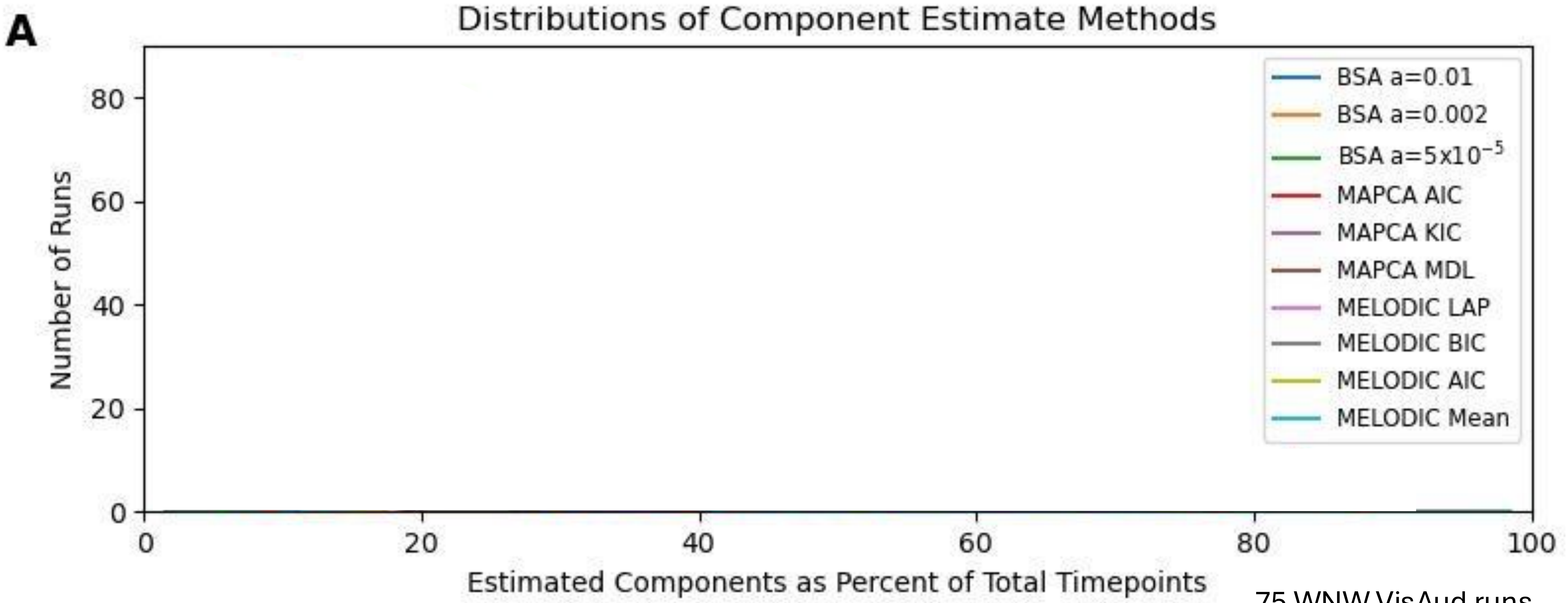
299 volumes per run

Breathing depth & rate





Comparing Methods for Component Number Estimation



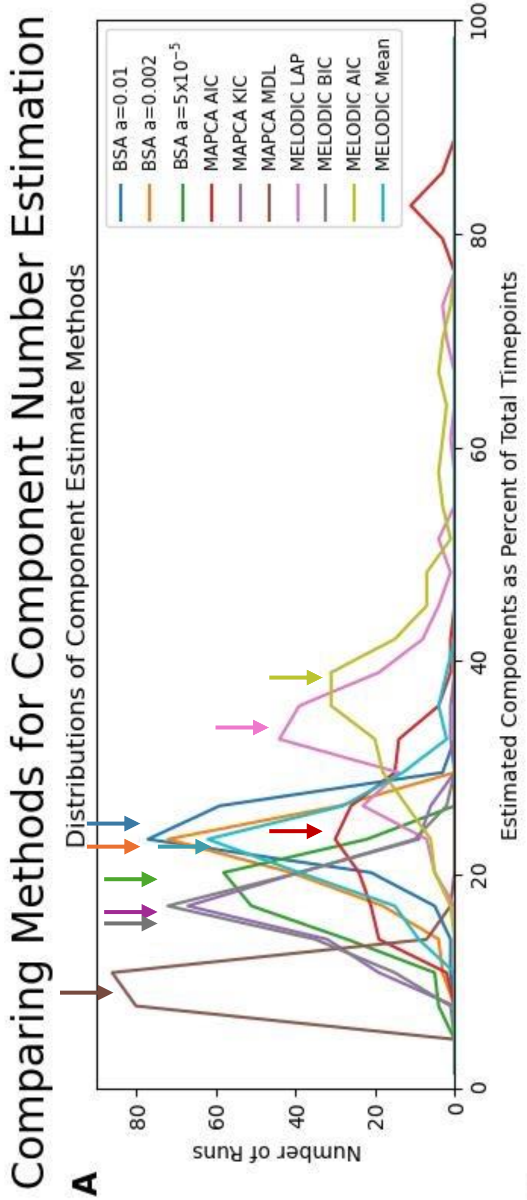
75 WNW VisAud runs
99 Breathing / Movie runs

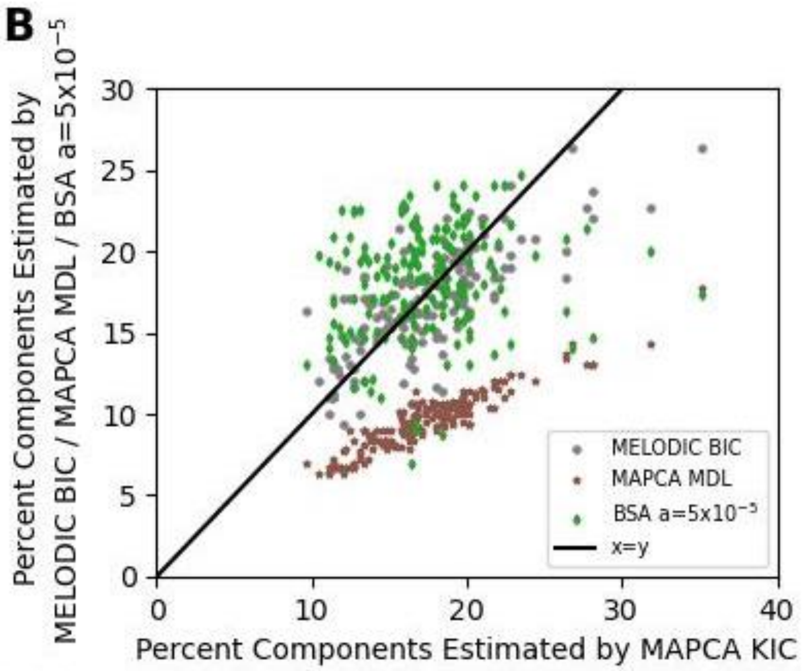
MAPCA = Used by tedana and a port of the methods in GIFT

MELODIC = Used by MELODIC in FSL. Some similar, some use Bayesian tools

BSA = Bootstrap Analysis (Majeed & Avison, PLoS ONE 2014) + coded & enhanced by Ka Chun Lam

Run-by-run comparisons of dimensionality estimates

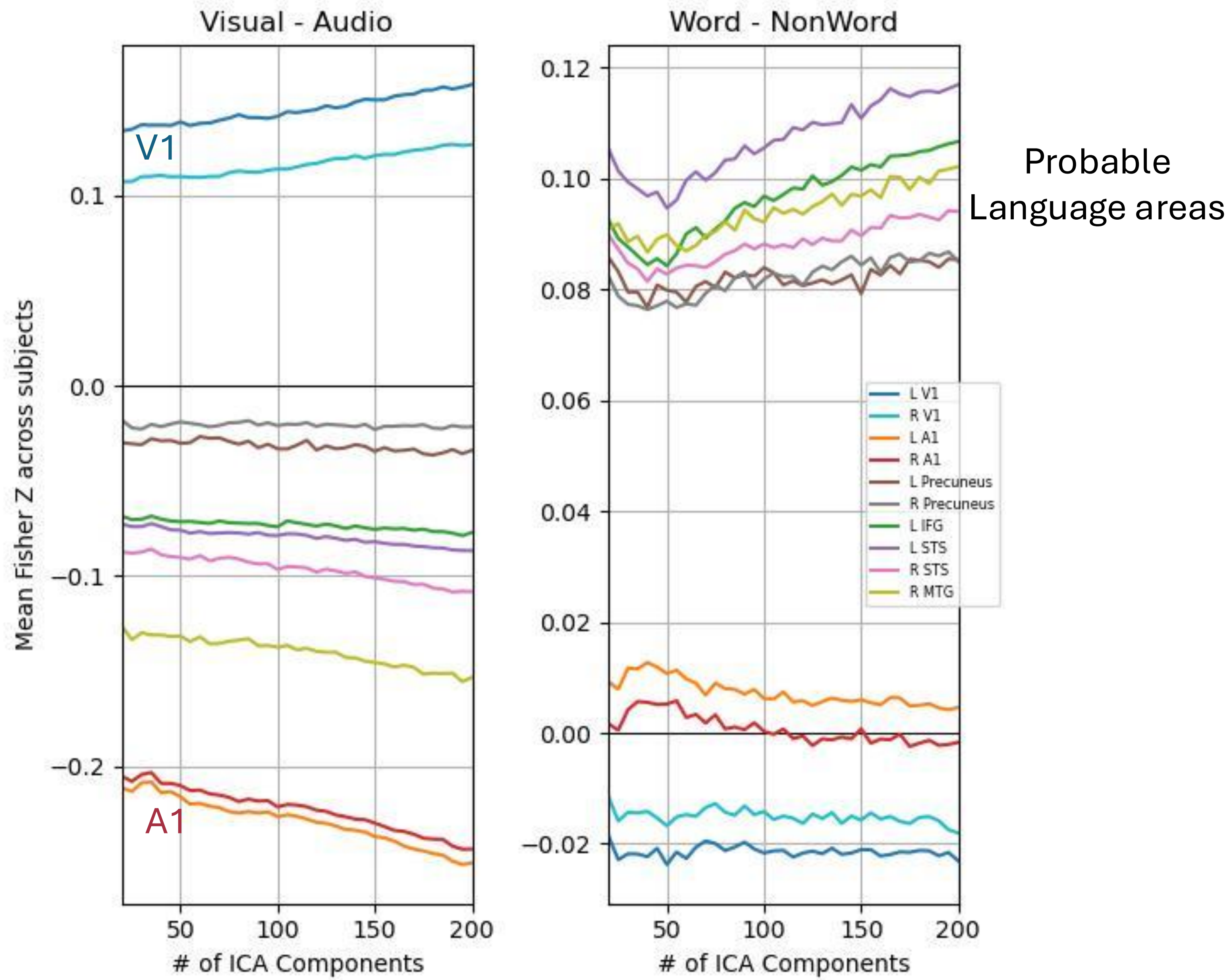




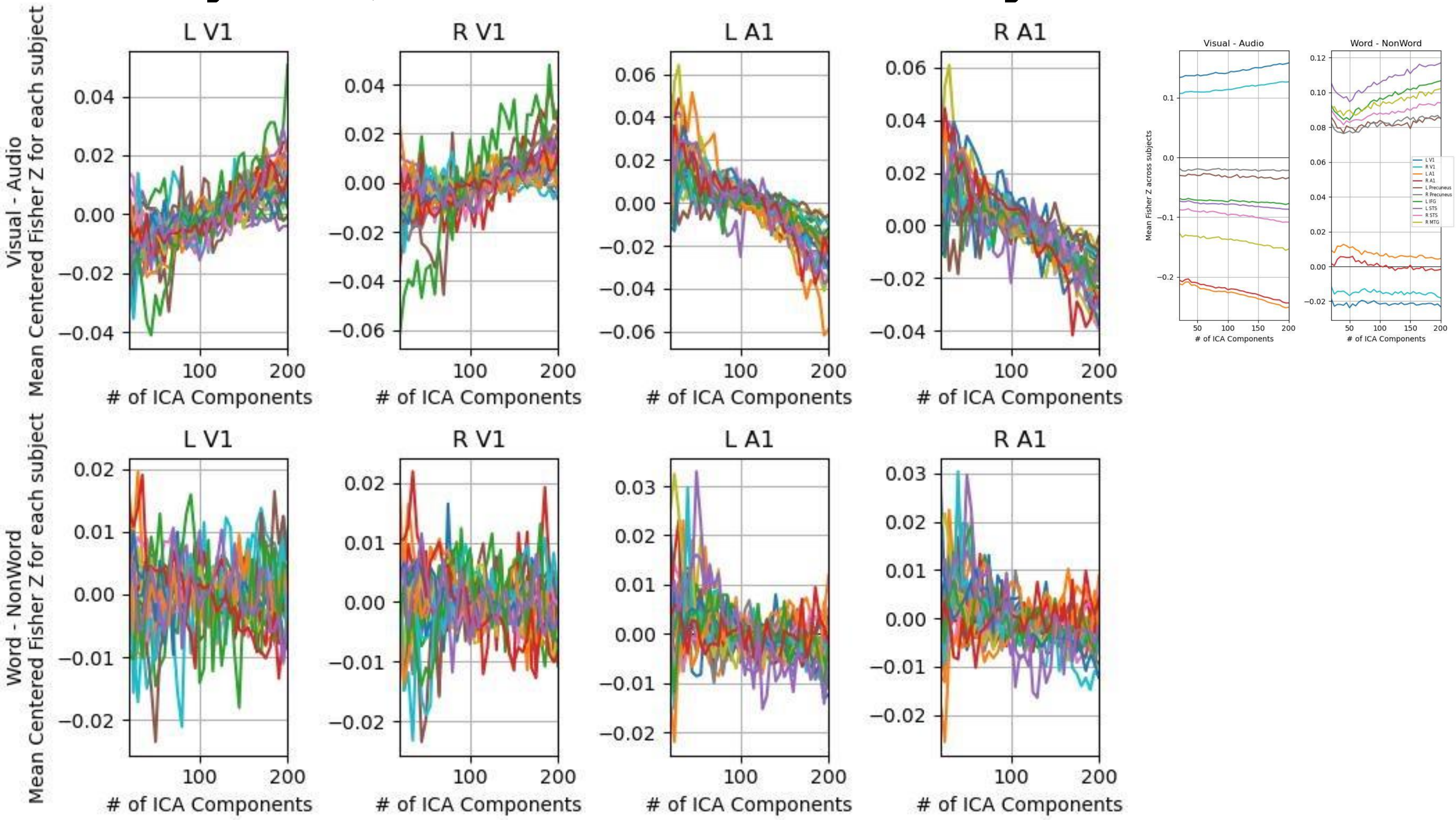
Many dimensionality estimations disagree

- We do not have a consensus estimate across methods
- Is one of these methods more accurate than others?
- What is accurate?
- Proxy measure: A good dimensionality estimate should result in better characterization of the data and better denoising
  - Using Word-Nonword, Vis-Aud task (340 volumes/run)
  - Run tedana with 20-200 ICA components pre-specified
  - Calculate $R^2 \rightarrow r \rightarrow$ Fisher Z
  - Subject-specific anatomically+functionally localized ROIs for each contrast
  - Contrast-to-Nosie measure: Average Fisher Z values for each subject and ROI
- What is the correct number of ICA components?

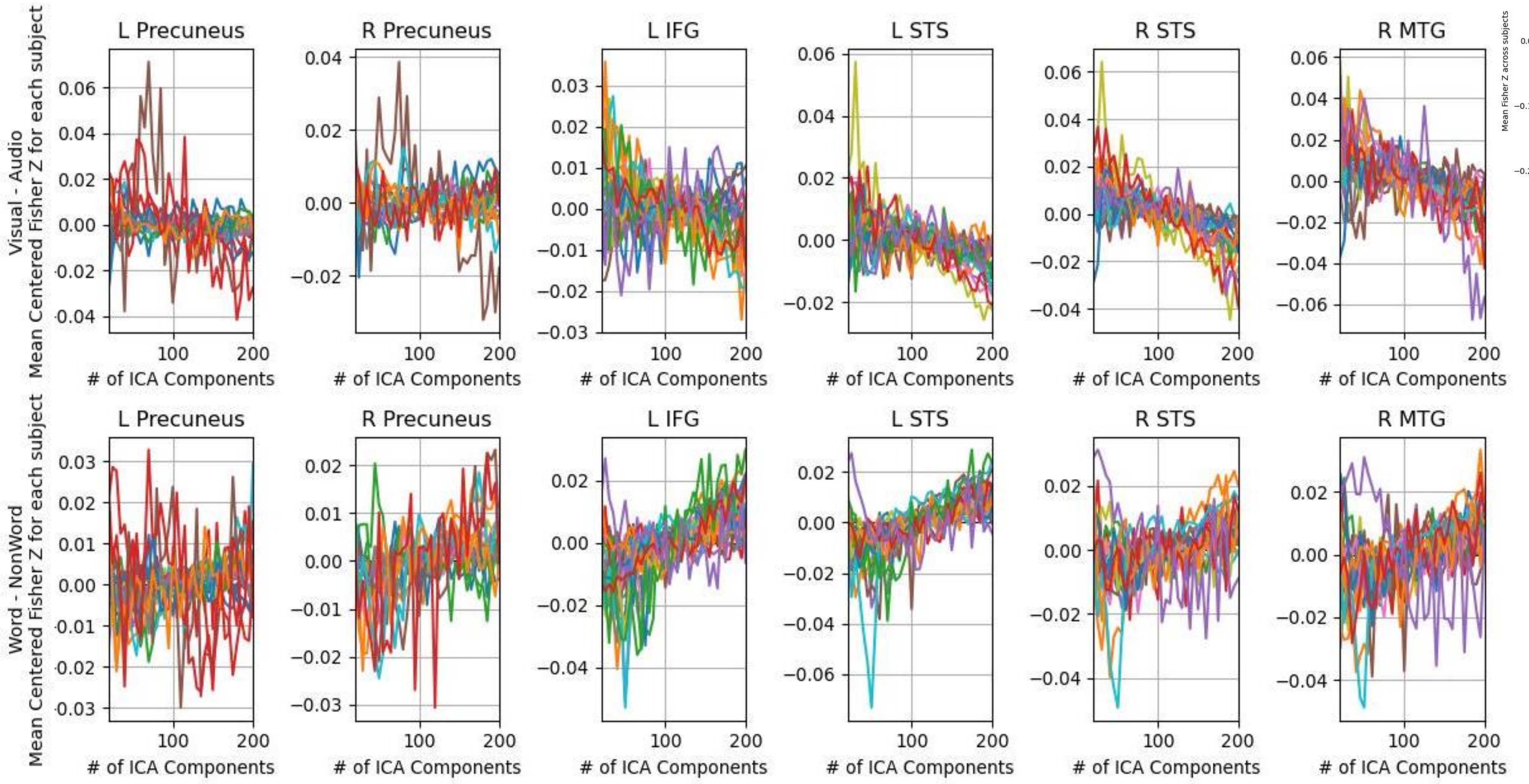
Contrast to noise vs # of ICA components

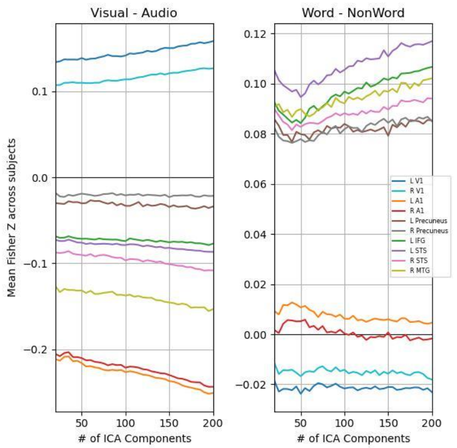


All subjects, Visual and Auditory ROIs

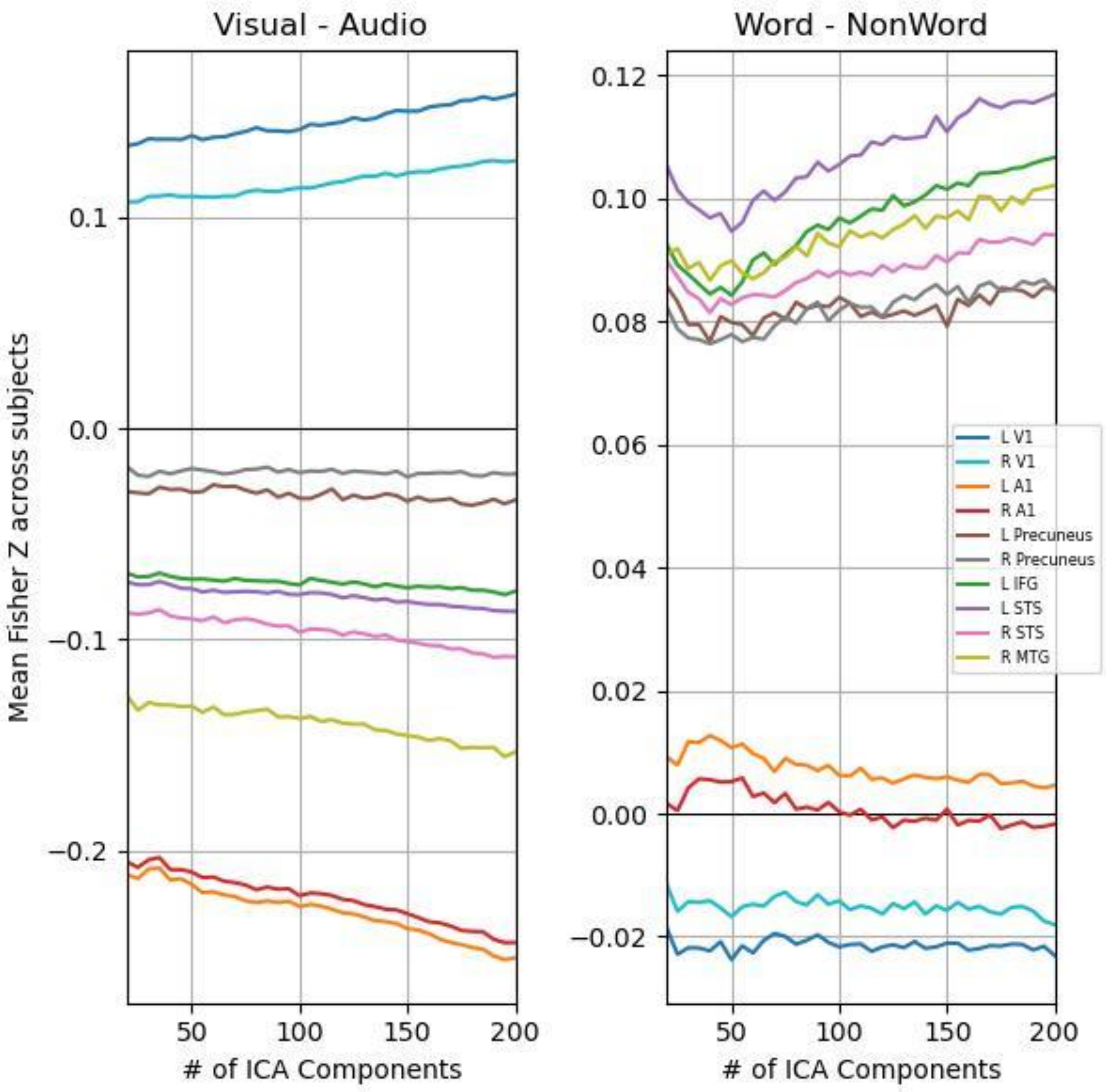


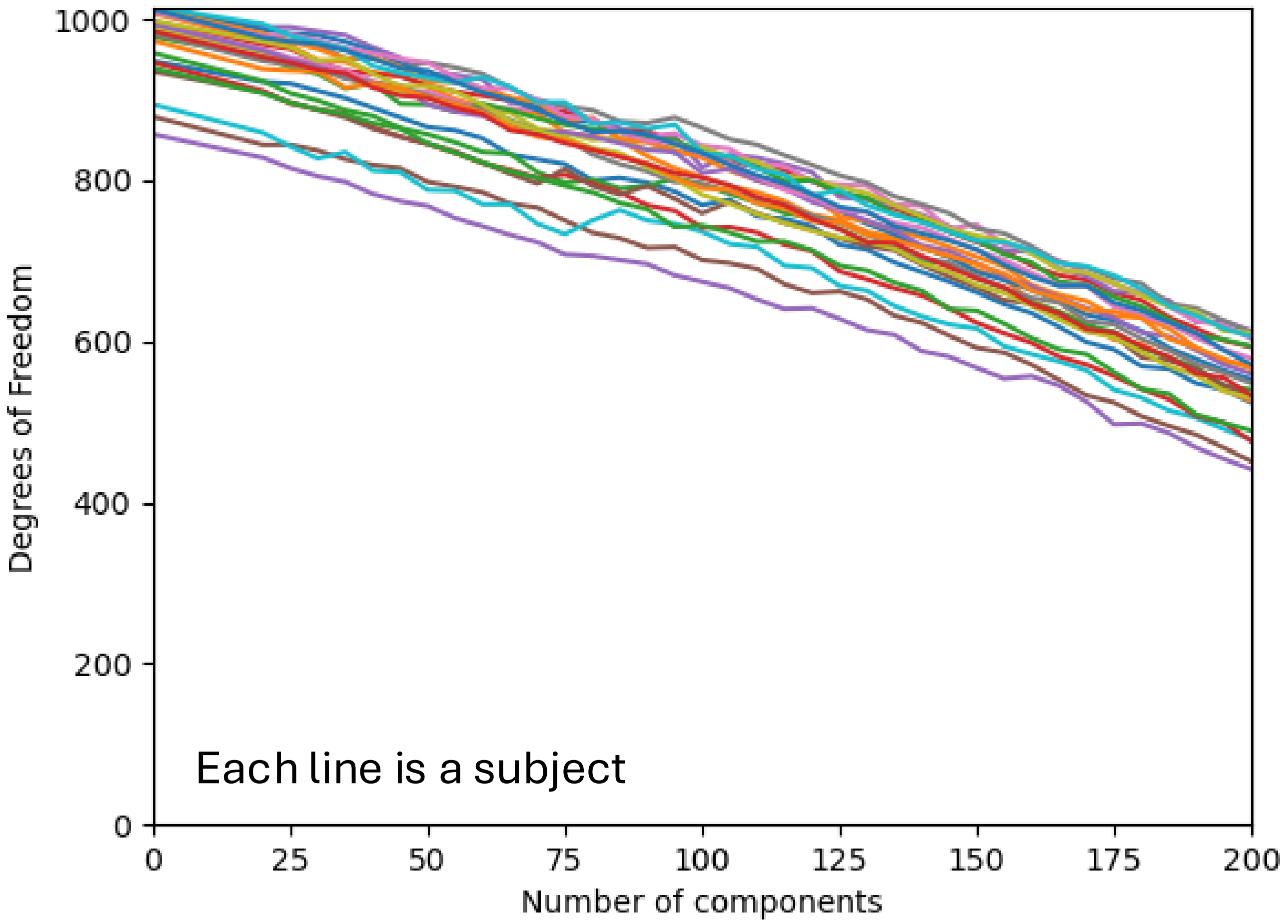
All subjects, language ROIS





Degrees of freedom decrease with more components





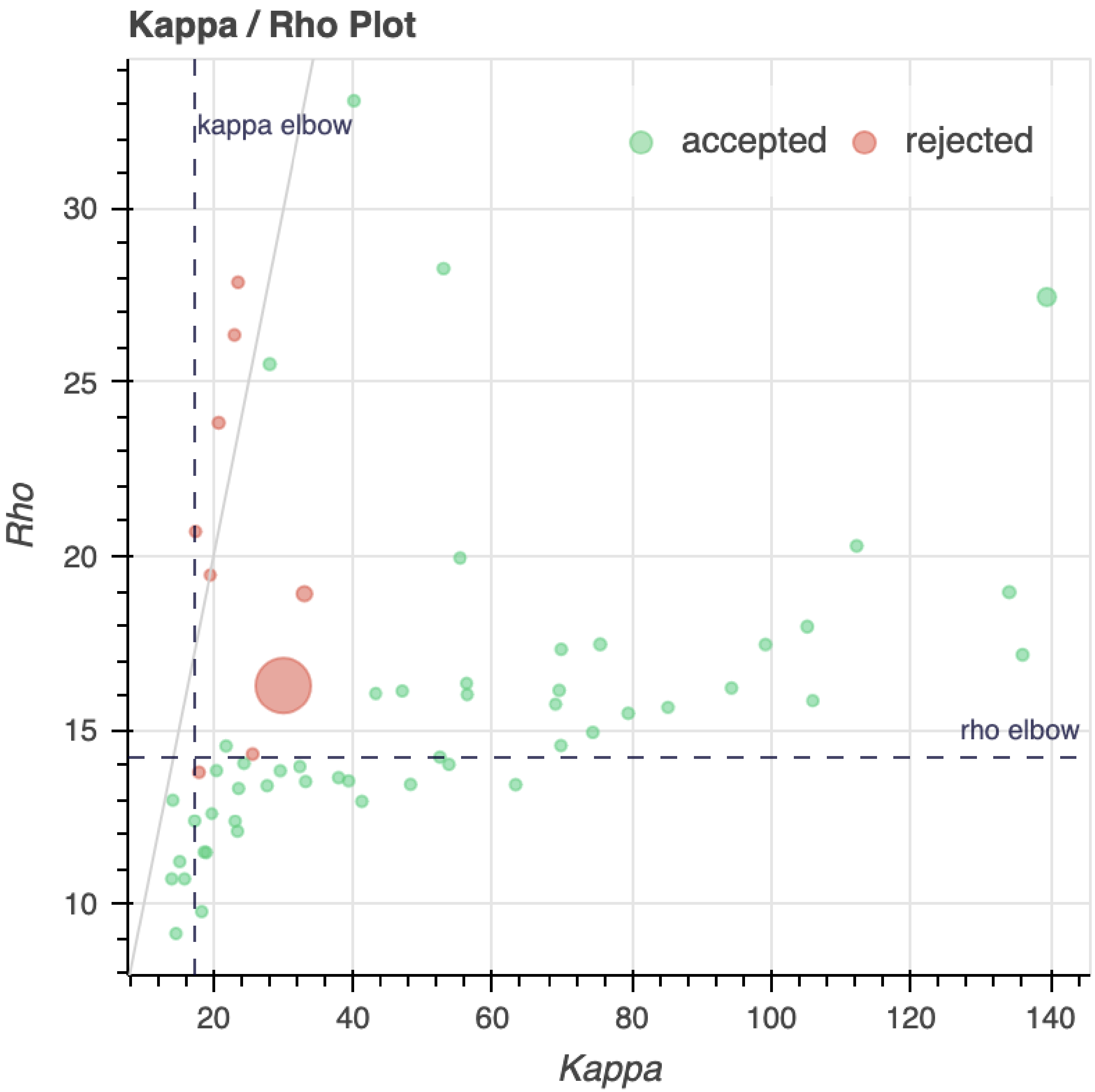
Current rec for selecting # of ICA components

- This choice will affect results, but don’t stress whether 50, 60, or 70, is more correct
- Pick something that makes sense across your dataset and runs in a sane amount of time
- ICA is “intelligent” signal averaging
- What is better than ICA?

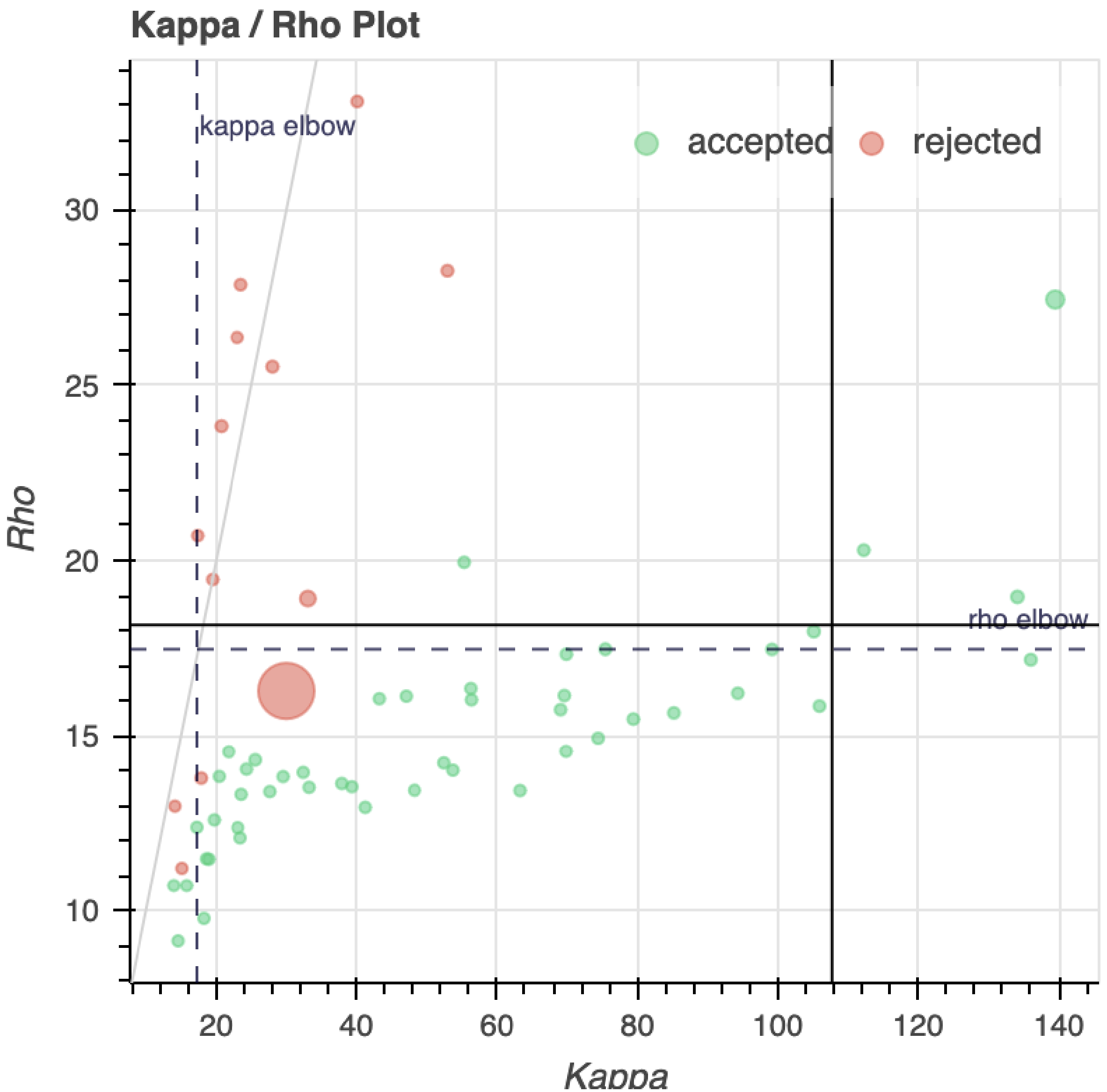
LBC Questions

Where to “cut” for good vs bad?

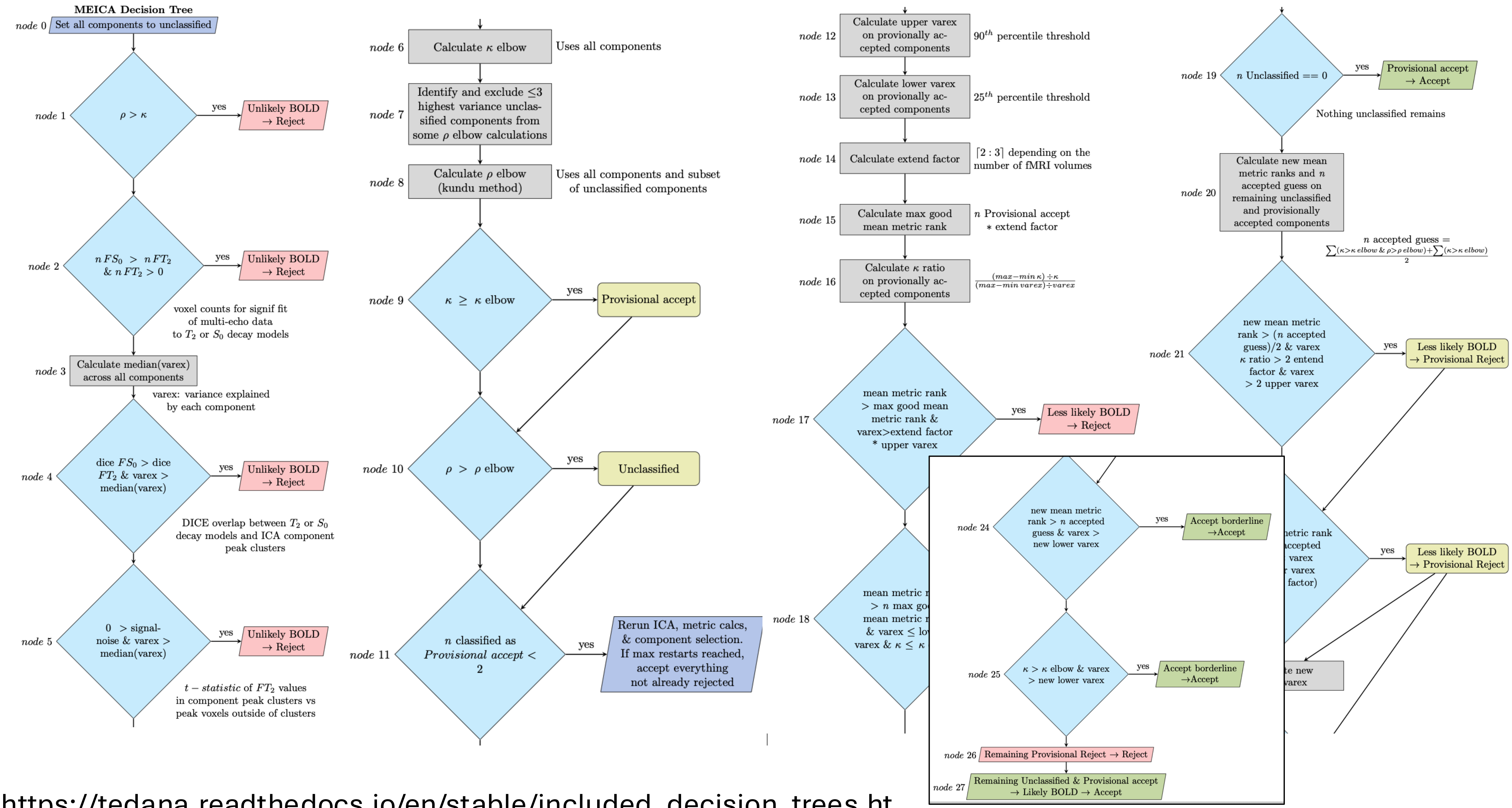
Original MEICA ”decision tree”



Tedana ”decision tree”

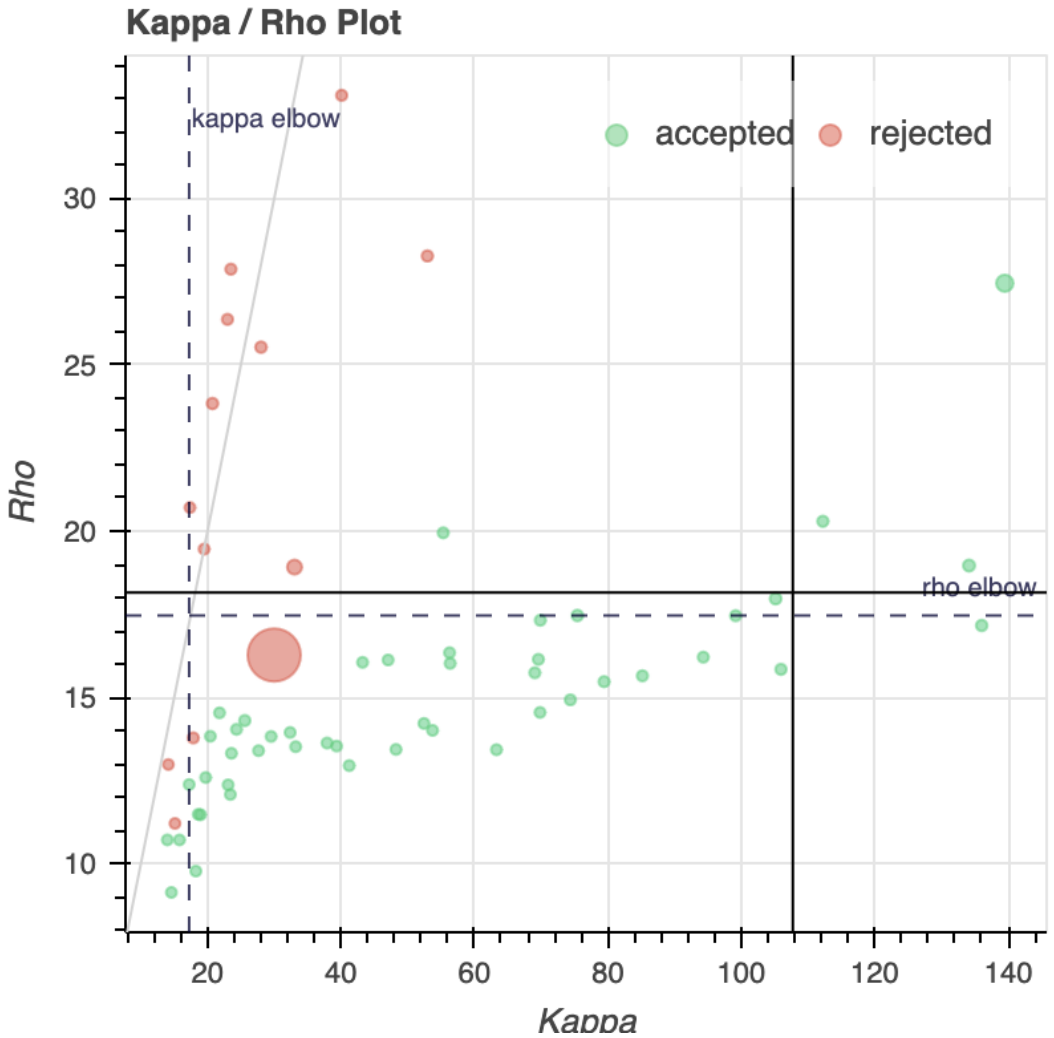


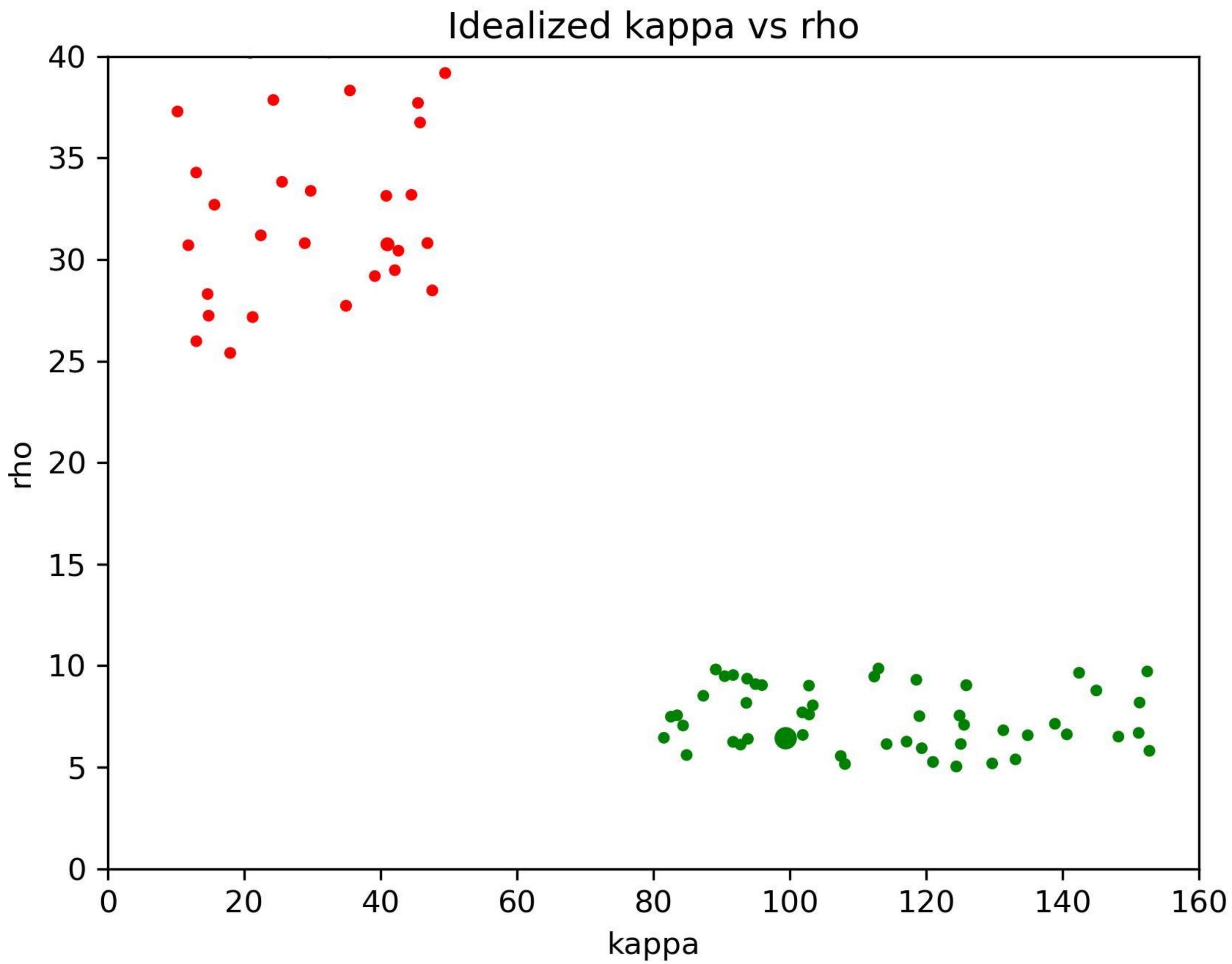
The meica decision process is… quirky



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

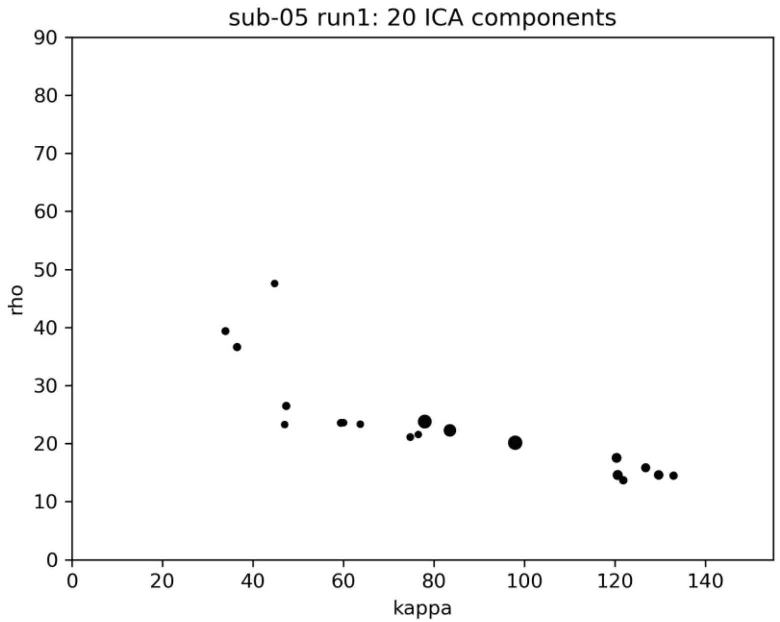
Why is the decision process unclear?

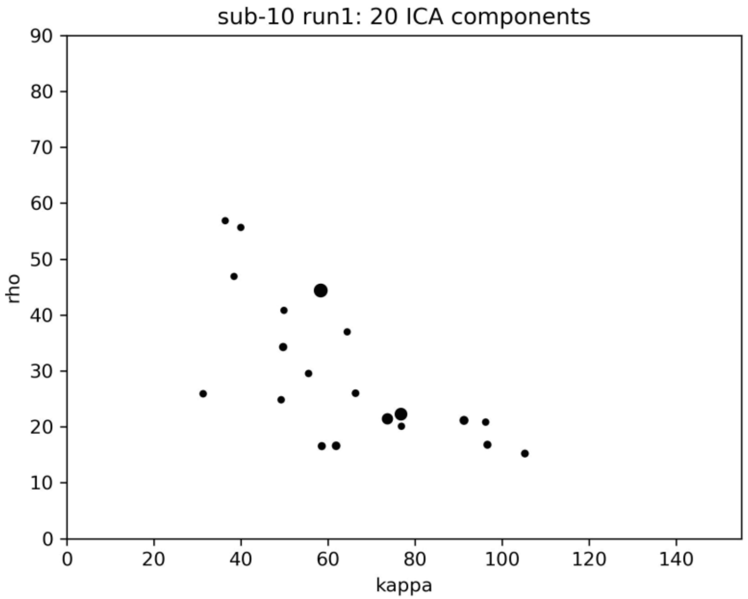




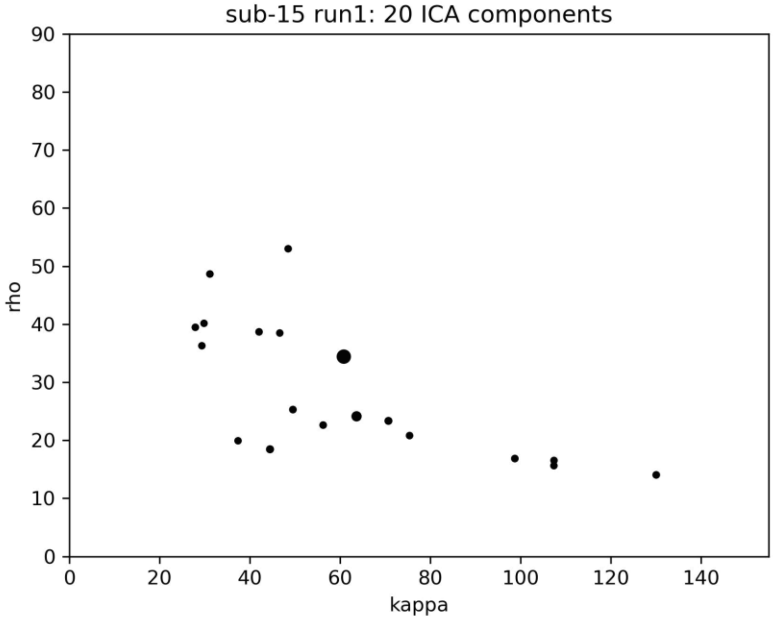
Everything far from the extremes is not only imprecise to classify, but is inherently a mix of signal we want and don't want

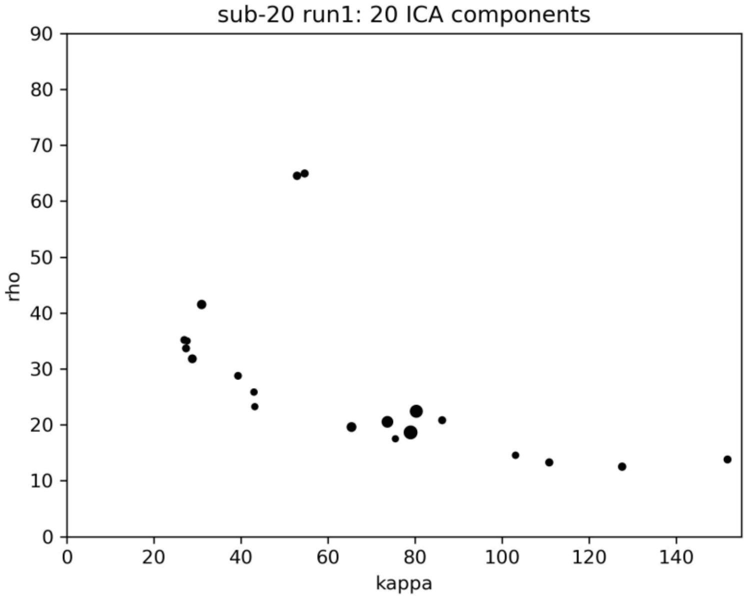
ICA is signal averaging, but are there better options?





Making the # of components study a bit more interesting





More components does bring more to extremes, but also more to closer to (0,0)

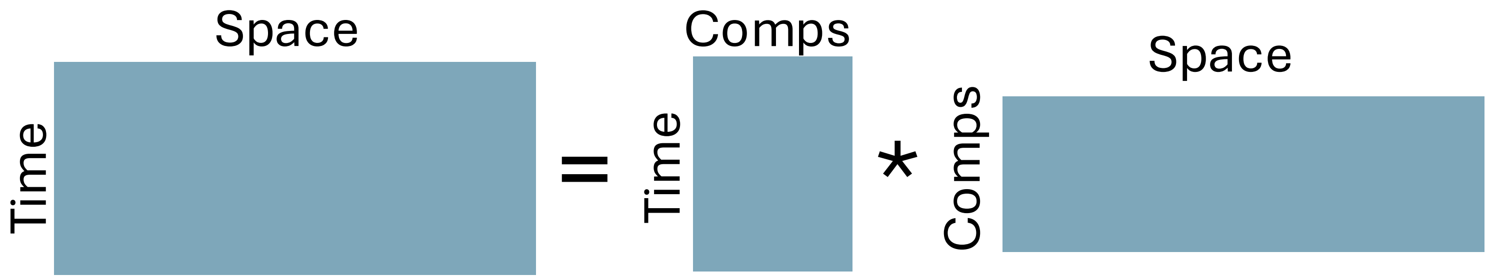
Other methods

The **VERY** preliminary & exploratory part of this talk

- Overall goal: A method that instead or in addition to optimizing for spatial statistical independence, optimizes for T2* vs S0 (kappa vs rho) separation

- **Tensorial ICA (tICA)**
- **Dynamic Mode Decomposition (DMD)**
- Iterative ICA to fit solutions with better separation
- Using T2* and S0 time series
- Machine Learning based approaches

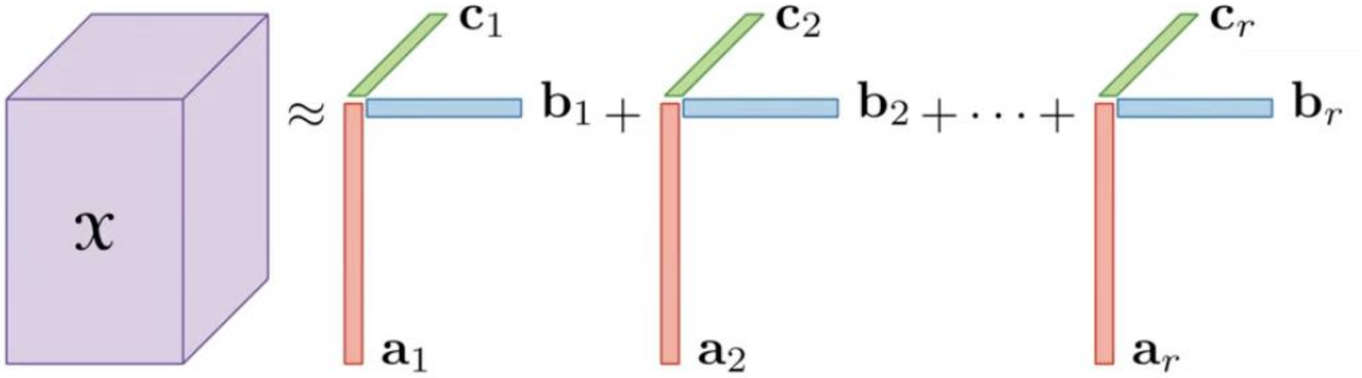
Standard ICA



Tensorial ICA

(Generalized)
Canonical Polyadic (CP)
Decomposition

a.k.a.
CANDECOMP or
PARAFAC

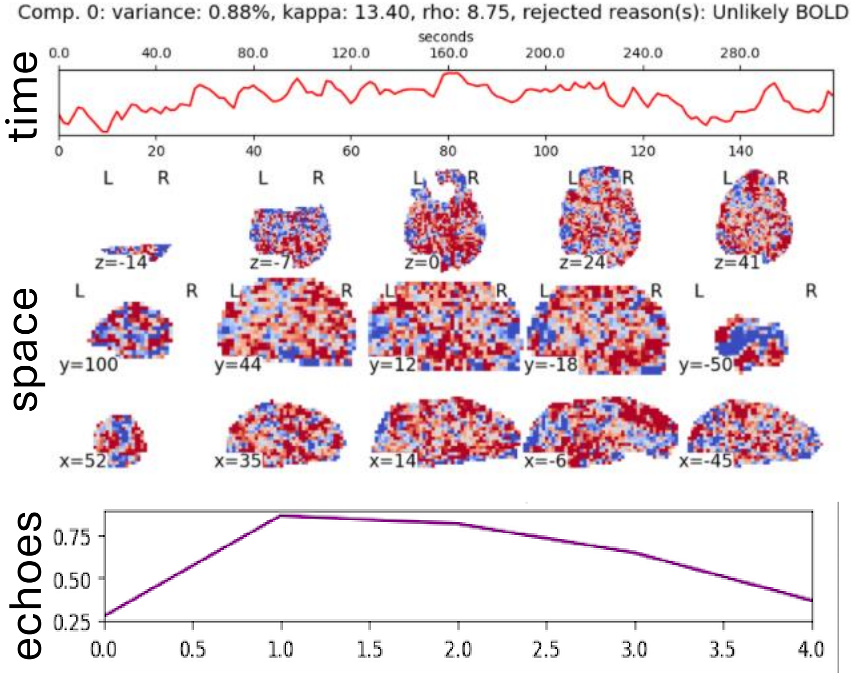


Potentially useful across echoes

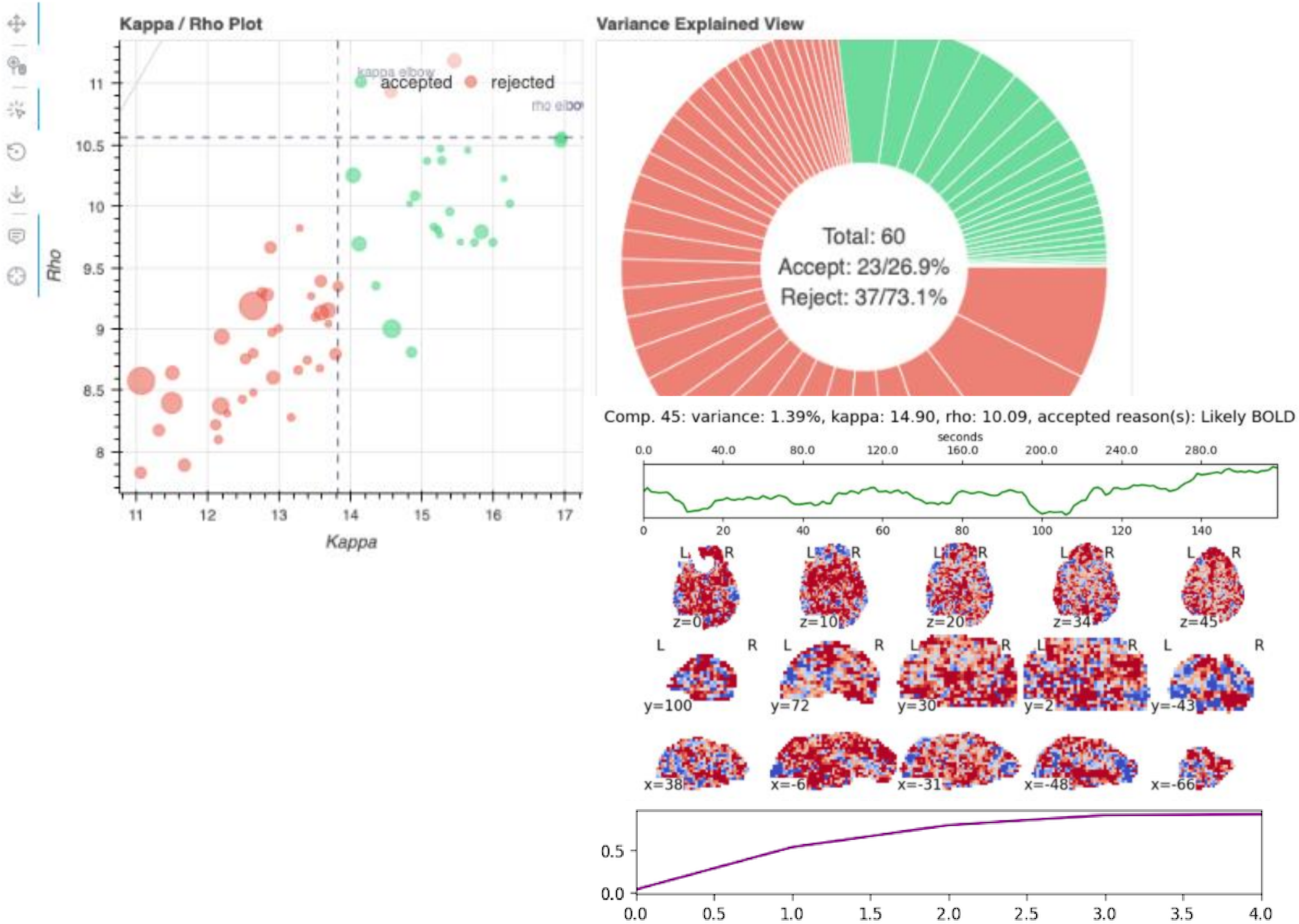
https://www.youtube.com/watch?v=V_ugq2iljxE

Tensorial ICA

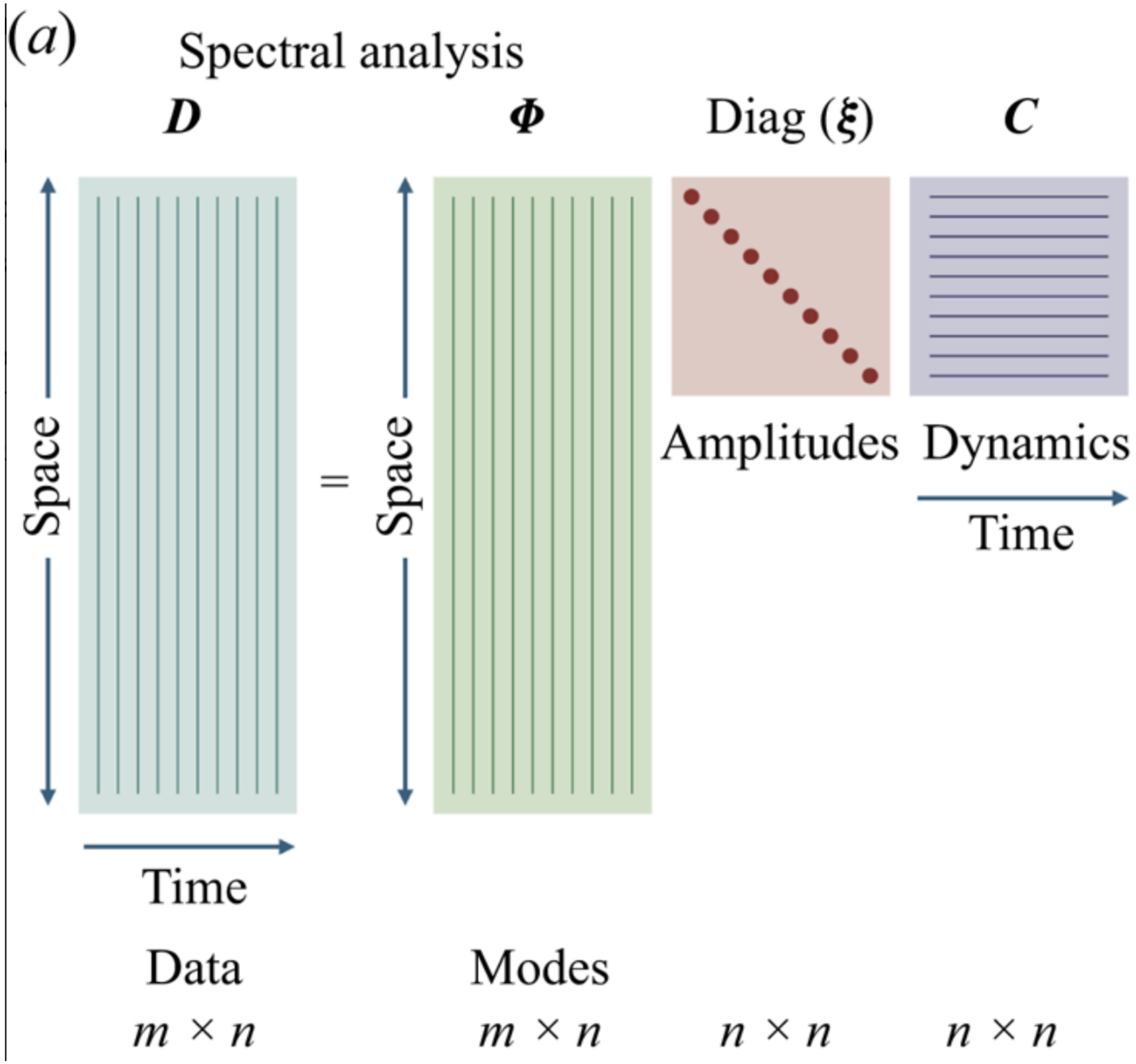
One mode (component)



ICA components



Dynamic Mode Decomposition

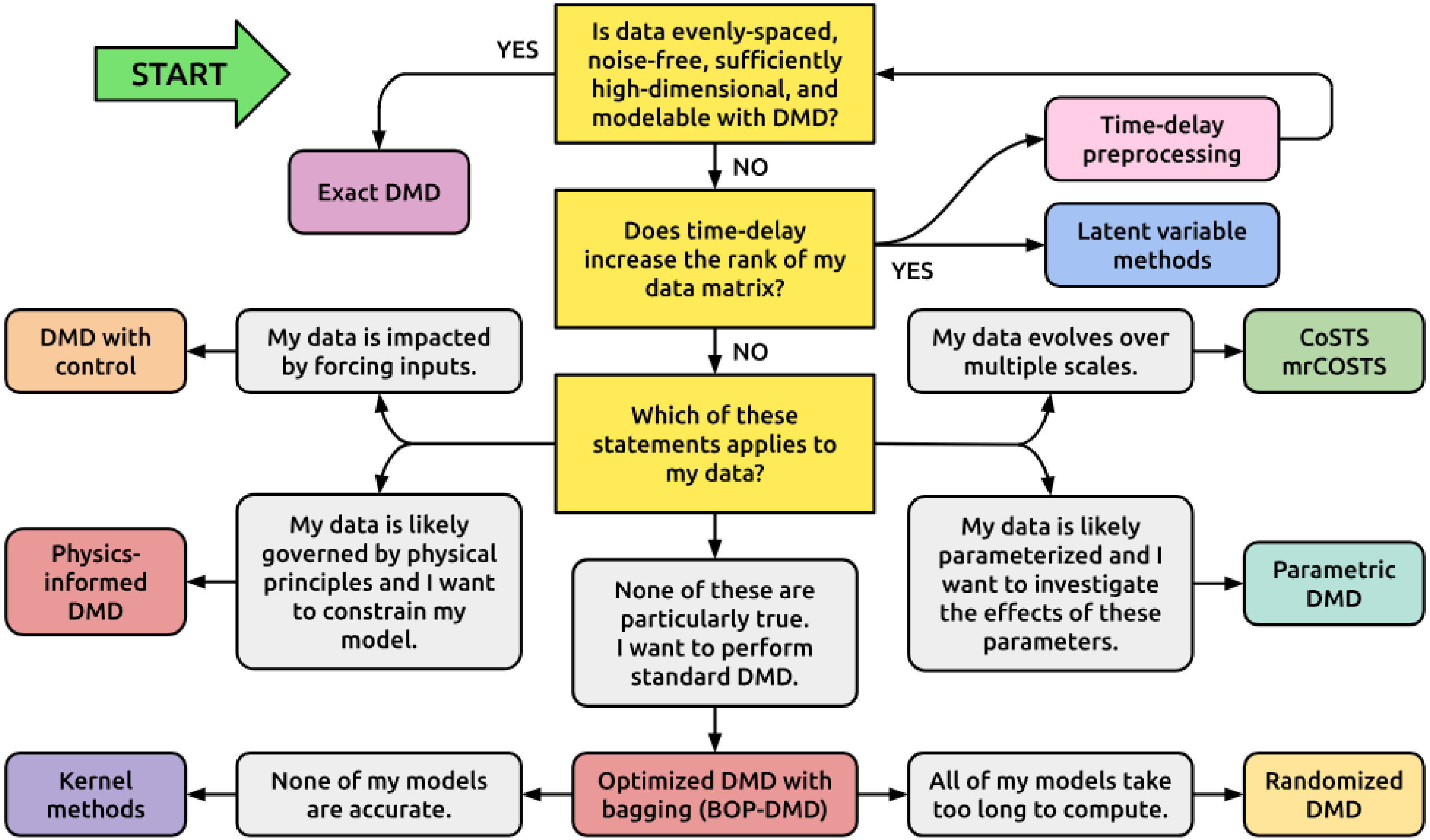


Dynamics is key, but how to define each can vary by data and goals

Also uses complex values which model phase and time delays

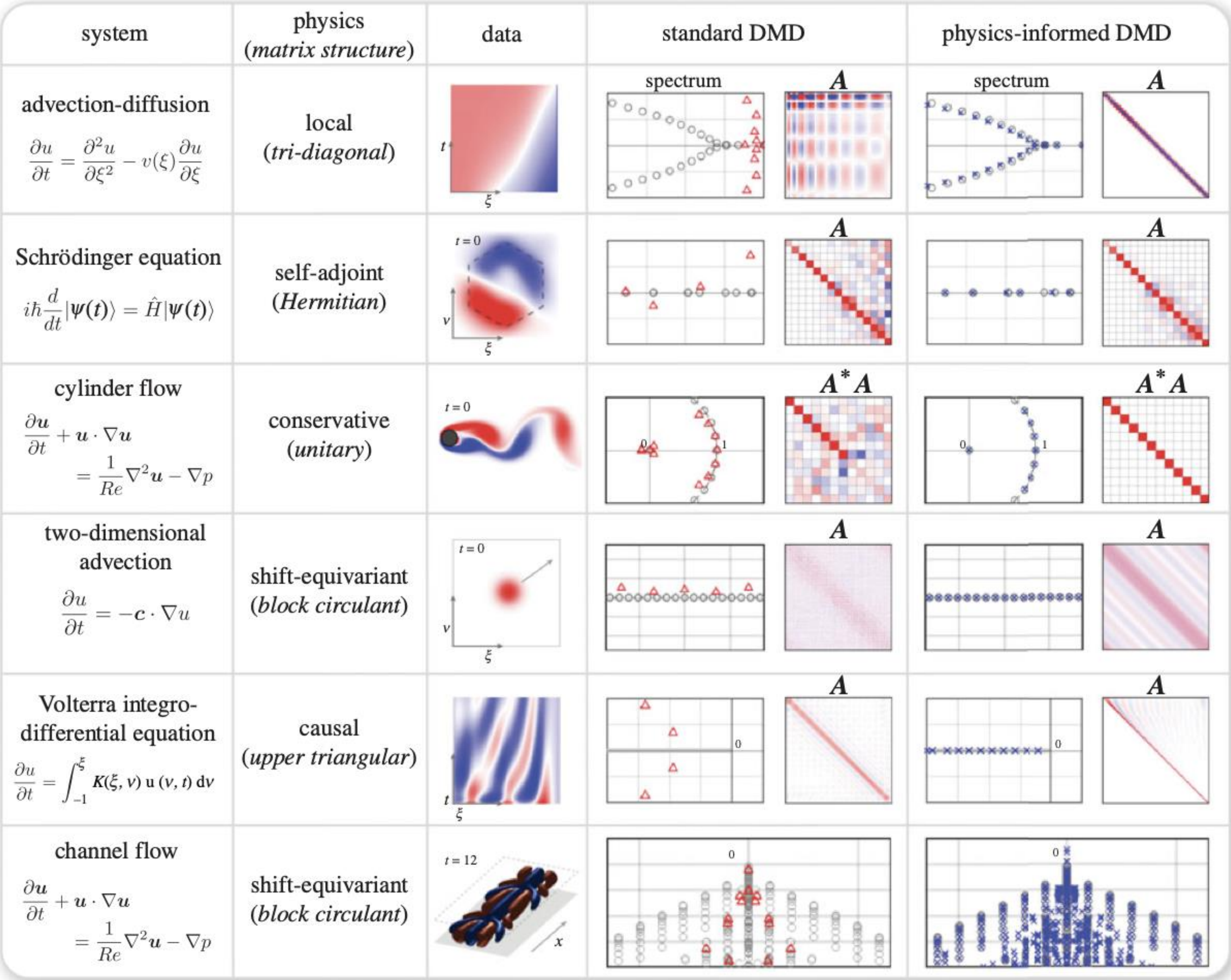
https://www.cambridge.org/core/journals/journal-of-fluid-mechanics/article/dynamic-mode-decomposition-for-analysis-of-timeseries-data/0C805EA6FDDE25CB823AFB8CC69B64AF

Many DMD options, but need to really understand application



https://github.com/PyDMD/PyDMD?tab=readme-ov-file

Physics informed DMD



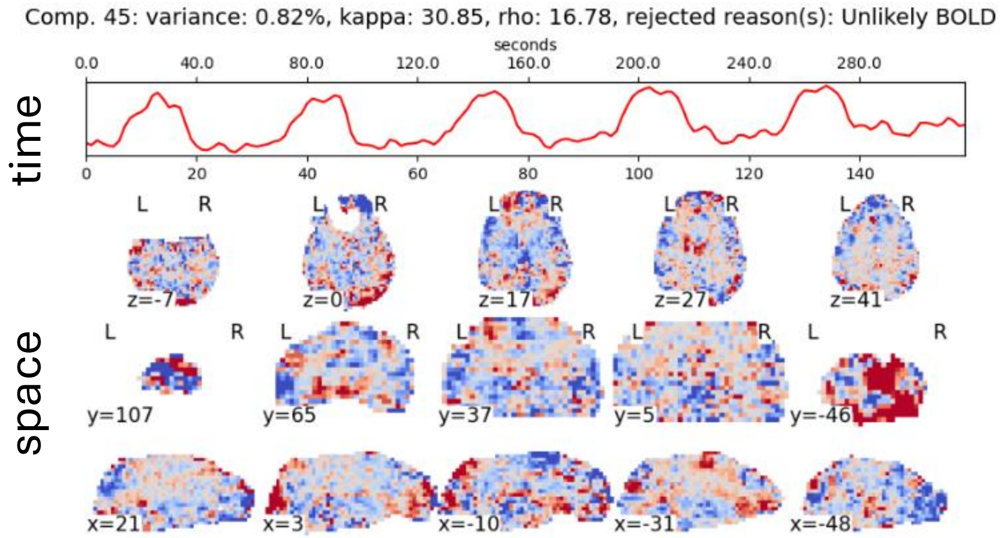
Sets up data in and set up equations to conform in particular ways.

Can we set up the dynamics to be modeled on known relationships across echoes?

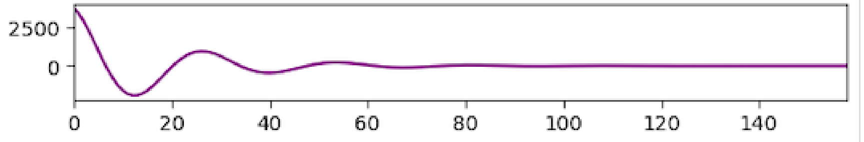
A test with Exact DMD

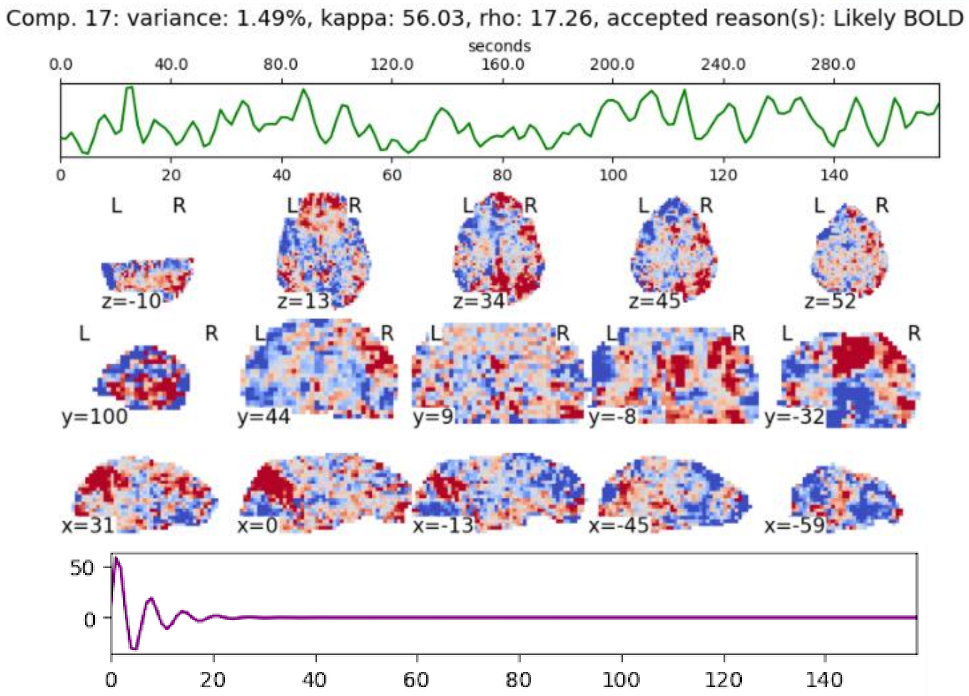
Modeling optimally combined data to same data one timepoint in the future

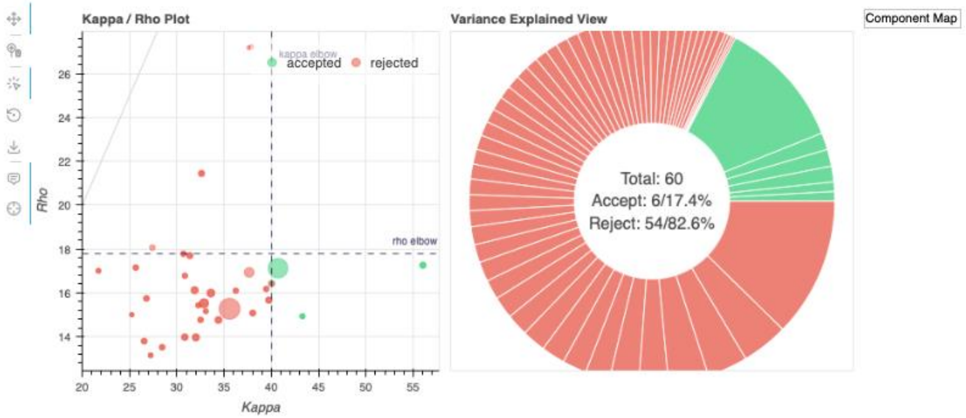
One mode



Time lagged relationship







Models some neurally related aspects of data, but currently worse kappa vs rho separation than ICA

Next steps

- Continuing to compile potential options for better methods
  - Try to understand the methods
  - Conduct tests of current and potential efficacy
- The properties of ICA give us nice pictures, but are statistically independent spatial maps really the best way to separate T2* and S0 signals.
- Potential for very different separation or clustering approaches?

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LBC Questions