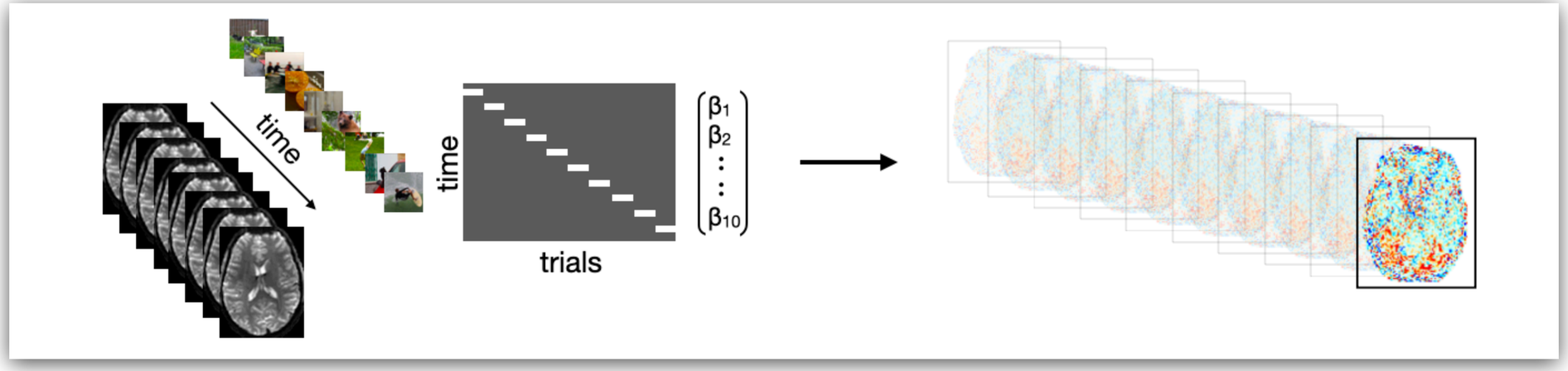
GLMsingle:

A toolbox for accurate single-trial fMRI response estimates



MIT BCS Computational Tutorial - April 2022

Jacob Prince, Ian Charest, Jan Kurzawski, John Pyles, Michael Tarr, Kendrick Kay

Overview

Why GLMsingle?

How does it work?

Demo!

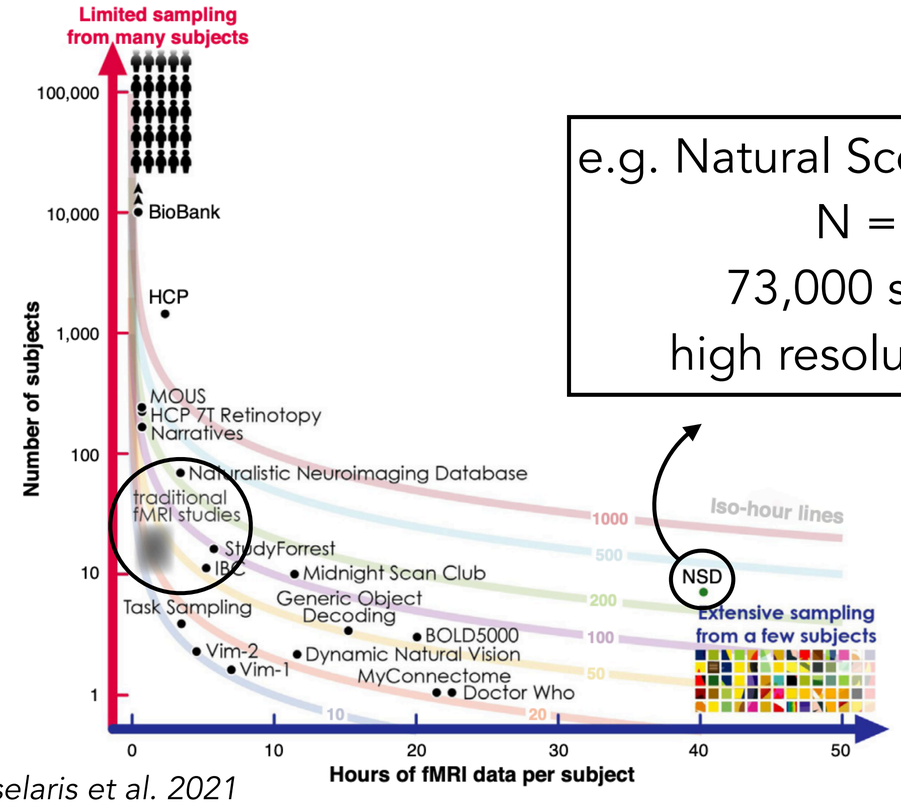
Implementation FAQ

Discussion

Why GLMsingle?

Paradigm shift toward data-hungry approaches…

Rapid increase in scale and depth of datasets…



Naselaris et al. 2021

e.g. Natural Scenes Dataset
N = 8
73,000 stimuli
high resolution (7T)

…reveal representational dimensions

…build encoding models

…characterize individual differences

…brain-constrained neural networks

…map cortical topography

…functional and structural conn

…investigate function of sub-cortex

…track developmental changes

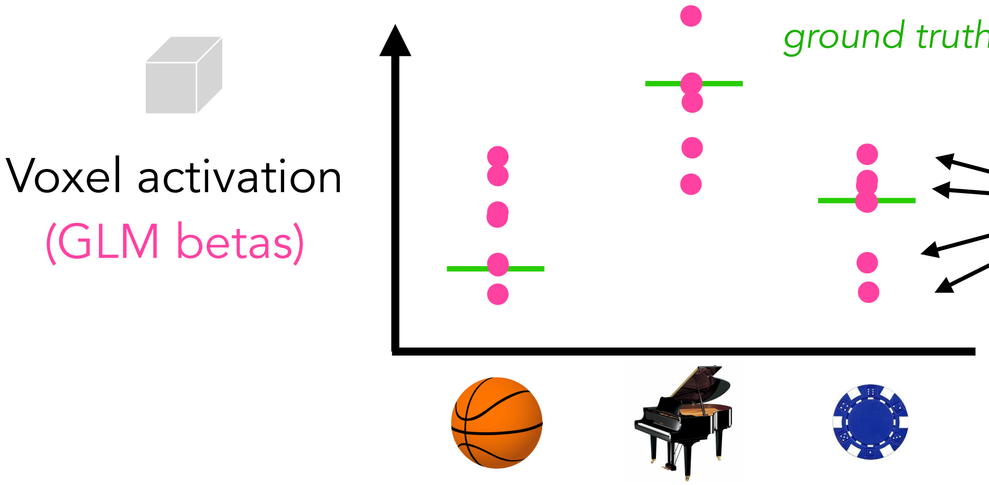
…cross-modal studies (fMRI, EEG, ECoG)

…develop new preprocessing + analysis methods

Noise is the fundamental limitation

Noise in fMRI signal estimation

Goal: general linear model (GLM) to estimate BOLD responses



variability in response estimates
over trial repetitions (noise)

many sources:

head motion

physiological noise

scanner noise

thermal noise

neural noise

…among others

condition-rich?

conditions per subject :(# repetitions per condition

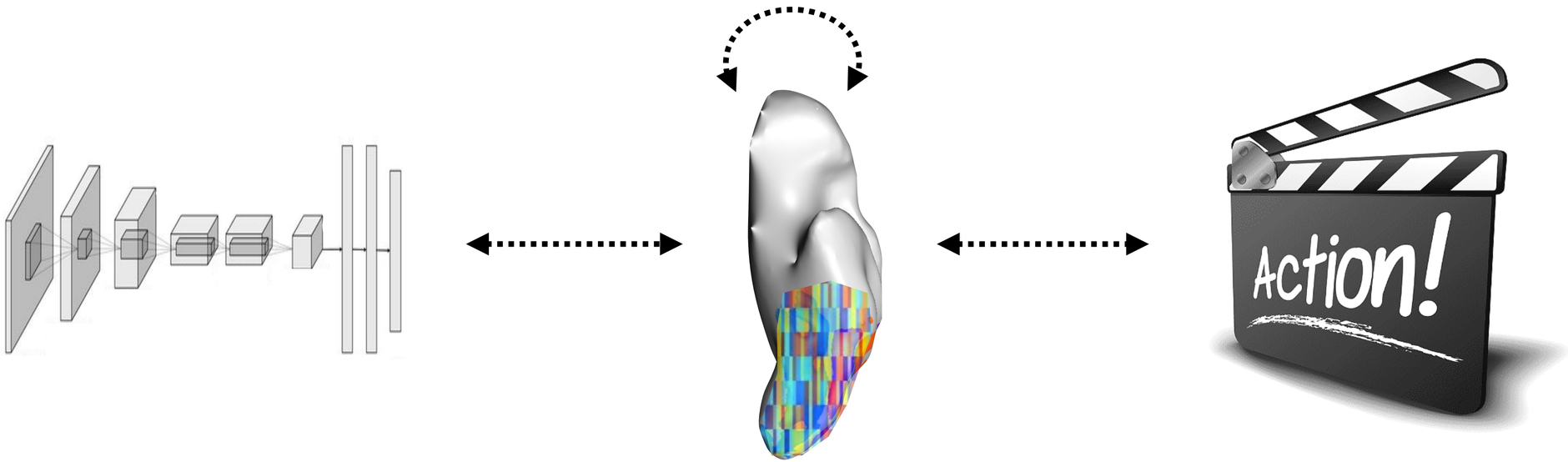
How can we combat noise to harness the potential of existing and future fMRI datasets?

How can we combat noise to harness the potential of existing and future fMRI datasets?

GLMsingle: a **flexible, data-driven** approach to denoising and signal estimation

Insight: noise structure **differs** between subjects, regions, voxels

Strategy: maximize data quality at level of **individual voxels** in **individual subjects**

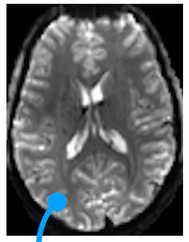


improving quality of signal estimates will positively impact downstream analysis outcomes

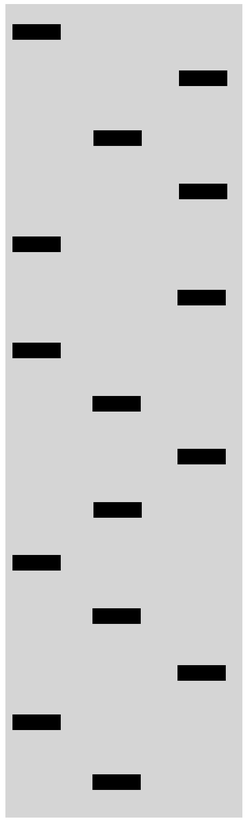
Estimating response amplitudes using GLMs

Goal: describe data from each voxel (Y) as linear combination of regressors (X)

coefficients (beta) reflect activation magnitude



time

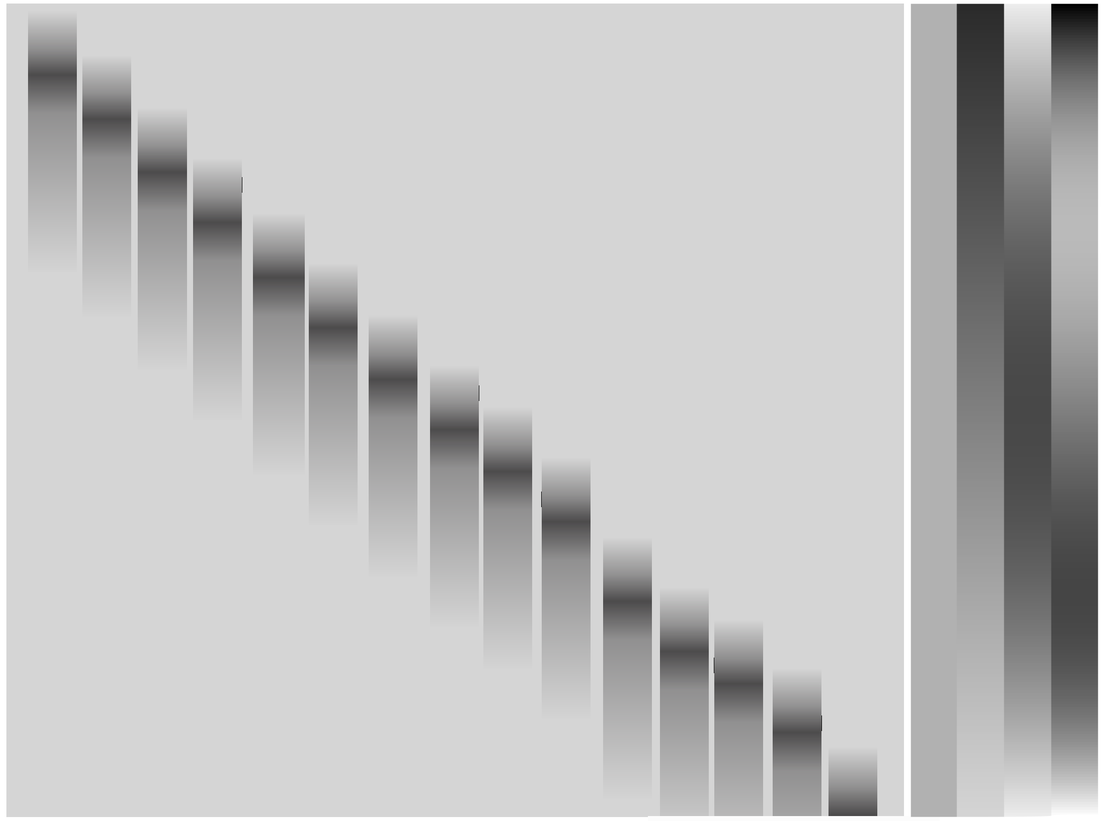


"single-trial":
one beta per trial

conditions

β_1 β_2 β_3 β_4 β_5 β_6 β_7 β_8 β_9 β_{10} β_{11} β_{12} β_{13} β_{14} β_{15} β β β β

time



trials

convolve

hemodynamic response function (HRF)

nuisance regressors

Inputs to GLMsingle:
fMRI time series and
trial onset matrix

Event-related, block,
& continuous designs
are compatible

Questions so far?

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How does GLMsingle work?

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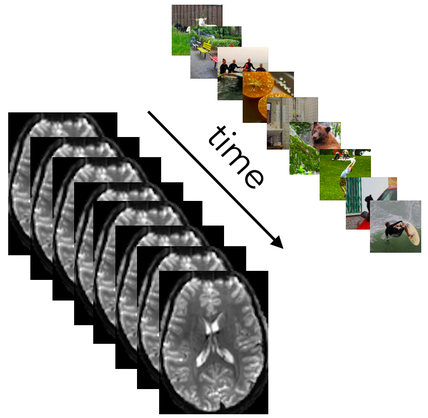

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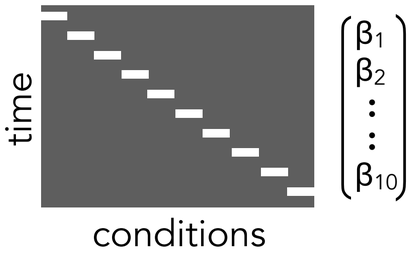
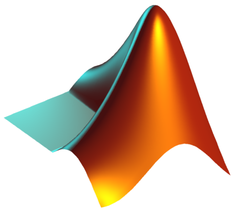
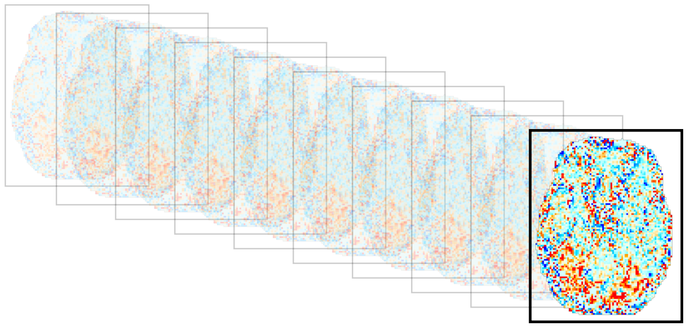




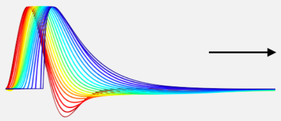
Outputs:

single-trial beta estimates



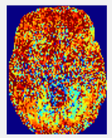
Library of HRFs

identify optimal HRF at each voxel



library of 20 HRFs

HRF indices

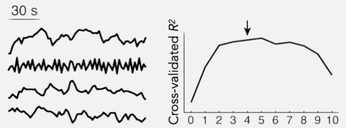


GLMdenoise

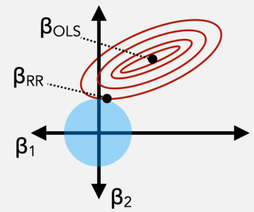
noise pool voxels

PCA

select number of noise regressors

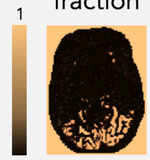


Fractional Ridge Regression



custom regularization at each voxel

shrinkage fraction



$$\frac{\| \beta_{RR} \|_2}{\| \beta_{OLS} \|_2}$$

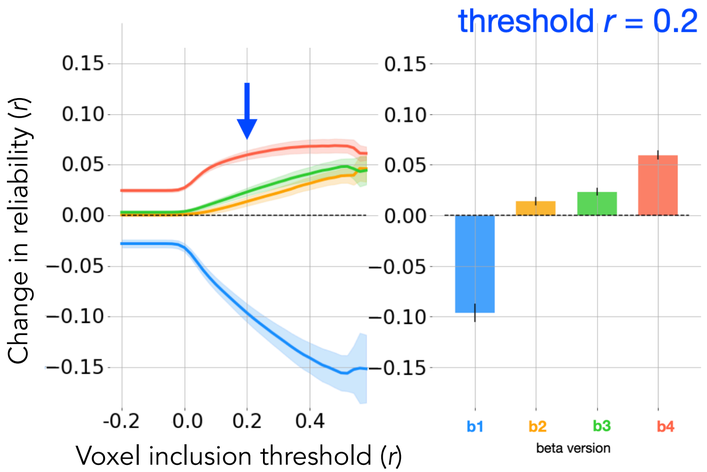
each procedure tackles a different component of the signal estimation pipeline

…can be turned on/off easily if the user desires…

Baseline GLM (b1)
GLMsingle (b4)

What is the downstream impact?

Improves reliability of response estimates



New Results

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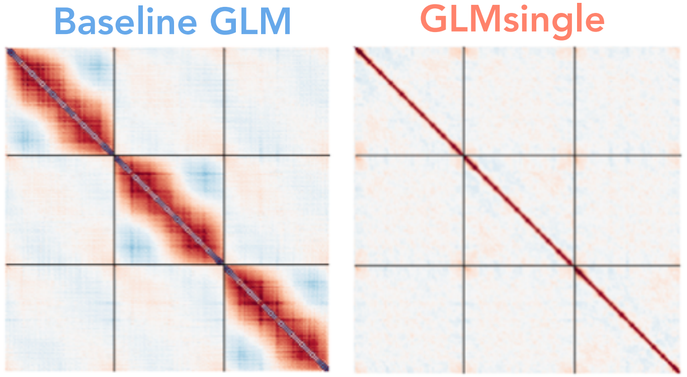
Jacob S. Prince, Ian Charest, Jan W. Kurzawski, John A. Pyles, Michael J. Tarr, Kendrick N. Kay

doi: https://doi.org/10.1101/2022.01.31.478431

This article is a preprint and has not been certified by peer review [what does this mean?].

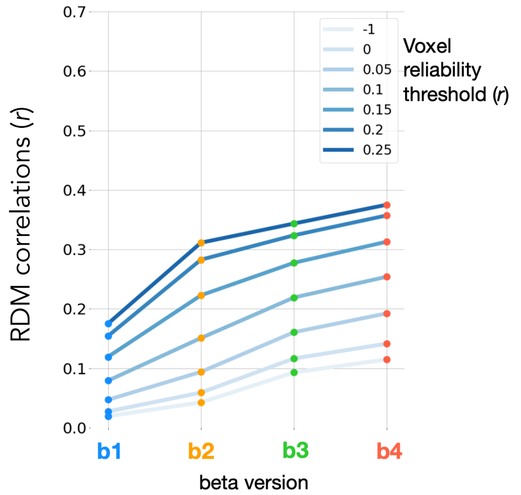
0 0 0 0 0 0 87

Reduces temporal autocorrelation

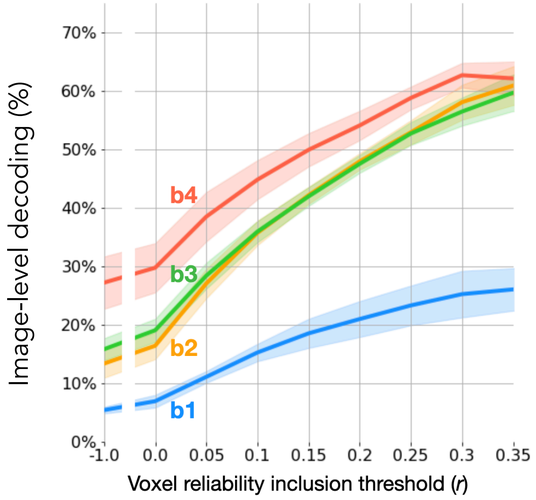


Mean temporal similarity (3 runs)

Enhances representational similarity between subjects



Improves decoding accuracy

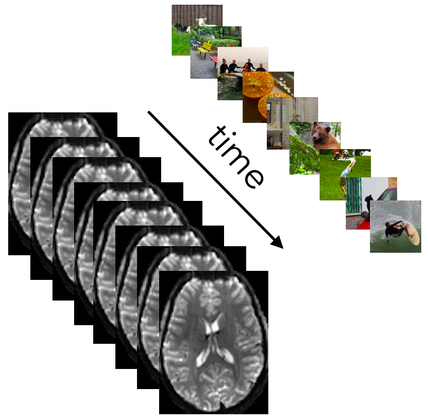


how does each component of GLMsingle work?

How does GLMsingle work?

Inputs:

fMRI time-series



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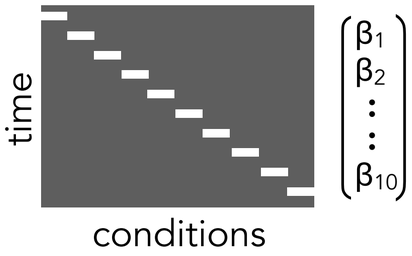

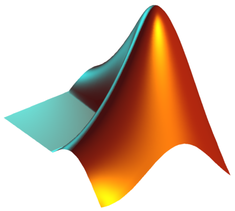

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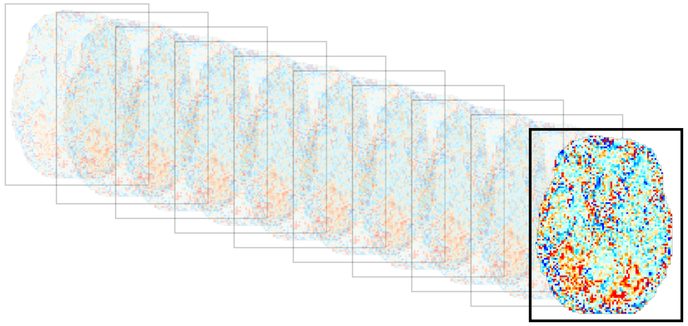
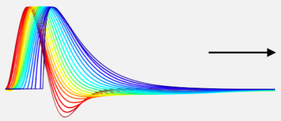


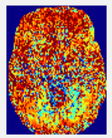
Library of HRFs

identify optimal HRF at each voxel



library of 20 HRFs

HRF indices

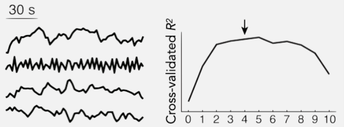


GLMdenoise

noise pool voxels

PCA

select number of noise regressors



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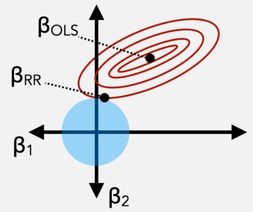


custom regularization at each voxel

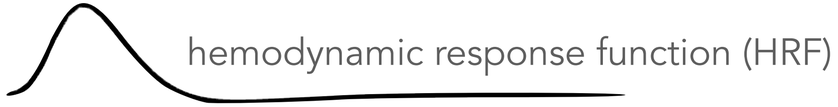
shrinkage fraction

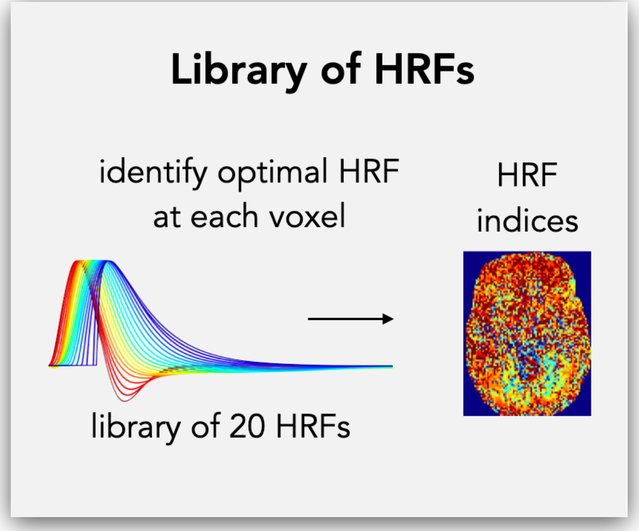
$$\frac{\| \beta_{RR} \|_2}{\| \beta_{OLS} \|_2}$$

each procedure tackles a different component of the signal estimation pipeline

Component #1: choice of HRF

Typical approach: assume same (canonical) HRF at each voxel





Problem: mis-modeling HRF can add noise to signal estimates

Insight: library approach relaxes assumption of canonical HRF at each voxel

Method: select an optimal HRF for each voxel

…iteratively fit input data using each candidate HRF

…for each voxel, inherit HRF with highest variance explained

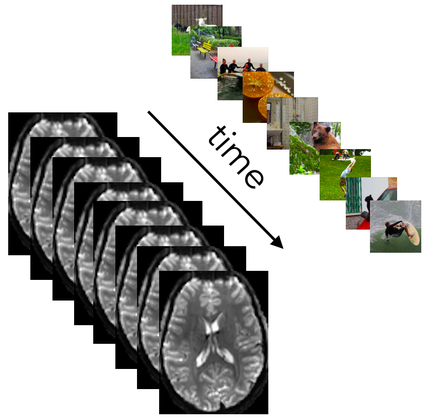
User can enable/disable, or add extra HRFs

questions?

How does GLMsingle work?

Inputs:

fMRI time-series



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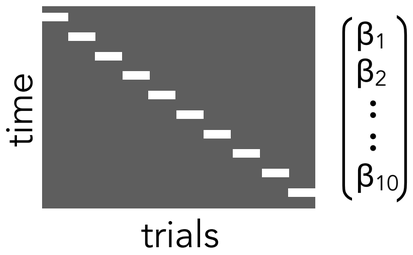

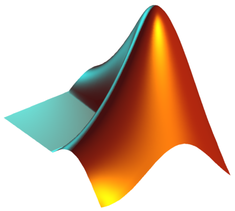

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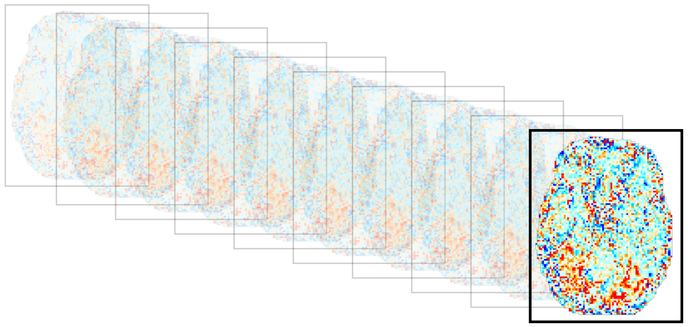

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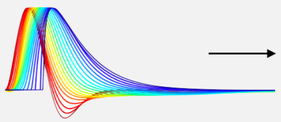
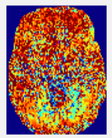


library of 20 HRFs

HRF indices

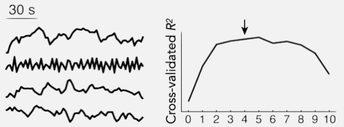


GLMdenoise

noise pool voxels

PCA

select number of noise regressors



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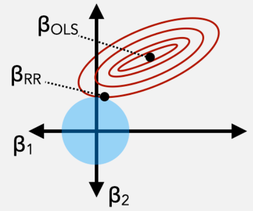


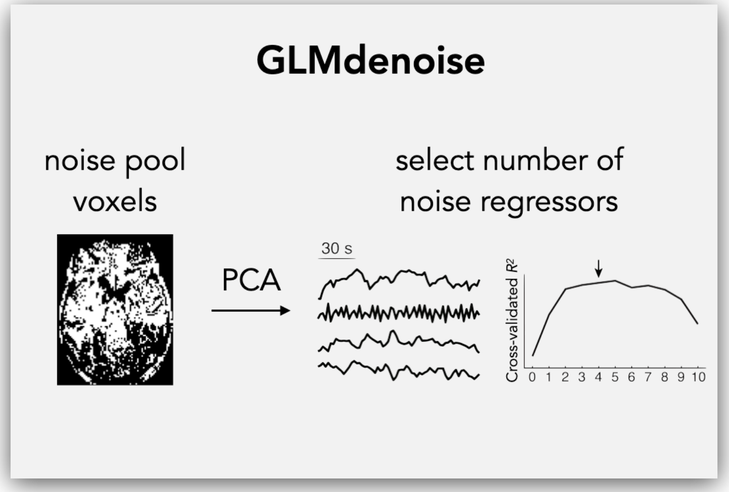
custom regularization at each voxel

shrinkage fraction

$$\frac{\| \beta_{RR} \|_2}{\| \beta_{OLS} \|_2}$$

each procedure tackles a different component of the signal estimation pipeline

Component #2: inclusion of nuisance regressors



Problem: data suffer from many sources of noise

Typical approach: include regressors capturing data fluctuations from skull, white matter, motion

Insight: directly model components of data likely to be noise

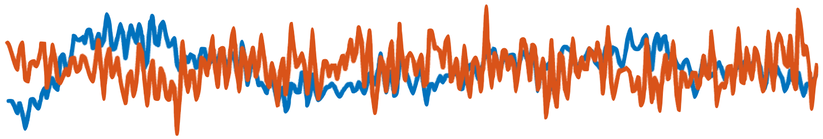
Method: derive optimal noise regressors using GLMdenoise *Kay et al., 2013*

…fit on-off GLM to identify parts of brain that are non-active (noise pool)

…apply PCA to time series data from noise pool voxels

…use cross-validation to iteratively include the top PCs as candidate noise regressors

…continue until variance explained is maximized



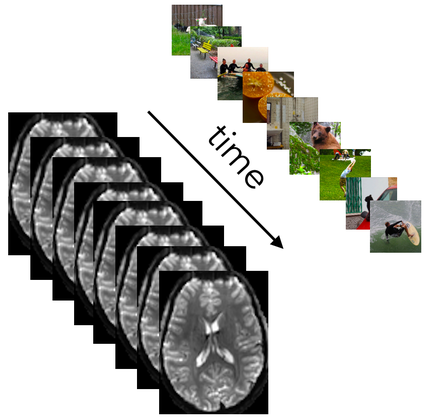
Outperforms other denoising techniques (Kay 2013); improves RSA/decoding outcomes (Charest 2018)

questions?

How does GLMsingle work?

Inputs:

fMRI time-series



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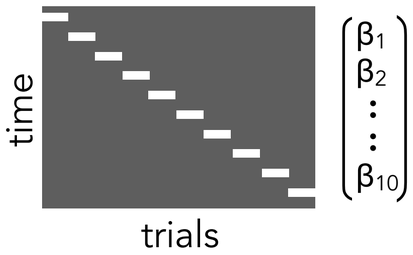

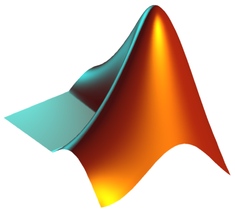

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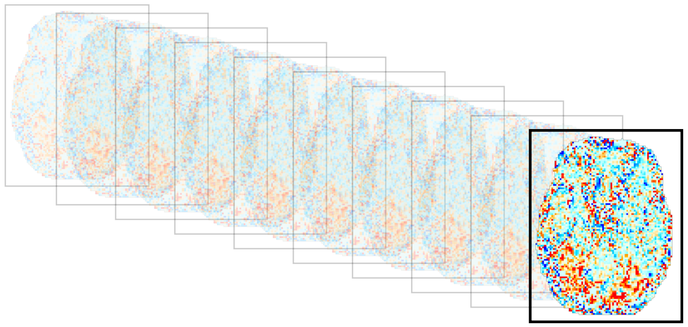

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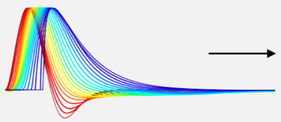
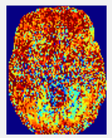


library of 20 HRFs

HRF indices



GLMdenoise

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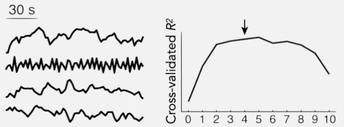

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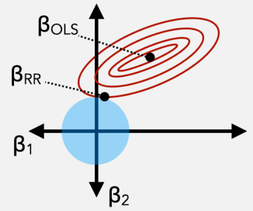

custom regularization at each voxel

shrinkage fraction

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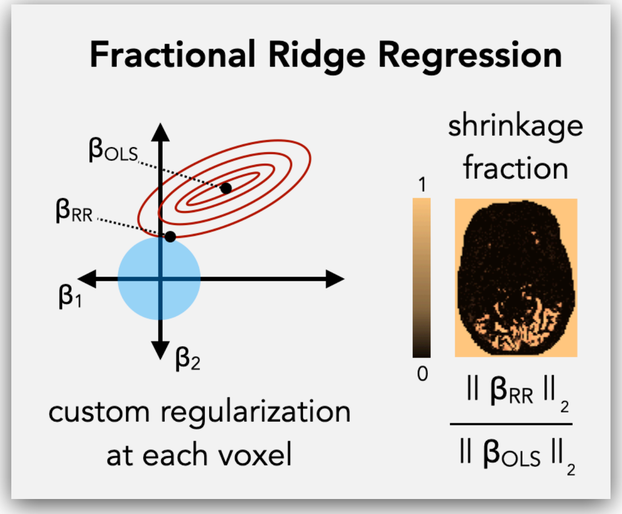
each procedure tackles a different component of the signal estimation pipeline

Component #3: response estimation (GLM fitting)

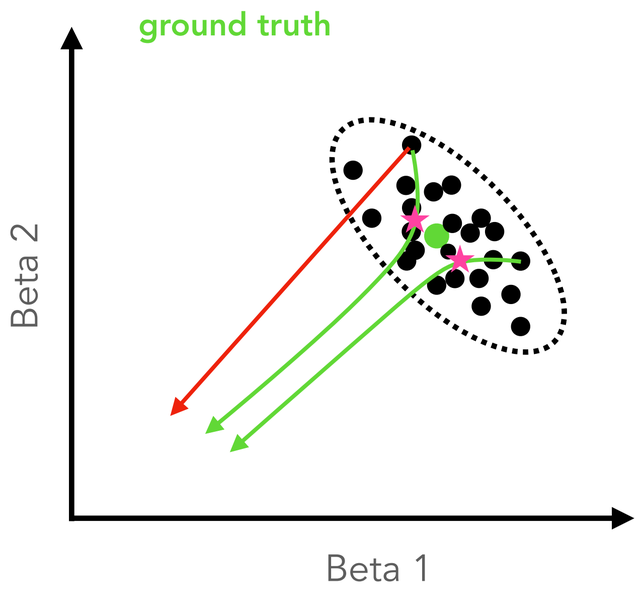


Typical approach: ordinary least squares (OLS) estimation

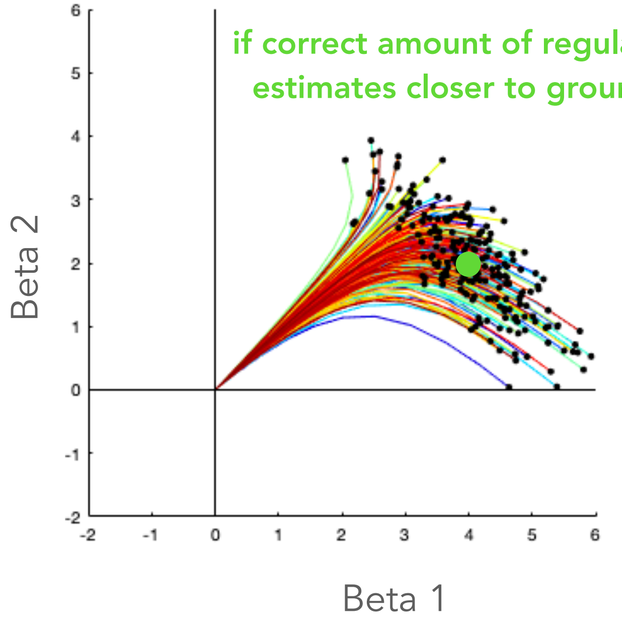
Problem: HRFs are slow (~30s) -> regression predictors overlap ->
ordinary least squares estimates are noisy due to multicollinearity

with correlated predictors, to minimize least squares: if one beta goes up, the other goes down (unstable)

OLS systematically mis-models brain responses



simulation: 200 experiments



Method: "fracridge" to efficiently learn optimal shrinkage value per voxel

Rokem and Kay, 2020

Provides a more effective sampling of different regularization levels than common approaches (e.g. grid search over log-spaced lambdas)

goal of regularization: shrink betas in a manner that biases toward ground truth

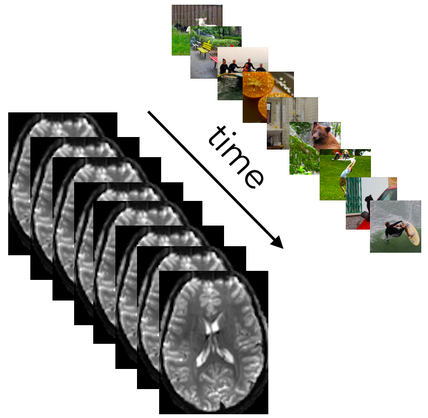
ridge regression with cross-validated shrinkage value achieves this!

questions?

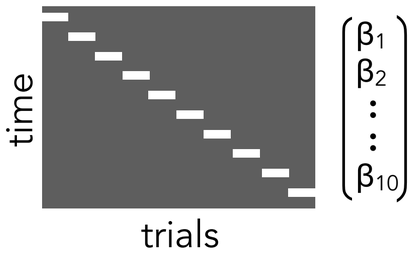
How does GLMsingle work?

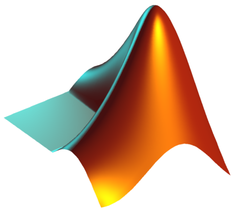
Inputs:

fMRI time-series



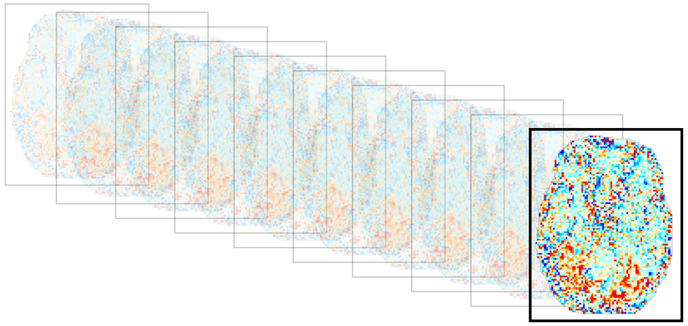
event matrix





Outputs:

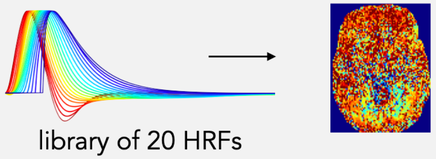
single-trial beta estimates



Library of HRFs

identify optimal HRF at each voxel

HRF indices



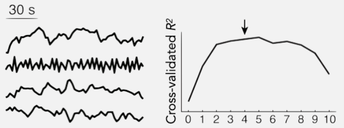
library of 20 HRFs

GLMdenoise

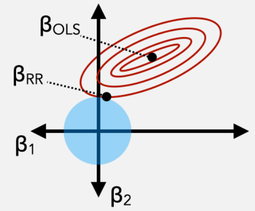
noise pool voxels

PCA

select number of noise regressors



Fractional Ridge Regression



custom regularization at each voxel

shrinkage fraction

$$\frac{\| \beta_{RR} \|_2}{\| \beta_{OLS} \|_2}$$

Overview

Why GLMsingle?

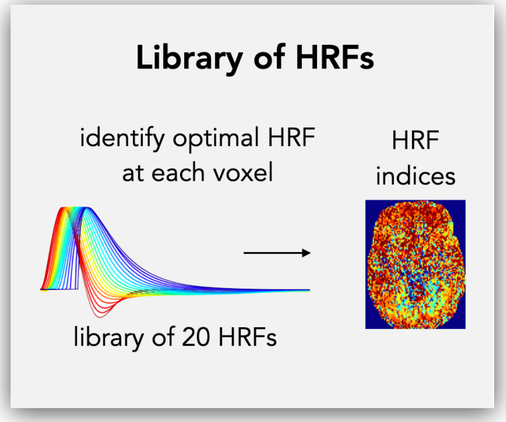
How does it work?

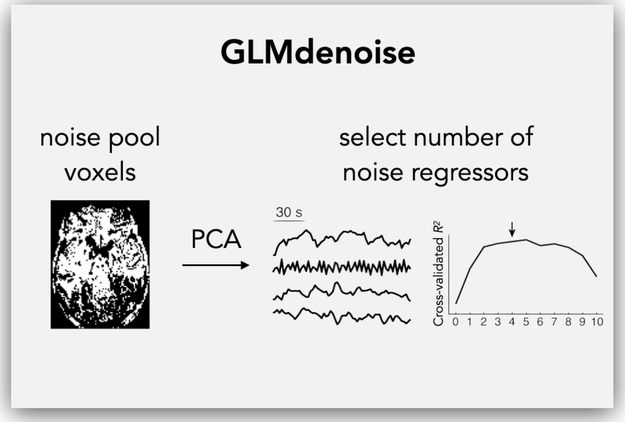
Demo!

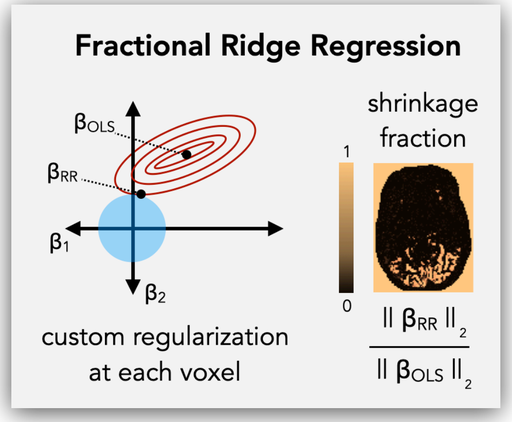
Implementation FAQ

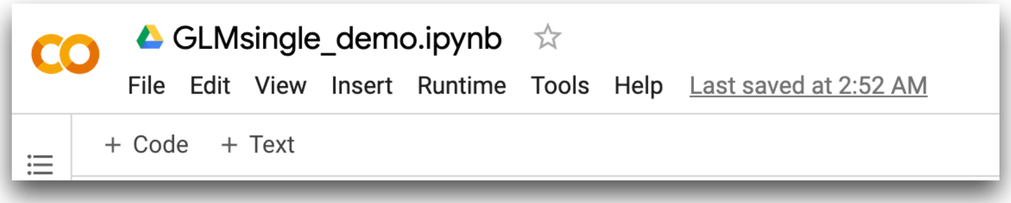
Discussion

GLMsingle Google Colab Demo





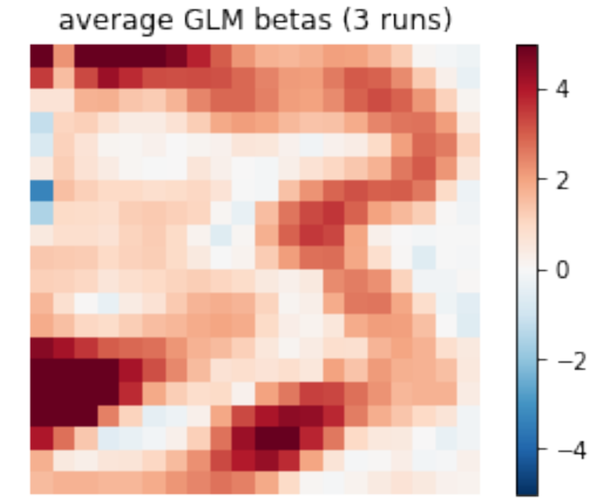


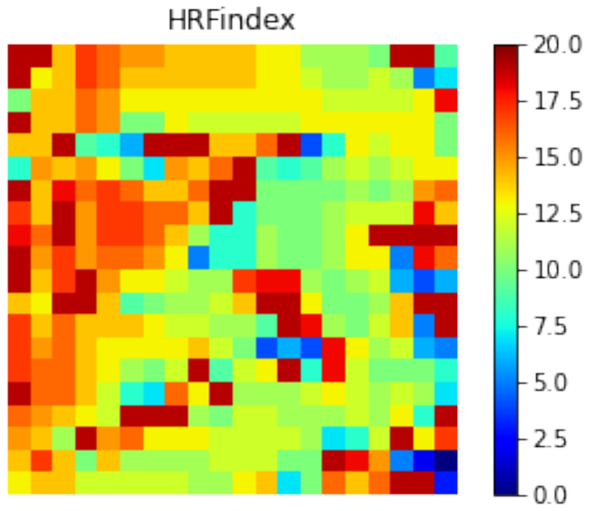


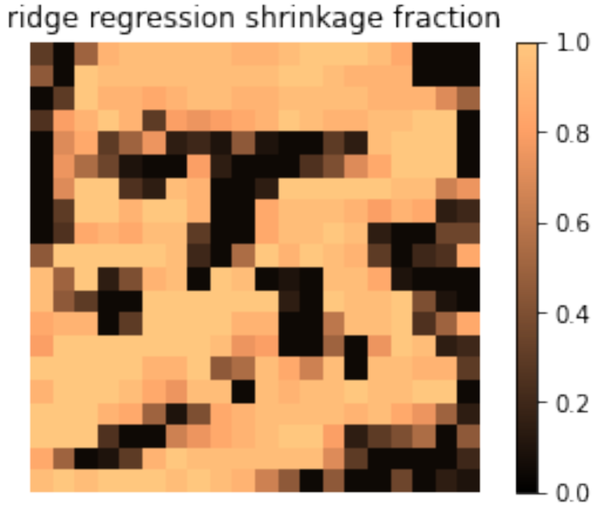
tinyurl.com/GLMsingle-demo

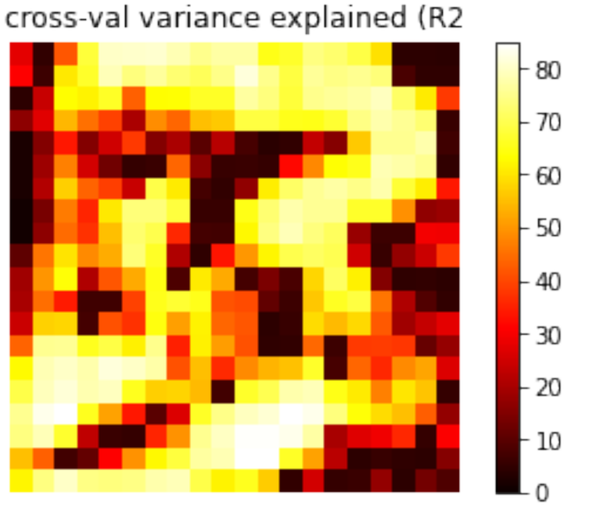
Click “File -> Save a copy in Drive”

How to interpret the GLMsingle figure outputs?









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Implementation FAQ

Which study designs are compatible with GLMsingle?

Event-related, block, continuous. No resting state.

How should fMRI time series be prepared?

Volumetric or surface data.

Motion, slice-time correction. No need for filtering.

Smoothing, registration are okay.

Why does GLMsingle expect condition repetitions?

Needed for x-val in GLMdenoise and fracridge.

More reps ideal, but not required.

Does GLMsingle fit with existing pipelines? (SPM, FSL, AFNI)

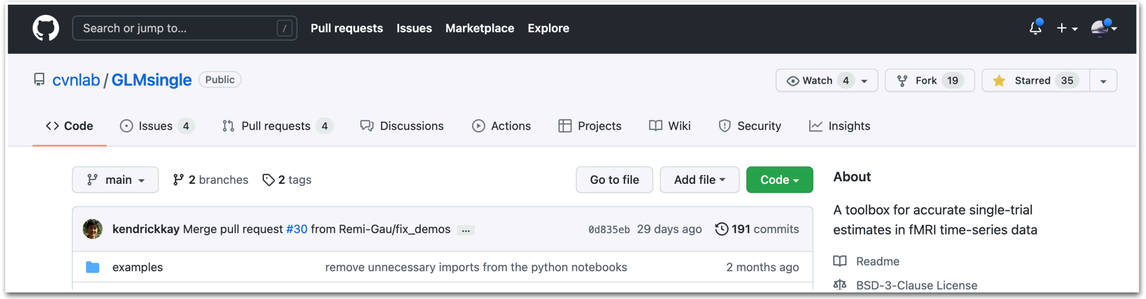
Could replace existing GLM components.

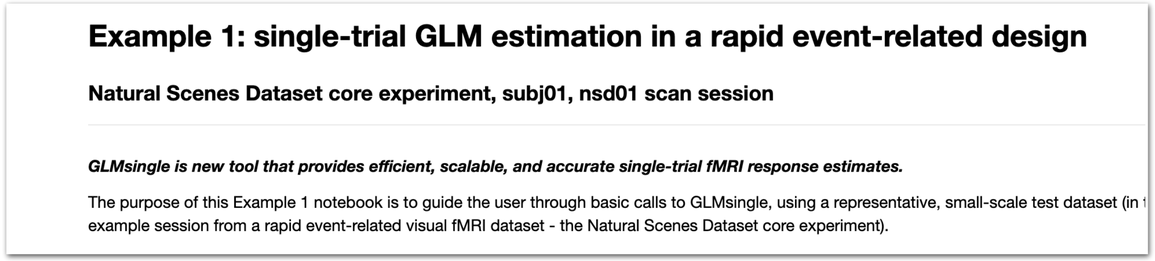
Or complement other preprocessing routines.

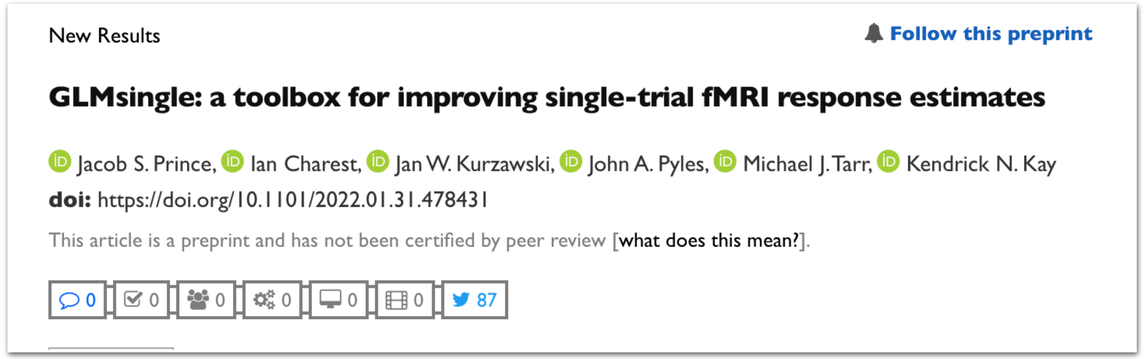
What if I only want certain components?

Easy, via hyperparameters.

What resources are available for users?







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Inputs:

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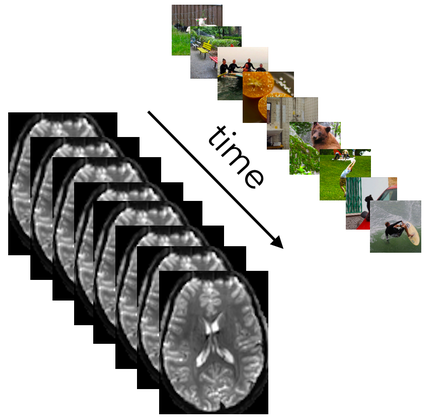

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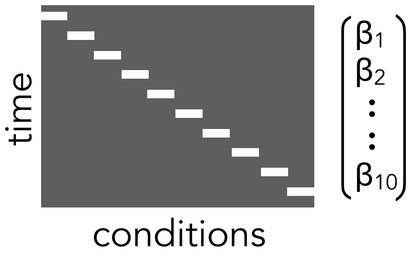

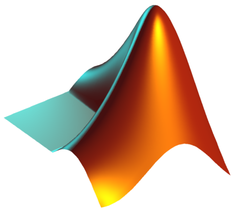

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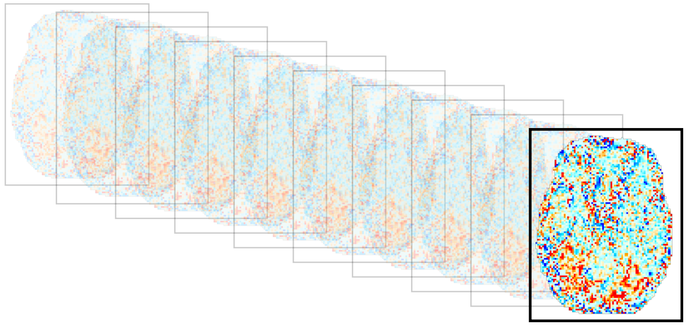
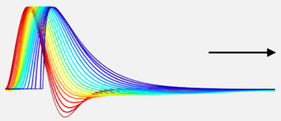


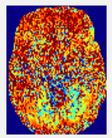
Library of HRFs

identify optimal HRF at each voxel



library of 20 HRFs

HRF indices

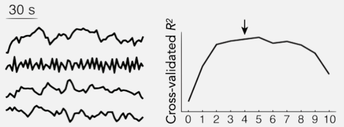


GLMdenoise

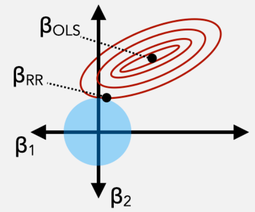
noise pool voxels

PCA

select number of noise regressors



Fractional Ridge Regression



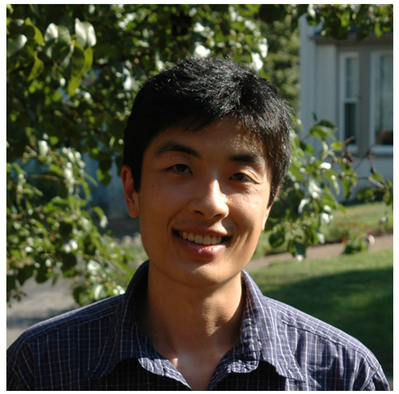
custom regularization at each voxel

shrinkage fraction

$$\frac{\| \beta_{RR} \|_2}{\| \beta_{OLS} \|_2}$$

each procedure tackles a different component of the signal estimation pipeline

Acknowledgements



Kendrick Kay
U. Minnesota

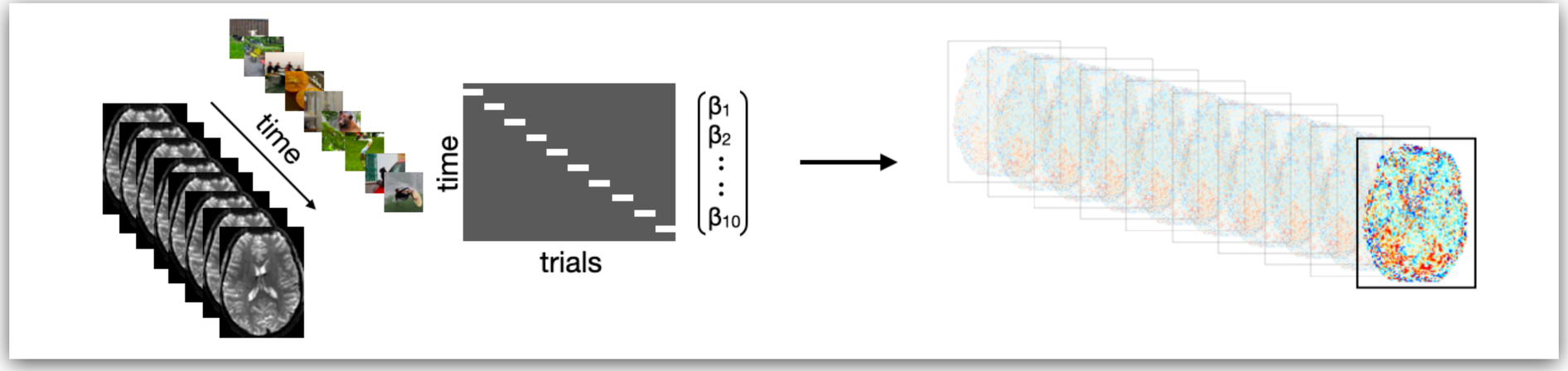
Ian Charest
U. of Montreal

Jan Kurzawski
NYU

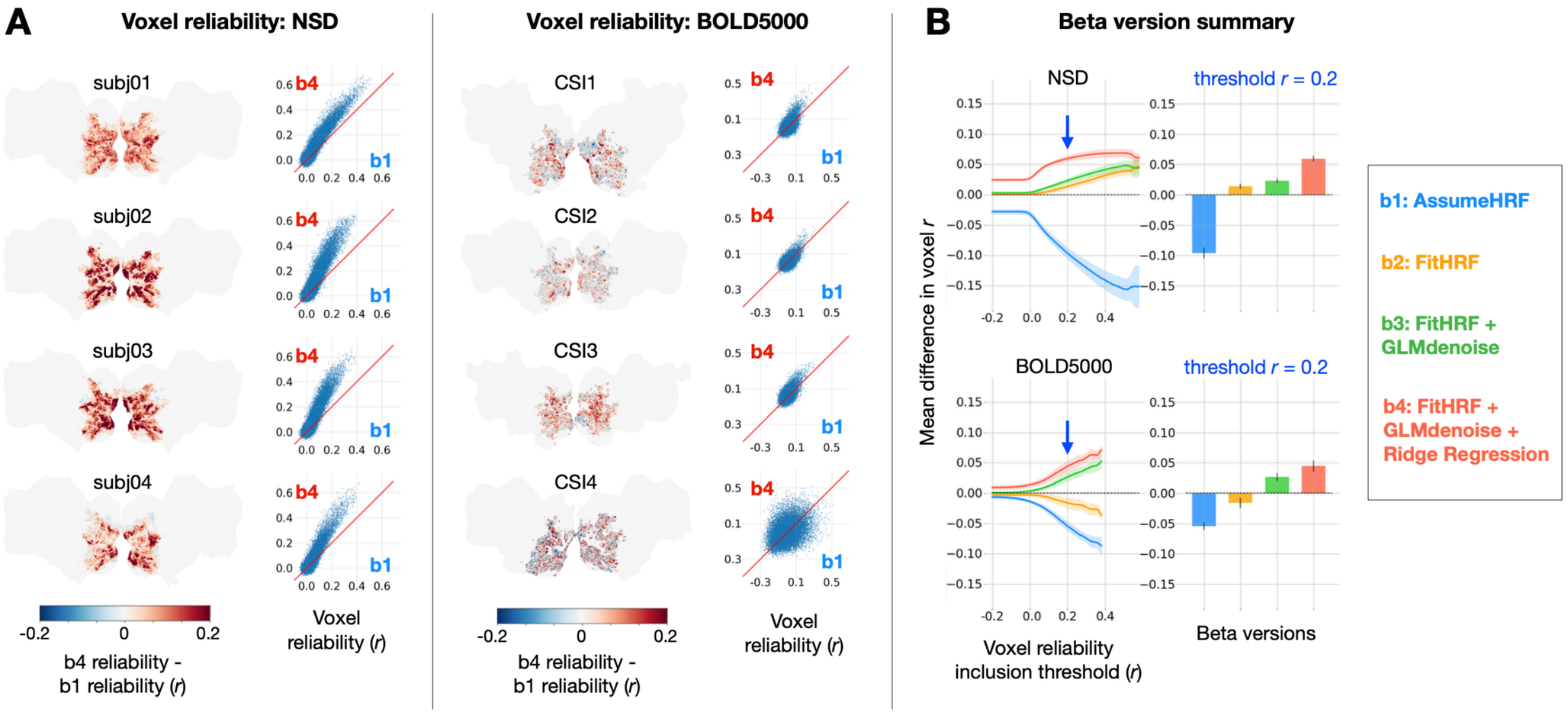
John Pyles
U. Washington

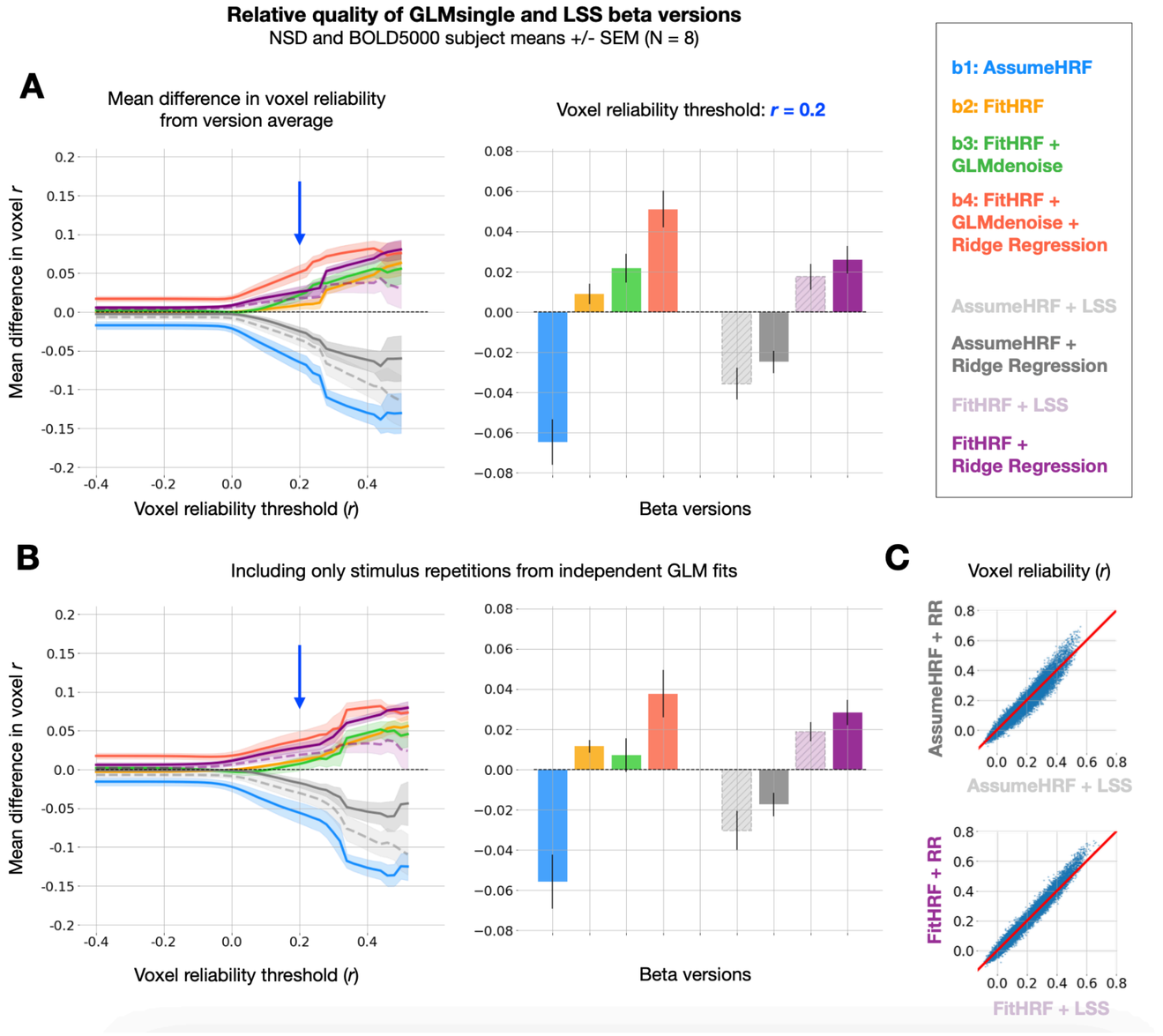
Mike Tarr
Carnegie Mellon

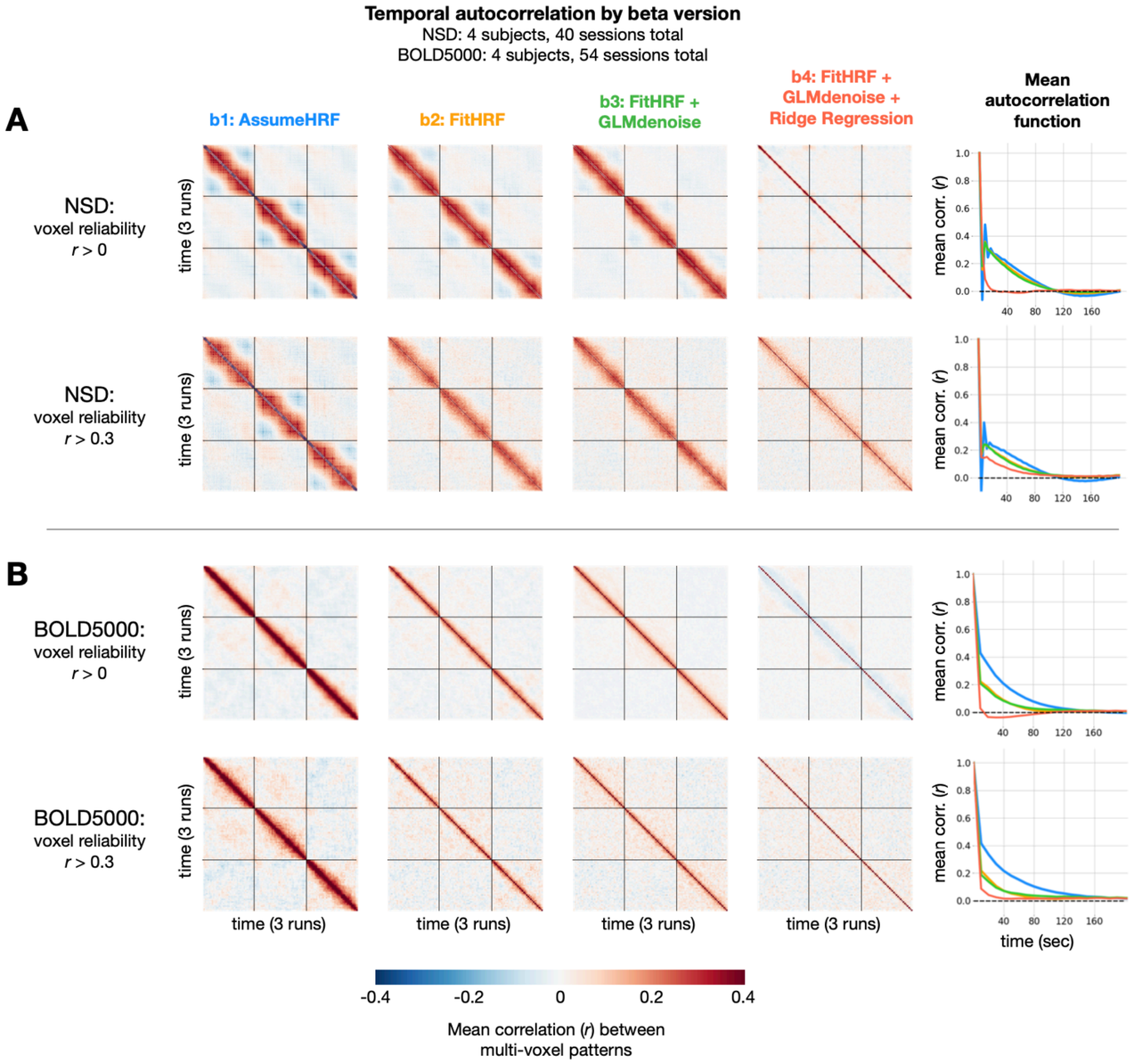
Thanks!

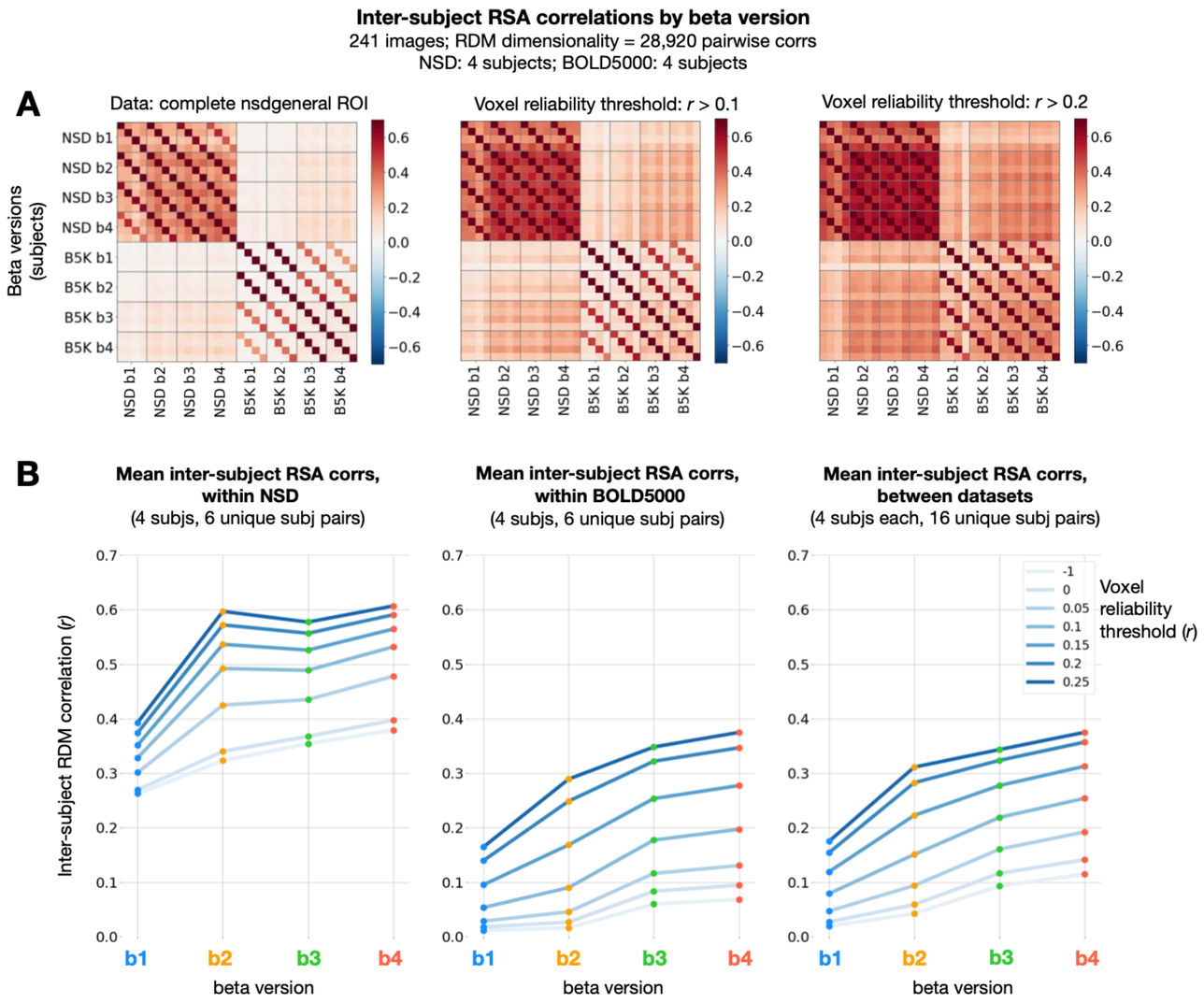


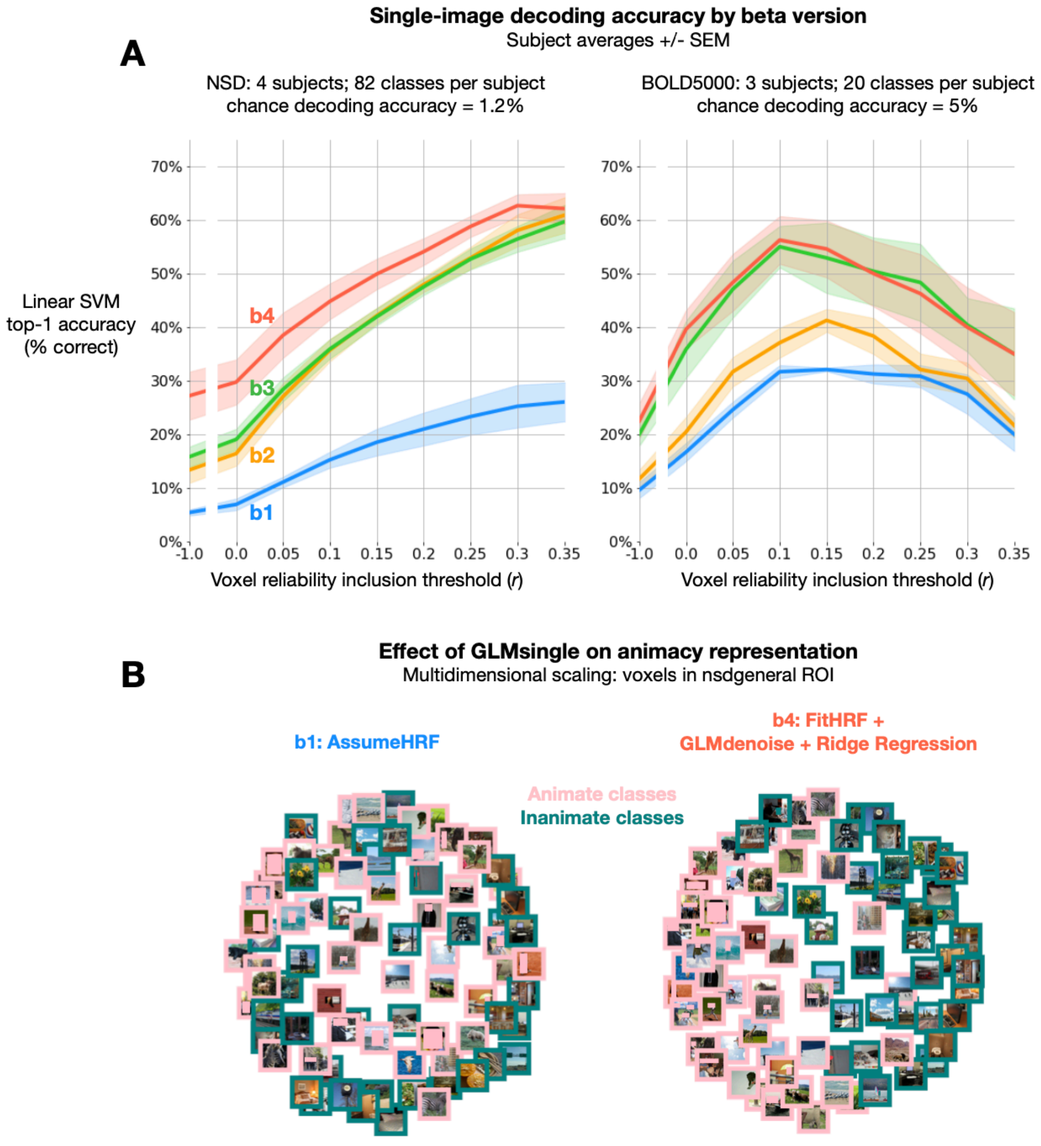
Supplementary slides


A
Voxel reliability: NSD
subj01
subj02
subj03
subj04
b4
b1
0.0 0.2 0.4 0.6
-0.2 0 0.2
b4 reliability - b1 reliability (r)
Voxel reliability (r)
Voxel reliability: BOLD5000
CSI1
CSI2
CSI3
CSI4
0.5 0.1 0.3
-0.3 0.1 0.5
B
Beta version summary
NSD
threshold r = 0.2
BOLD5000
Mean difference in voxel r
Voxel reliability inclusion threshold (r)
Beta versions
b1: AssumeHRF
b2: FitHRF
b3: FitHRF + GLMdenoise
b4: FitHRF + GLMdenoise + Ridge Regression


Relative quality of GLMsingle and LSS beta versions
NSD and BOLD5000 subject means +/- SEM (N = 8)
A
Mean difference in voxel reliability from version average
Mean difference in voxel r
Voxel reliability threshold (r)
Voxel reliability threshold: r = 0.2
Beta versions
b1: AssumeHRF
b2: FitHRF
b3: FitHRF + GLMdenoise
b4: FitHRF + GLMdenoise + Ridge Regression
AssumeHRF + LSS
AssumeHRF + Ridge Regression
FitHRF + LSS
FitHRF + Ridge Regression
B
Including only stimulus repetitions from independent GLM fits
C
Voxel reliability (r)
AssumeHRF + RR
AssumeHRF + LSS
FitHRF + RR
FitHRF + LSS


Temporal autocorrelation by beta version
NSD: 4 subjects, 40 sessions total
BOLD5000: 4 subjects, 54 sessions total
A
B
b1: AssumeHRF
b2: FitHRF
b3: FitHRF + GLMdenoise
b4: FitHRF + GLMdenoise + Ridge Regression
Mean autocorrelation function
NSD: voxel reliability r > 0
NSD: voxel reliability r > 0.3
BOLD5000: voxel reliability r > 0
BOLD5000: voxel reliability r > 0.3
time (3 runs)
mean corr. (r)
time (sec)
-0.4
-0.2
0
0.2
0.4
Mean correlation (r) between multi-voxel patterns


Inter-subject RSA correlations by beta version
241 images; RDM dimensionality = 28,920 pairwise corrs
NSD: 4 subjects; BOLD5000: 4 subjects
A
Data: complete nsdgeneral ROI
Voxel reliability threshold: r > 0.1
Voxel reliability threshold: r > 0.2
Beta versions (subjects)
NSD b1
NSD b2
NSD b3
NSD b4
B5K b1
B5K b2
B5K b3
B5K b4
0.6
0.4
0.2
0.0
−0.2
−0.4
−0.6
B
Mean inter-subject RSA corrs, within NSD
(4 subjs, 6 unique subj pairs)
Mean inter-subject RSA corrs, within BOLD5000
(4 subjs, 6 unique subj pairs)
Mean inter-subject RSA corrs, between datasets
(4 subjs each, 16 unique subj pairs)
Inter-subject RDM correlation (r)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
b1
b2
b3
b4
beta version
-1
0
0.05
0.1
0.15
0.2
0.25
Voxel reliability threshold (r)


A
Single-image decoding accuracy by beta version
Subject averages +/- SEM
NSD: 4 subjects; 82 classes per subject
chance decoding accuracy = 1.2%
BOLD5000: 3 subjects; 20 classes per subject
chance decoding accuracy = 5%
Linear SVM
top-1 accuracy
(% correct)
70%
60%
50%
40%
30%
20%
10%
0%
b4
b3
b2
b1
-1.0 0.0 0.05 0.1 0.15 0.2 0.25 0.3 0.35
Voxel reliability inclusion threshold (r)
B
Effect of GLMsingle on animacy representation
Multidimensional scaling: voxels in nsdgeneral ROI
b1: AssumeHRF
b4: FitHRF +
GLMdenoise + Ridge Regression
Animate classes
Inanimate classes