fMRI Reproducibility in *R*

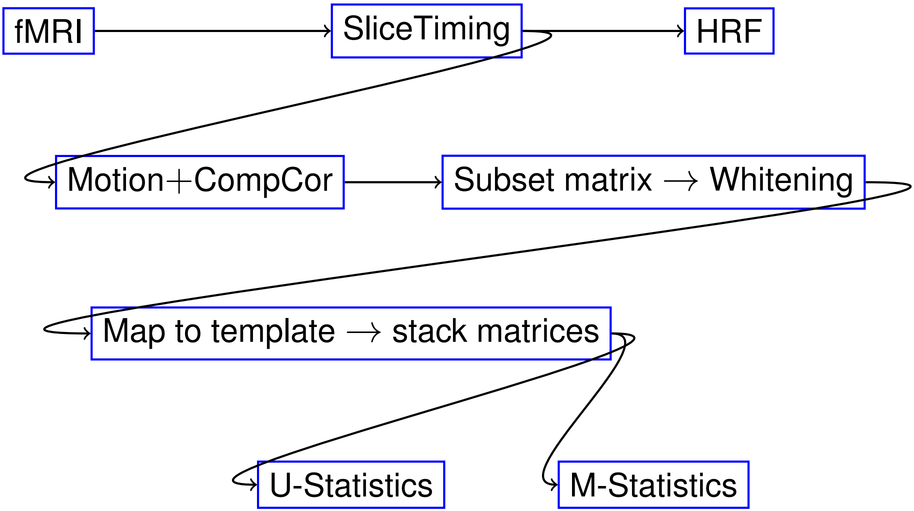
Brian B. Avants

PENN Image Computing & Science Laboratory
Dept. of Radiology, University of Pennsylvania
Philadelphia, PA, 19104 [1]

November 7, 2013

[1] for KRNS project

ANTsR group-wise fMRI: BOBO[2]



[2] processing based on bold only

Reproducibility Datasets

Dataset 1 : Gorgolewski n=10

Dataset 2 : Duncan n > 35

```
run1 <- rnorm(100)
run2 <- rnorm(100)
cor.test(run1, run2)


##
##  Pearson's product-moment correlation
##
## data:  run1 and run2
## t = -0.3046, df = 98, p-value = 0.7613
## alternative hypothesis: true correlation is not equal to 0
## 95 percent confidence interval:
##  -0.2258  0.1667
## sample estimates:
##       cor
## -0.03076
```

R Processing

Use *R* to test processing strategies for fMRI

- Pre-processing minimal connectome strategies
- Univariate: GLM with CompCor and ANTs motion correction.
- Multivariate: fMRI application of SCCAN
- Multi/Univariate use same pre-processing and includes outlier detection based on global signal.
- Employ a group-wise fixed effects analysis — requires mapping to a common template space.
- Template is BOLD and includes AAL neuroanatomical labels.

R Processing

Use *R* to test processing strategies for fMRI

- Pre-processing minimal connectome strategies
- Univariate: GLM with CompCor and ANTs motion correction.
- Multivariate: fMRI application of SCCAN
- Multi/Univariate use same pre-processing and includes outlier detection based on global signal.
- Employ a group-wise fixed effects analysis — requires mapping to a common template space.
- Template is BOLD and includes AAL neuroanatomical labels.

R Processing

Use *R* to test processing strategies for fMRI

- Pre-processing minimal connectome strategies
- Univariate: GLM with CompCor and ANTs motion correction.
- Multivariate: fMRI application of SCCAN
- Multi/Univariate use same pre-processing and includes outlier detection based on global signal.
- Employ a group-wise fixed effects analysis — requires mapping to a common template space.
- Template is BOLD and includes AAL neuroanatomical labels.

R Processing

Use *R* to test processing strategies for fMRI

- Pre-processing minimal connectome strategies
- Univariate: GLM with CompCor and ANTs motion correction.
- Multivariate: fMRI application of SCCAN
- Multi/Univariate use same pre-processing and includes outlier detection based on global signal.
- Employ a group-wise fixed effects analysis — requires mapping to a common template space.
- Template is BOLD and includes AAL neuroanatomical labels.

R Processing

Use *R* to test processing strategies for fMRI

- Pre-processing minimal connectome strategies
- Univariate: GLM with CompCor and ANTs motion correction.
- Multivariate: fMRI application of SCCAN
- Multi/Univariate use same pre-processing and includes outlier detection based on global signal.
- Employ a group-wise fixed effects analysis — requires mapping to a common template space.
- Template is BOLD and includes AAL neuroanatomical labels.

R Processing

Use *R* to test processing strategies for fMRI

- Pre-processing minimal connectome strategies
- Univariate: GLM with CompCor and ANTs motion correction.
- Multivariate: fMRI application of SCCAN
- Multi/Univariate use same pre-processing and includes outlier detection based on global signal.
- Employ a group-wise fixed effects analysis — requires mapping to a common template space.
- Template is BOLD and includes AAL neuroanatomical labels.

Signal Reproducibility Measurements

Validation Mechanisms

- Univar: Threshold statistical map consistently: ~~top x% of β map~~ $\rightarrow$ threshold at constant β = 1.5, 2.0, 2.5 .... across two different runs.
- Multivar: Measure spatial coincidence of sparse multivariate predictors across runs.
- Measure signal overlap (Dice) between clusters in thresholded beta map.
- ~~Minimum distance sum (MDS) between clusters in thresholded beta map between two runs~~

Prediction

Subject-level and group-wise feature selection followed by subject-specific prediction.

Signal Reproducibility Measurements

Validation Mechanisms

- Univar: Threshold statistical map consistently: ~~top x% of β map~~ $\rightarrow$ threshold at constant β = 1.5, 2.0, 2.5 .... across two different runs.
- Multivar: Measure spatial coincidence of sparse multivariate predictors across runs.
- Measure signal overlap (Dice) between clusters in thresholded beta map.
- ~~Minimum distance sum (MDS) between clusters in thresholded beta map between two runs~~

Prediction

Subject-level and group-wise feature selection followed by subject-specific prediction.

Signal Reproducibility Measurements

Validation Mechanisms

- Univar: Threshold statistical map consistently: ~~top x% of~~ $\cancel{\beta}$ ~~map~~ $\rightarrow$ threshold at constant β = 1.5, 2.0, 2.5 .... across two different runs.
- Multivar: Measure spatial coincidence of sparse multivariate predictors across runs.
- Measure signal overlap (Dice) between clusters in thresholded beta map.
- ~~Minimum distance sum (MDS) between clusters in thresholded beta map between two runs~~

Prediction

Subject-level and group-wise feature selection followed by subject-specific prediction.

Signal Reproducibility Measurements

Validation Mechanisms

- Univar: Threshold statistical map consistently: ~~top x% of β map~~ $\rightarrow$ threshold at constant β = 1.5, 2.0, 2.5 .... across two different runs.
- Multivar: Measure spatial coincidence of sparse multivariate predictors across runs.
- Measure signal overlap (Dice) between clusters in thresholded beta map.
- ~~Minimum distance sum (MDS) between clusters in thresholded beta map between two runs~~

Prediction

Subject-level and group-wise feature selection followed by subject-specific prediction.

Signal Reproducibility Measurements

Validation Mechanisms

- Univar: Threshold statistical map consistently: ~~top x% of~~ $\cancel{\beta}$ ~~map~~ $\rightarrow$ threshold at constant β = 1.5, 2.0, 2.5 .... across two different runs.
- Multivar: Measure spatial coincidence of sparse multivariate predictors across runs.
- Measure signal overlap (Dice) between clusters in thresholded beta map.
- ~~Minimum distance sum (MDS) between clusters in thresholded beta map between two runs~~

Prediction

Subject-level and group-wise feature selection followed by subject-specific prediction.

Analysis Scripts in RfMRI

- ants_2_template.sh — maps BOLD to template space.
- process_bold.R — bold processing for one run ... outputs hrf, matrices and (thresholded) beta maps
- After above steps, univar_multivar_fmri_consistency.sh produces group-wise reproducibility numbers.
- Models are of form: voxel $\approx$ hrf $+ motion1 + motion2 + motion3 + compcor1 + compcor2 + compcor3 + globalsignal +$ SubjectID
- Input data is the "stacked" matrix i.e. if we have n subjects, each with a $t \times p$ (time by space) matrix , then the input matrix for this study would be of size $nt \times p$.

Analysis Scripts in RfMRI

- ants_2_template.sh — maps BOLD to template space.
- process_bold.R — bold processing for one run ... outputs hrf, matrices and (thresholded) beta maps
- After above steps, univar_multivar_fmri_consistency.sh produces group-wise reproducibility numbers.
- Models are of form: voxel $\approx$ hrf $+ motion1 + motion2 + motion3 + compcor1 + compcor2 + compcor3 + globalsignal +$ SubjectID
- Input data is the "stacked" matrix i.e. if we have n subjects, each with a $t \times p$ (time by space) matrix , then the input matrix for this study would be of size $nt \times p$.

Analysis Scripts in RfMRI

- ants_2_template.sh — maps BOLD to template space.
- process_bold.R — bold processing for one run ... outputs hrf, matrices and (thresholded) beta maps
- After above steps, univar_multivar_fmri_consistency.sh produces group-wise reproducibility numbers.
- Models are of form: voxel $\approx$ hrf $+ motion1 + motion2 + motion3 + compcor1 + compcor2 + compcor3 + globalsignal +$ SubjectID
- Input data is the "stacked" matrix i.e. if we have n subjects, each with a $t \times p$ (time by space) matrix , then the input matrix for this study would be of size $nt \times p$.

Analysis Scripts in RfMRI

- ants_2_template.sh — maps BOLD to template space.
- process_bold.R — bold processing for one run ... outputs hrf, matrices and (thresholded) beta maps
- After above steps, univar_multivar_fmri_consistency.sh produces group-wise reproducibility numbers.
- Models are of form: voxel $\approx$ hrf $+ motion1 + motion2 + motion3 + compcor1 + compcor2 + compcor3 + globalsignal +$ SubjectID
- Input data is the "stacked" matrix i.e. if we have n subjects, each with a $t \times p$ (time by space) matrix , then the input matrix for this study would be of size $nt \times p$.

Analysis Scripts in RfMRI

- ants_2_template.sh — maps BOLD to template space.
- process_bold.R — bold processing for one run ... outputs hrf, matrices and (thresholded) beta maps
- After above steps, univar_multivar_fmri_consistency.sh produces group-wise reproducibility numbers.
- Models are of form: voxel $\approx$ hrf $+ motion1 + motion2 + motion3 + compcor1 + compcor2 + compcor3 + globalsignal +$ SubjectID
- Input data is the "stacked" matrix i.e. if we have n subjects, each with a $t \times p$ (time by space) matrix , then the input matrix for this study would be of size $nt \times p$.

Repeatability: Univariate

10 subjects

- Analyzed covert verb generation and finger tapping.
- Do β maps overlap? Depends on threshold and task.
- Finger tapping overlap: Max ≈ 0.4 at threshold Y.
- Covert verb: Less sensitive to threshold. Max ≈ 0.7 at threshold 2.

Repeatability: Univariate

10 subjects

- Analyzed covert verb generation and finger tapping.
- Do β maps overlap? Depends on threshold and task.
- Finger tapping overlap: Max ≈ 0.4 at threshold Y.
- Covert verb: Less sensitive to threshold. Max ≈ 0.7 at threshold 2.

Repeatability: Univariate

10 subjects

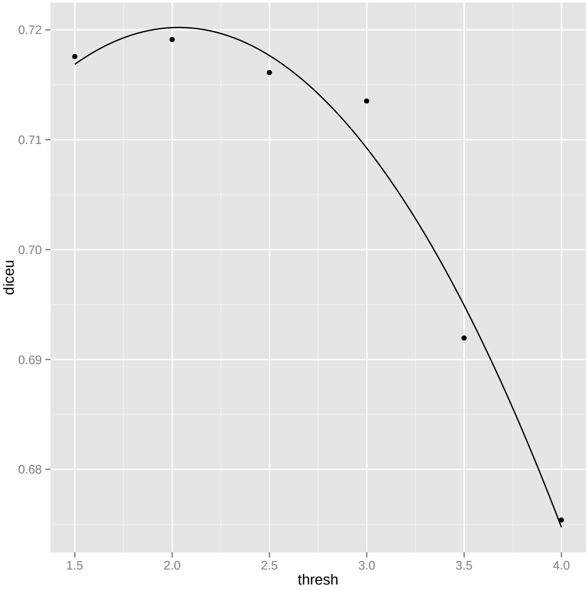
- Analyzed covert verb generation and finger tapping.
- Do β maps overlap? Depends on threshold and task.
- Finger tapping overlap: Max ≈ 0.4 at threshold Y.
- Covert verb: Less sensitive to threshold. Max ≈ 0.7 at threshold 2.

Repeatability: Univariate

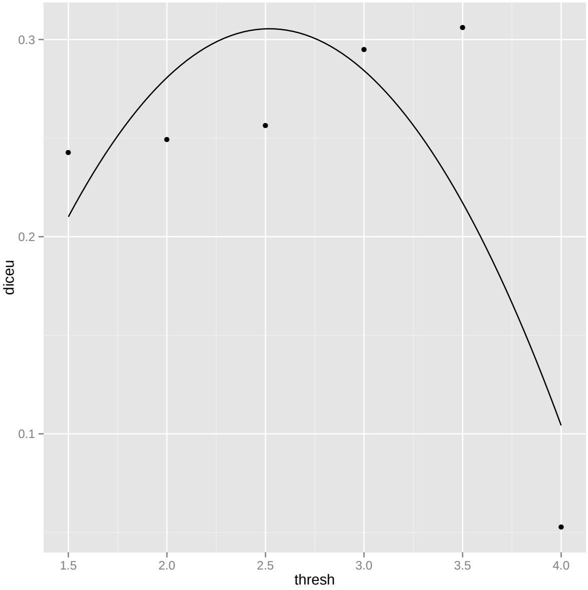
10 subjects

- Analyzed covert verb generation and finger tapping.
- Do β maps overlap? Depends on threshold and task.
- Finger tapping overlap: Max ≈ 0.4 at threshold Y.
- Covert verb: Less sensitive to threshold. Max ≈ 0.7 at threshold 2.

Univariate Overlap: Covert Verb



Univariate Overlap: Finger Tapping



Repeatability: Multivariate

10 subjects

- Analyzed covert verb generation and finger tapping.
- Do sparse-components overlap? Depends on threshold and task.
- A sparse component, u, maximizes
  $$\text{PearsonCorrelation}(Xu, \text{HRF}_{\text{model(s)}}v) - \omega\|u\|_1$$
  where we ℓ_1 penalize non-zero components of u and X is the BOLD matrix.
- Finger tapping overlap: "focal network," max ≈ 0.7 at threshold 2% of brain.
- Covert verb: "bigger network," max ≈ 0.8 at threshold 12% of brain.

Repeatability: Multivariate

10 subjects

- Analyzed covert verb generation and finger tapping.
- Do sparse-components overlap? Depends on threshold and task.
- A sparse component, u, maximizes
  $$\text{PearsonCorrelation}(Xu, \text{HRF}_{\text{model(s)}}v) - \omega\|u\|_1$$
  where we ℓ_1 penalize non-zero components of u and X is the BOLD matrix.
- Finger tapping overlap: "focal network," max ≈ 0.7 at threshold 2% of brain.
- Covert verb: "bigger network," max ≈ 0.8 at threshold 12% of brain.

Repeatability: Multivariate

10 subjects

- Analyzed covert verb generation and finger tapping.
- Do sparse-components overlap? Depends on threshold and task.
- A sparse component, u, maximizes
  $$\text{PearsonCorrelation}(Xu, \text{HRF}_{\text{model(s)}} v) - \omega \|u\|_1$$
  where we ℓ_1 penalize non-zero components of u and X is the BOLD matrix.
- Finger tapping overlap: "focal network," max ≈ 0.7 at threshold 2% of brain.
- Covert verb: "bigger network," max ≈ 0.8 at threshold 12% of brain.

Repeatability: Multivariate

10 subjects

- Analyzed covert verb generation and finger tapping.
- Do sparse-components overlap? Depends on threshold and task.
- A sparse component, u, maximizes

  $$\text{PearsonCorrelation}(Xu, \text{HRF}_{\text{model(s)}}v) - \omega\|u\|_1$$

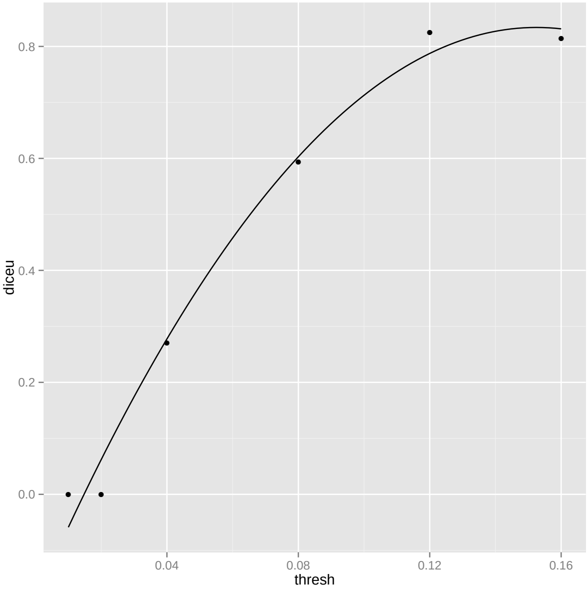
  where we ℓ_1 penalize non-zero components of u and X is the BOLD matrix.
- Finger tapping overlap: ”focal network,” max ≈ 0.7 at threshold 2% of brain.
- Covert verb: ”bigger network,” max ≈ 0.8 at threshold 12% of brain.

Repeatability: Multivariate

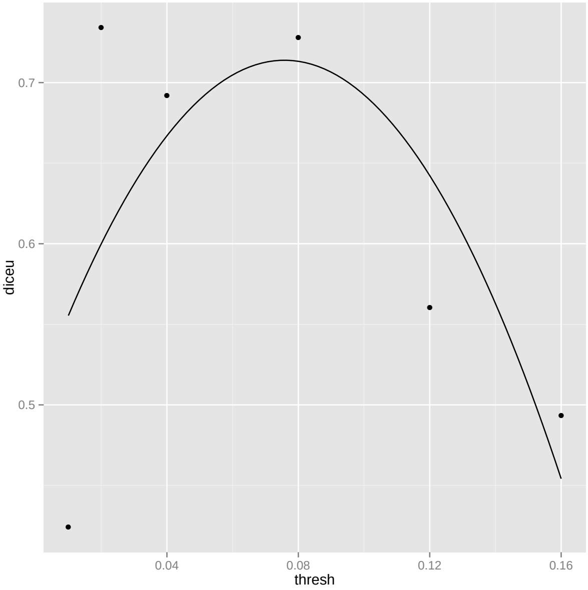
10 subjects

- Analyzed covert verb generation and finger tapping.
- Do sparse-components overlap? Depends on threshold and task.
- A sparse component, u, maximizes
  $$\text{PearsonCorrelation}(Xu, \text{HRF}_{\text{model(s)}}v) - \omega\|u\|_1$$
  where we ℓ_1 penalize non-zero components of u and X is the BOLD matrix.
- Finger tapping overlap: ”focal network,” max ≈ 0.7 at threshold 2% of brain.
- Covert verb: ”bigger network,” max ≈ 0.8 at threshold 12% of brain.

Multivariate Overlap: Covert Verb

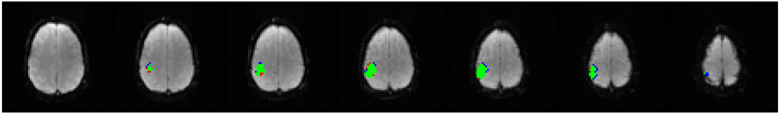


Multivariate Overlap: Finger Tapping



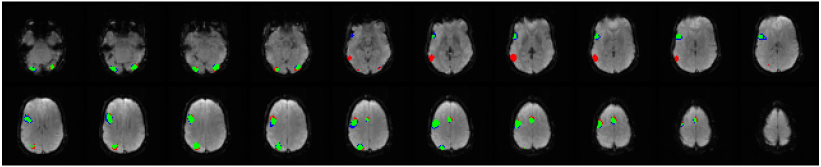
Finger Tapping: M-Spatial Maps

Figure : Finger tapping reproducibility — 3 color, red:run1, blue:run2, green:both. Dice ≈ 0.87.



Covert Verb Generation: M-Spatial Maps

Figure : Covert verb generation reproducibility — 3 color, red:run1, blue:run2, green:both. Dice ≈ 0.83.



Discussion

- Multivariate approach appears to be more repeatable: 0.8 vs 0.7 (covert verb) and 0.7 vs 0.4 (finger tapping).
- This may be due to the data-driven and spatially-informed smoothing within the multivariate optimization.
- Optimized spatial smoothing for univariate data may work better.
- Spatiotemporal smoothing improves overlap for both univariate (vg:0.74, ft:0.38) & multivariate (vg:0.83, ft: 0.87) approaches.

Discussion

- Multivariate approach appears to be more repeatable: 0.8 vs 0.7 (covert verb) and 0.7 vs 0.4 (finger tapping).
- This may be due to the data-driven and spatially-informed smoothing within the multivariate optimization.
- Optimized spatial smoothing for univariate data may work better.
- Spatiotemporal smoothing improves overlap for both univariate (vg:0.74, ft:0.38) & multivariate (vg:0.83, ft: 0.87) approaches.

Discussion

- Multivariate approach appears to be more repeatable: 0.8 vs 0.7 (covert verb) and 0.7 vs 0.4 (finger tapping).
- This may be due to the data-driven and spatially-informed smoothing within the multivariate optimization.
- Optimized spatial smoothing for univariate data may work better.
- Spatiotemporal smoothing improves overlap for both univariate (vg:0.74, ft:0.38) & multivariate (vg:0.83, ft: 0.87) approaches.

Discussion

- Multivariate approach appears to be more repeatable: 0.8 vs 0.7 (covert verb) and 0.7 vs 0.4 (finger tapping).
- This may be due to the data-driven and spatially-informed smoothing within the multivariate optimization.
- Optimized spatial smoothing for univariate data may work better.
- Spatiotemporal smoothing improves overlap for both univariate (vg:0.74, ft:0.38) & multivariate (vg:0.83, ft: 0.87) approaches.

Discussion 2

- SCCAN allows combination of block and HRF models to drive prediction — may also help reproducibility.
- Subject-level reproducibility: *not bad* (needs work to quantify further via prediction).
- Many processing decisions made by observation, knowledge from literature and educated guesses.

Discussion 2

- SCCAN allows combination of block and HRF models to drive prediction — may also help reproducibility.
- Subject-level reproducibility: *not bad* (needs work to quantify further via prediction).
- Many processing decisions made by observation, knowledge from literature and educated guesses.

Discussion 2

- SCCAN allows combination of block and HRF models to drive prediction — may also help reproducibility.
- Subject-level reproducibility: *not bad* (needs work to quantify further via prediction).
- Many processing decisions made by observation, knowledge from literature and educated guesses.

Summary of Findings

Novel BOLD-fMRI study comparing the reliability of multivariate and univariate group-level analysis

- Both finger-tapping and CovVerbGen result in Dice overlap > 0.83. The upper limit in reliability is *unknown*. [a]
- CovVerbGen involves a more distributed network of effects and is therefore less reliable yet is consistent @ both group-level and subject-level.

---

[a] Including GlobalSignal appears to increase or, at minimum, not hurt, reliability.

Summary of Findings

Novel BOLD-fMRI study comparing the reliability of multivariate and univariate group-level analysis

- Both finger-tapping and CovVerbGen result in Dice overlap > 0.83. The upper limit in reliability is *unknown*. [a]
- CovVerbGen involves a more distributed network of effects and is therefore less reliable yet is consistent @ both group-level and subject-level.

[a] Including GlobalSignal appears to increase or, at minimum, not hurt, reliability.

Future Work

- Study impact of pre-processing for both univariate and multivariate approaches.
- Random effects in univariate? Optimized smoothing in univariate?
- Test decoding of 3 simple tasks with both univariate and multivariate feature selection: *"dictionary" or "template"*?
- Given results of above, process Haxby data.

Future Work

- Study impact of pre-processing for both univariate and multivariate approaches.
- Random effects in univariate? Optimized smoothing in univariate?
- Test decoding of 3 simple tasks with both univariate and multivariate feature selection: *“dictionary” or “template”?*
- Given results of above, process Haxby data.

Future Work

- Study impact of pre-processing for both univariate and multivariate approaches.
- Random effects in univariate? Optimized smoothing in univariate?
- Test decoding of 3 simple tasks with both univariate and multivariate feature selection: *“dictionary” or “template”*?
- Given results of above, process Haxby data.

Future Work

- Study impact of pre-processing for both univariate and multivariate approaches.
- Random effects in univariate? Optimized smoothing in univariate?
- Test decoding of 3 simple tasks with both univariate and multivariate feature selection: *“dictionary” or “template”?*
- Given results of above, process Haxby data.

Trivial Preliminary Results: Decoding *S1*

Train on Run 1 and test on Run 2 — finger, mouth, foot interleaved with rest. Prediction from group and subject features via *R* and *SCCAN*.

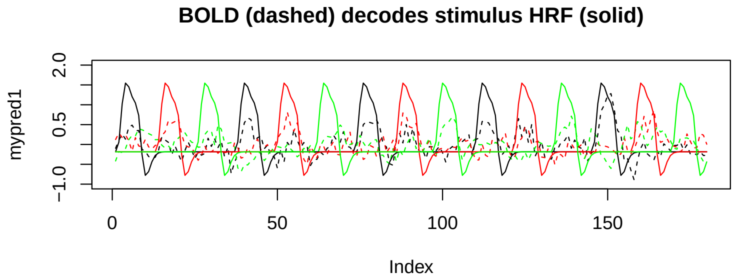


Figure : Subject 1.

Prior constraints and voting will improve results.

Trivial Preliminary Results: Decoding *S2*

Train on Run 1 and test on Run 2 — finger, mouth, foot interleaved with rest. Prediction from group and subject features via *R* and *SCCAN*.

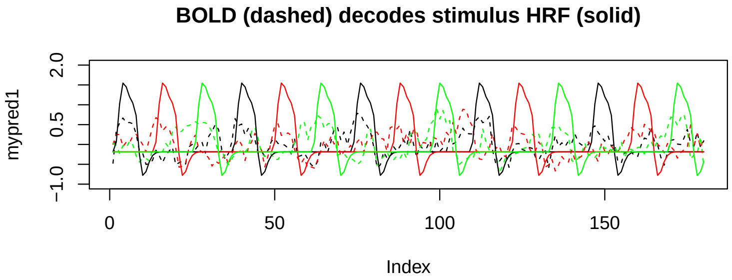


Figure : Subject 2.

Prior constraints and voting will improve results.