#### fMRI Reproducibility in R

#### **Brian B. Avants**

PENN Image Computing & Science Laboratory Dept. of Radiology, University of Pennsylvania Philadelphia, PA, 19104 <sup>1</sup>

November 7, 2013

<sup>&</sup>lt;sup>1</sup>for KRNS project

# This presentation is copyrighted by The **ANTs software consortium**

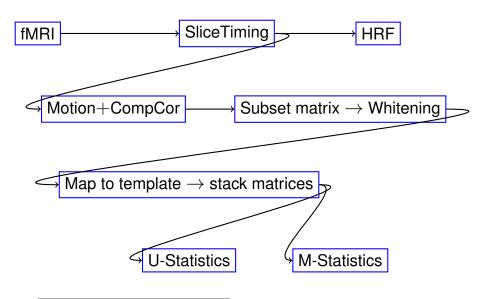
distributed under the

Creative Commons by Attribution License 3.0

http:

//creativecommons.org/licenses/by/3.0

### ANTsR group-wise fMRI: BOBO<sup>2</sup>



<sup>&</sup>lt;sup>2</sup>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 = -1.112, df = 98, p-value = 0.2689
## alternative hypothesis: true correlation is not equal to 0
## 95 percent confidence interval:
## -0.30142 0.08671
## sample estimates:
##
       cor
## -0.1116
```

- 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.

- 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.

- 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.

- 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.

- 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.

- 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.

#### Validation Mechanisms

- ▶ Univar: Threshold statistical map consistently: top x% of  $\beta$  map  $\rightarrow$  threshold at constant  $\beta$  = 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.

#### Validation Mechanisms

- ▶ Univar: Threshold statistical map consistently: top x% of  $\beta$  map  $\rightarrow$  threshold at constant  $\beta$  = 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 followec by subject-specific prediction.

#### Validation Mechanisms

- ▶ Univar: Threshold statistical map consistently: top x% of  $\beta$  map  $\rightarrow$  threshold at constant  $\beta$  = 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 followec by subject-specific prediction.

#### Validation Mechanisms

- ▶ Univar: Threshold statistical map consistently: top x% of  $\beta$  map  $\rightarrow$  threshold at constant  $\beta$  = 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.

#### Validation Mechanisms

- ▶ Univar: Threshold statistical map consistently: top x% of  $\beta$  map  $\rightarrow$  threshold at constant  $\beta$  = 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.

- 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,
   <u>univar\_multivar\_fmri\_consistency.sh</u> produces
   group-wise reproducibility numbers.
- ▶ Models are of form: voxel  $\approx$  hrf + motion1 + motion2 + motion3 + compcor1 + compcor2 + compcor3 + global signal + 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  $nt \times n$

- 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, <u>univar\_multivar\_fmri\_consistency.sh</u> produces group-wise reproducibility numbers.
- ▶ Models are of form: voxel  $\approx$  hrf + motion1 + motion2 + motion3 + compcor1 + compcor2 + compcor3 + global signal + 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  $nt \times p$ .

- 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, <u>univar\_multivar\_fmri\_consistency.sh</u> produces group-wise reproducibility numbers.
- ▶ Models are of form: voxel  $\approx$  hrf + motion1 + motion2 + motion3 + compcor1 + compcor2 + compcor3 + global signal + 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  $nt \times p$ .

- 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, <u>univar\_multivar\_fmri\_consistency.sh</u> produces group-wise reproducibility numbers.
- ▶ Models are of form: voxel  $\approx$  hrf + motion1 + motion2 + motion3 + compcor1 + compcor2 + compcor3 + global signal + 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  $nt \times p$ .

- 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, <u>univar\_multivar\_fmri\_consistency.sh</u> 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  $nt \times p$ .

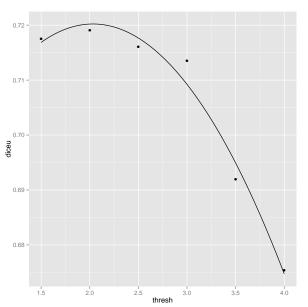
- Analyzed covert verb generation and finger tapping.
- ▶ Do  $\beta$  maps overlap? Depends on threshold and task.
- Finger tapping overlap: Max pprox 0.4 at threshold Y.
- Covert verb: Less sensitive to threshold. Max  $\approx 0.7$  at threshold 2.

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

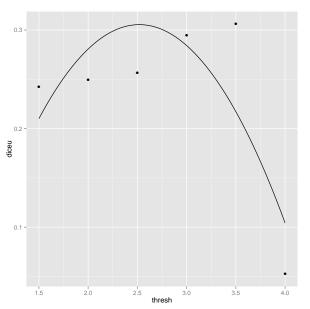
- Analyzed covert verb generation and finger tapping.
- Do β maps overlap? Depends on threshold and task.
- Finger tapping overlap: Max  $\approx 0.4$  at threshold Y.
- Covert verb: Less sensitive to threshold. Max  $\approx 0.7$  at threshold 2.

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

# Univariate Overlap: Covert Verb



# Univariate Overlap: Finger Tapping



- Analyzed covert verb generation and finger tapping.
- Do sparse-components overlap? Depends on threshold and task.
- A sparse component, u, maximizes PearsonCorrelation $(Xu, \mathsf{HRF}_{\mathsf{model}(\mathsf{s})}v) \omega \|u\|_1$  where we  $\ell_1$  penalize non-zero components of u and X is the BOLD matrix.
- Finger tapping overlap: "focal network," max  $\approx 0.7$  at threshold 2% of brain.
- ► Covert verb: "bigger network," max  $\approx 0.8$  at threshold 12% of brain.

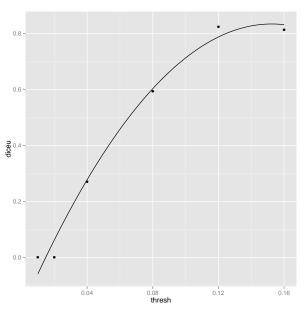
- Analyzed covert verb generation and finger tapping.
- Do sparse-components overlap? Depends on threshold and task.
- A sparse component, u, maximizes PearsonCorrelation $(Xu, \mathsf{HRF}_{\mathsf{model}(\mathsf{s})}v) \omega \|u\|_1$  where we  $\ell_1$  penalize non-zero components of u and X is the BOLD matrix.
- Finger tapping overlap: "focal network," max  $\approx 0.7$  at threshold 2% of brain.
- ► Covert verb: "bigger network," max  $\approx 0.8$  at threshold 12% of brain.

- Analyzed covert verb generation and finger tapping.
- Do sparse-components overlap? Depends on threshold and task.
- A sparse component, u, maximizes PearsonCorrelation $(Xu, \mathsf{HRF}_{\mathsf{model}(\mathsf{s})}v) \omega \|u\|_1$  where we  $\ell_1$  penalize non-zero components of u and X is the BOLD matrix.
- Finger tapping overlap: "focal network," max  $\approx 0.7$  at threshold 2% of brain.
- ► Covert verb: "bigger network," max  $\approx 0.8$  at threshold 12% of brain.

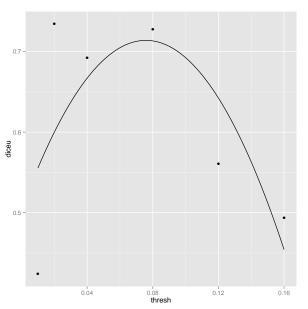
- Analyzed covert verb generation and finger tapping.
- Do sparse-components overlap? Depends on threshold and task.
- A sparse component, u, maximizes PearsonCorrelation $(Xu, \mathsf{HRF}_{\mathsf{model}(\mathsf{s})}v) \omega \|u\|_1$  where we  $\ell_1$  penalize non-zero components of u and X is the BOLD matrix.
- Finger tapping overlap: "focal network," max  $\approx 0.7$  at threshold 2% of brain.
- ► Covert verb: "bigger network," max  $\approx 0.8$  at threshold 12% of brain.

- Analyzed covert verb generation and finger tapping.
- Do sparse-components overlap? Depends on threshold and task.
- A sparse component, u, maximizes PearsonCorrelation $(Xu, \mathsf{HRF}_{\mathsf{model}(\mathsf{s})}v) \omega \|u\|_1$  where we  $\ell_1$  penalize non-zero components of u and X is the BOLD matrix.
- Finger tapping overlap: "focal network," max  $\approx 0.7$  at threshold 2% of brain.
- ► Covert verb: "bigger network," max  $\approx 0.8$  at threshold 12% of brain.

# Multivariate Overlap: Covert Verb

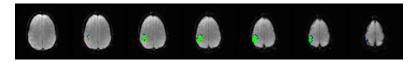


# Multivariate Overlap: Finger Tapping



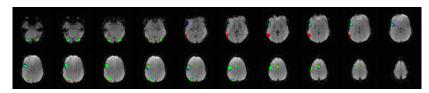
#### Finger Tapping: M-Spatial Maps

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



#### Covert Verb Generation: M-Spatial Maps

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



#### 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.

- 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.

- 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.

- 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.

- 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.

- 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.

- 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. <sup>a</sup>
- CovVerbGen involves a more distributed network of effects and is therefore less reliable yet is consistent @ both group-level and subject-level.

<sup>a</sup>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. <sup>a</sup>
- CovVerbGen involves a more distributed network of effects and is therefore less reliable yet is consistent @ both group-level and subject-level.

<sup>a</sup>Including GlobalSignal appears to increase or, at minimum, not hurt, reliability.

- 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.

- 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.

- 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.

- 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*.

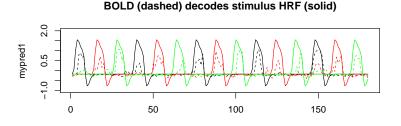


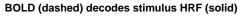
Figure: Subject 1.

Index

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*.



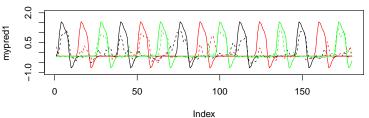


Figure: Subject 2.

Prior constraints and voting will improve results.