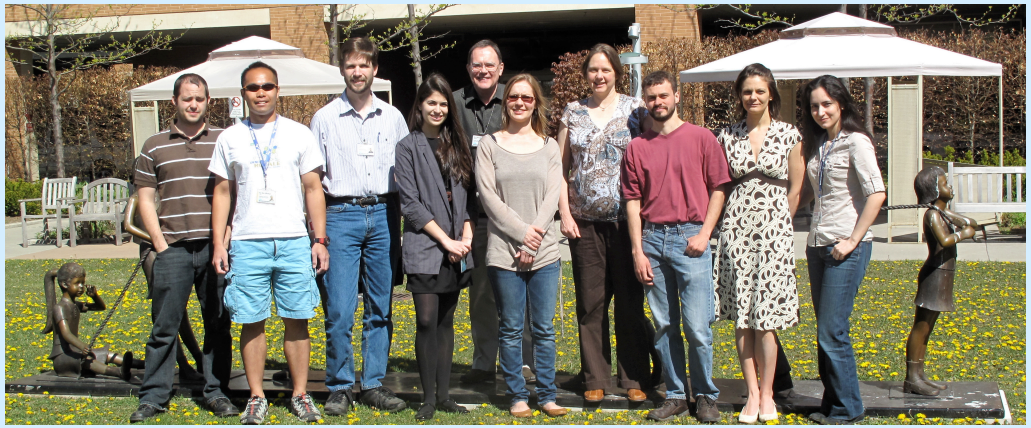
The NPAIRS Computational Statistics Framework for Data Analysis in Neuroimaging

The Strother Laboratory and Grady Laboratory



Rotman Research Institute, Baycrest Centre, and Medical Biophysics, University of Toronto
and Centre for Stroke Recovery, Heart and Stroke Foundation of Onatrio

Principal Funding Sources: NIH Human Brain Project, James S. McDonnell Foundation, Heart & Stroke Foundation of Ontario, Canadian Institutes for Health Research

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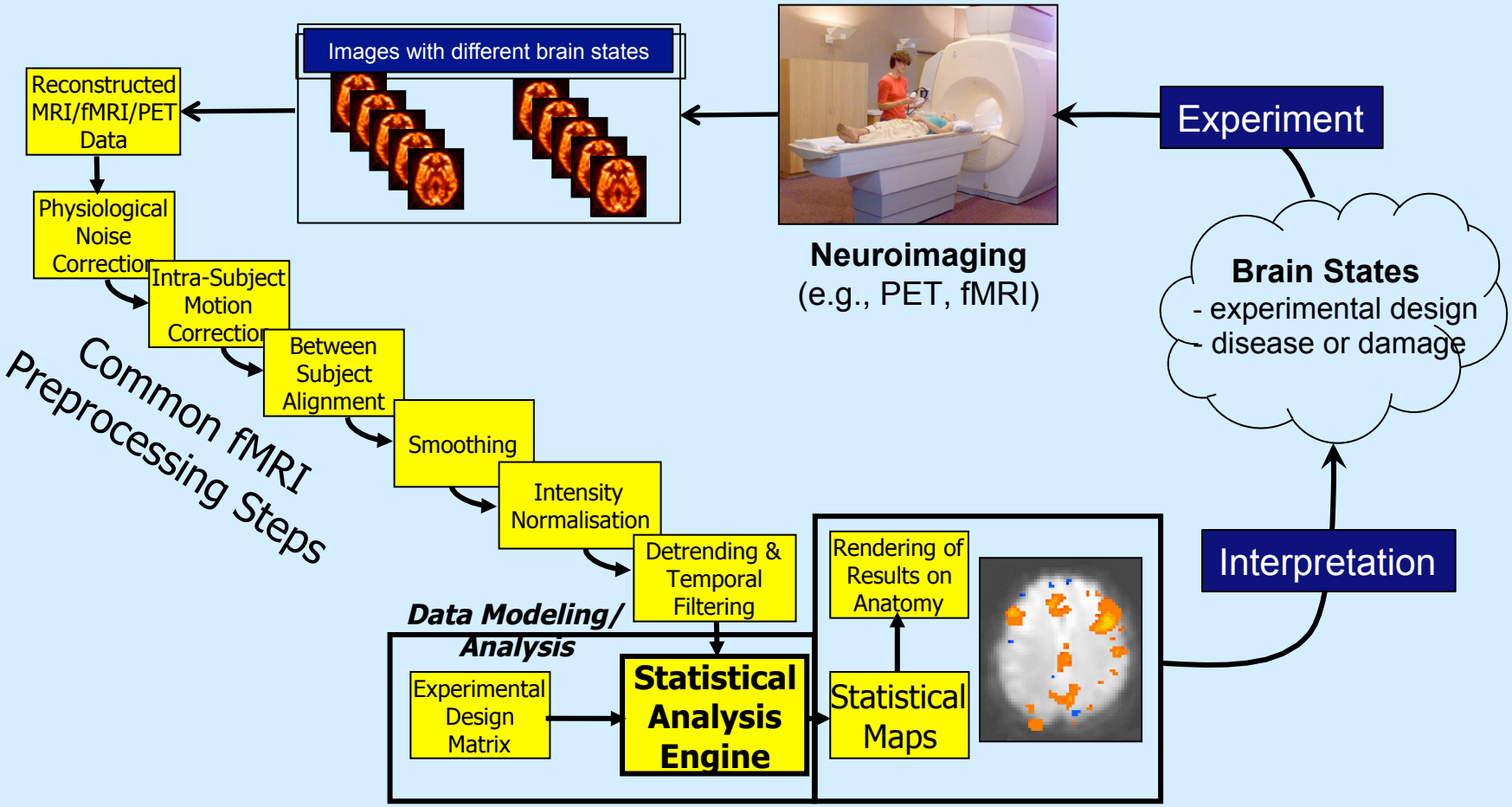
Baycrest Enriching Care Enhancing Knowledge Enlightening Minds

Outline

- BOLD fMRI pipelines and the implicit pipeline hypothesis: is there a problem?
- The NonParametric Activation and Influence Reproducibility reSampling (NPAIRS) framework for testing pipeline utility:
  - prediction and reproducibiliy performance metrics
- BOLD fMRI pipelines with Canonical Variates Analysis (CVA) discriminants on a principal component analysis (PCA) basis.
- Prediction vs. reproducibility plots as data-driven, pseudo ROC curves:
  - Impact of preprocessing pipeline choices.
  - Optimal PCA dimensionality as a function of age and multiple memory tasks.
- Conclusions

Neuroimaging Pipelines



Testing Processing and Analysis Pipelines

- Difficult to simulate realistic pipeline effects
- Focus on real-data performance measures
- All models are wrong but some are useful (Box)
- How do we measure utility of results without knowledge of "true" and "false" signal response?
- Use data-driven metrics:
  - **Reproducibility** of parameter estimates, i.e., activation maps
  - **Prediction** of experimental conditions

Strother SC, et al. Hum Brain Mapp, 5:312-316, 1997.
Strother SC, et al. Neuroimage 15:747-771, 2002.
Kjems U, et al. Neuroimage 15:772-786, 2002.

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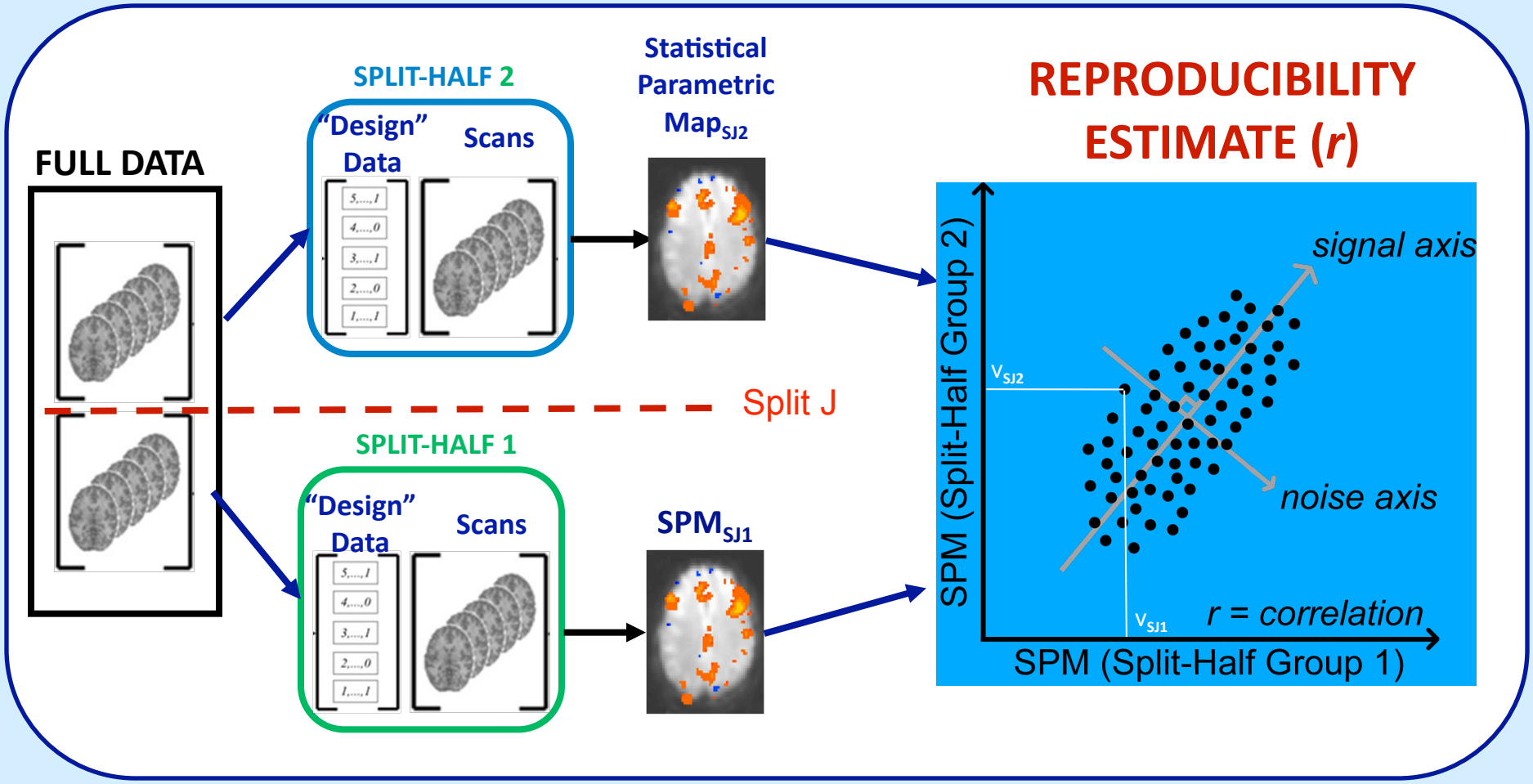
NPAIRS Reproducibility (*r*)



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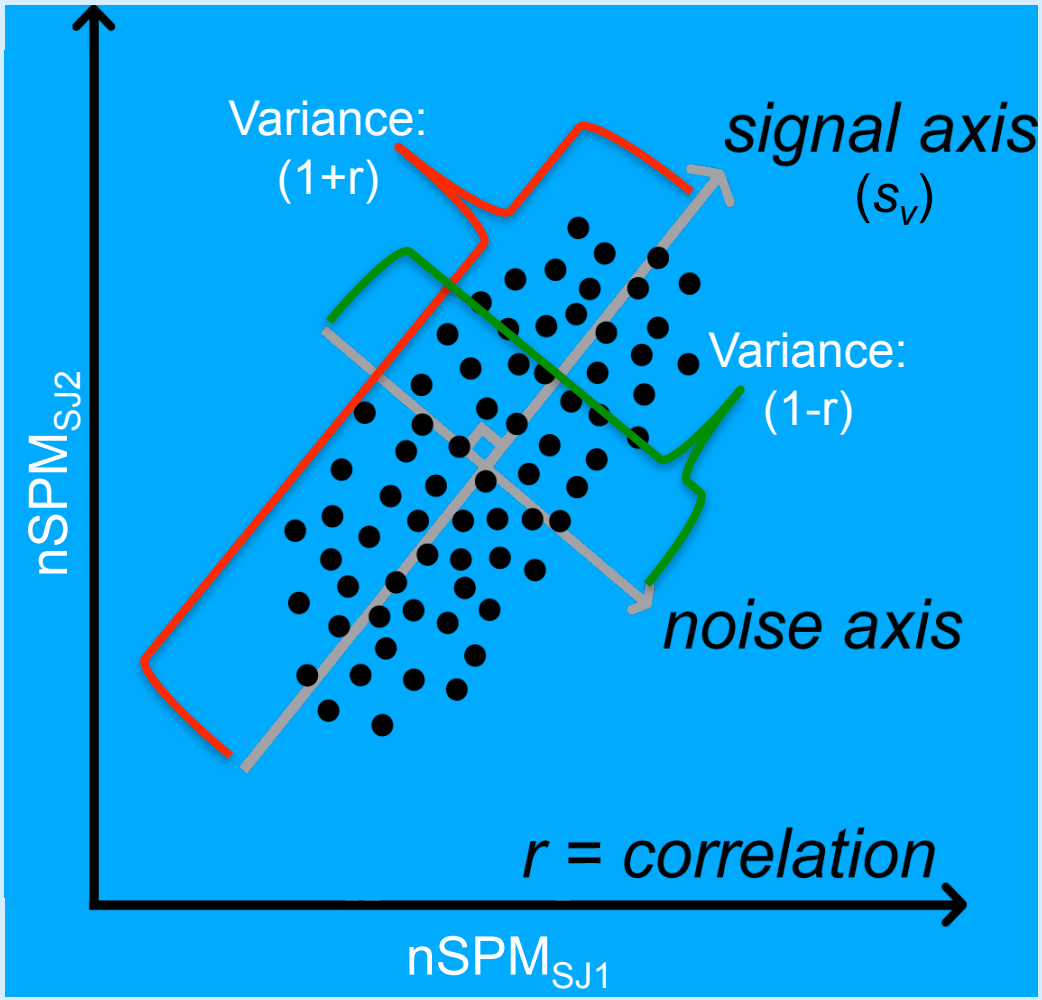
Global SNR and Robust rSPM(z)



For split J, and voxel v_J

1. **Normalize Split-Half SPMs**

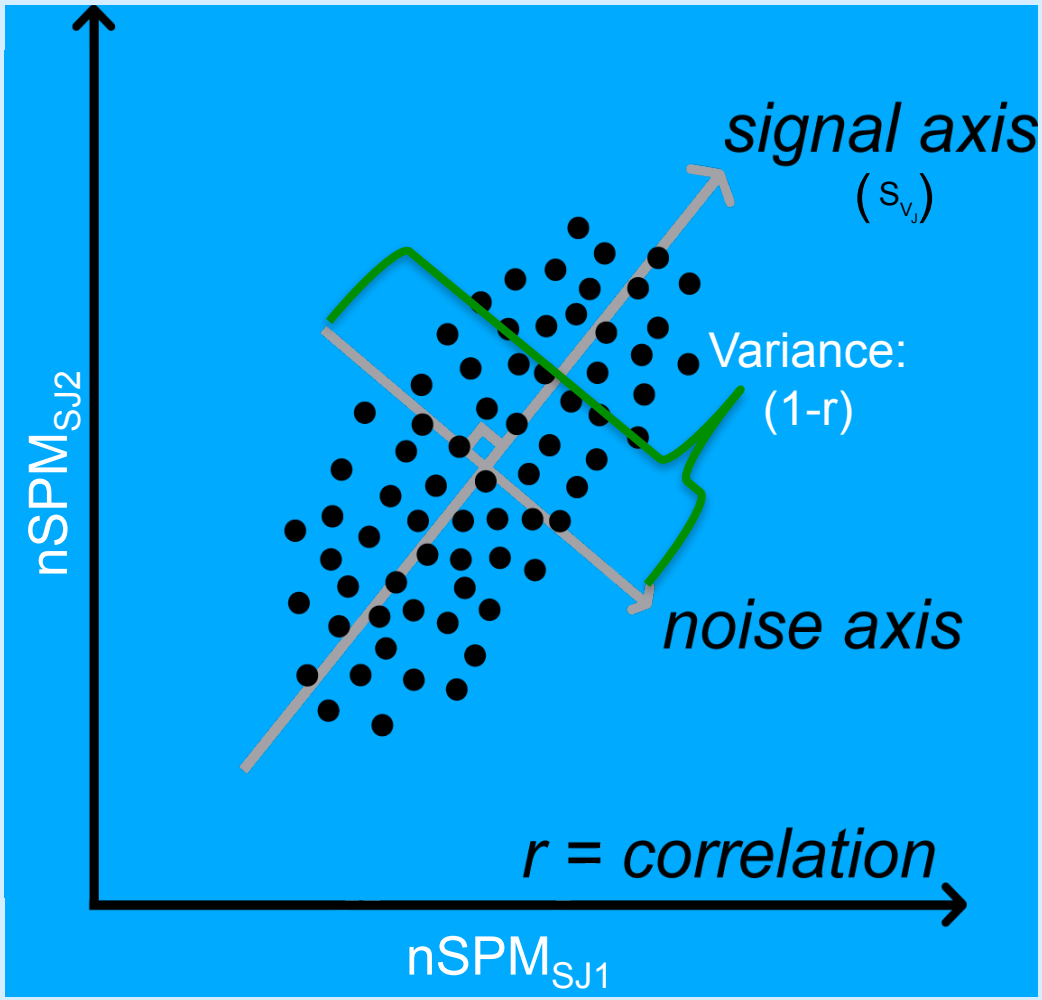
$$nSPM_{SJ1} = \left(SPM_{SJ1} - \overline{SPM}_{SJ1}\right) \Big/ \widehat{\sigma}_{SPM_{SJ1}}$$

2. **Global SNR for pipeline**

$$gSNR = \sqrt{(1+r)\text{-}(1-r) \Big/ (1-r)}$$

$$= \sqrt{2r \Big/ (1-r)}$$

Global SNR and Robust rSPM(z)



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$$= \sqrt{2r\big/(1-r)}$$

3. **Robust Concensus rSPM(z)**

$$rSPM(z)_J = s_{v_J} \Big/ \sqrt{(1-r_J)}$$

$$rSPM(z) = \sum_J rSPM(z)_J$$

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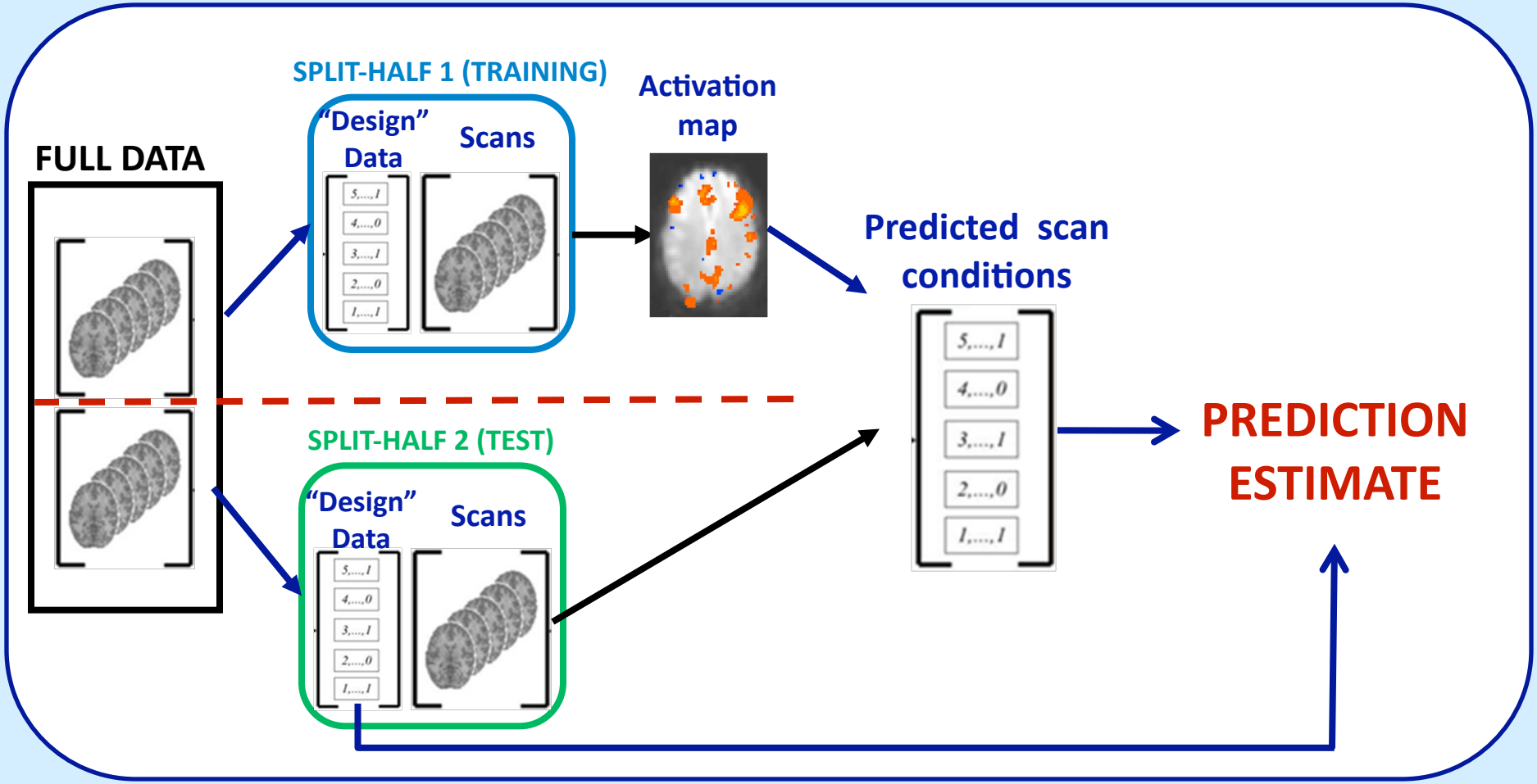
NPAIRS Prediction



Lautrup B, et al. From tomography to neural networks, (Hermann HJ, Wolf DE, Poeppel E, eds.) World Scientific, 137-148, 1995.

Morch N, et al. Lecture Notes in Computer Science 1230: Information Processing in Medical Imaging. Springer-Verlag, pp.259-270 1997.

Hansen LK,et al. Neuroimage, 9:534-544, 1999.

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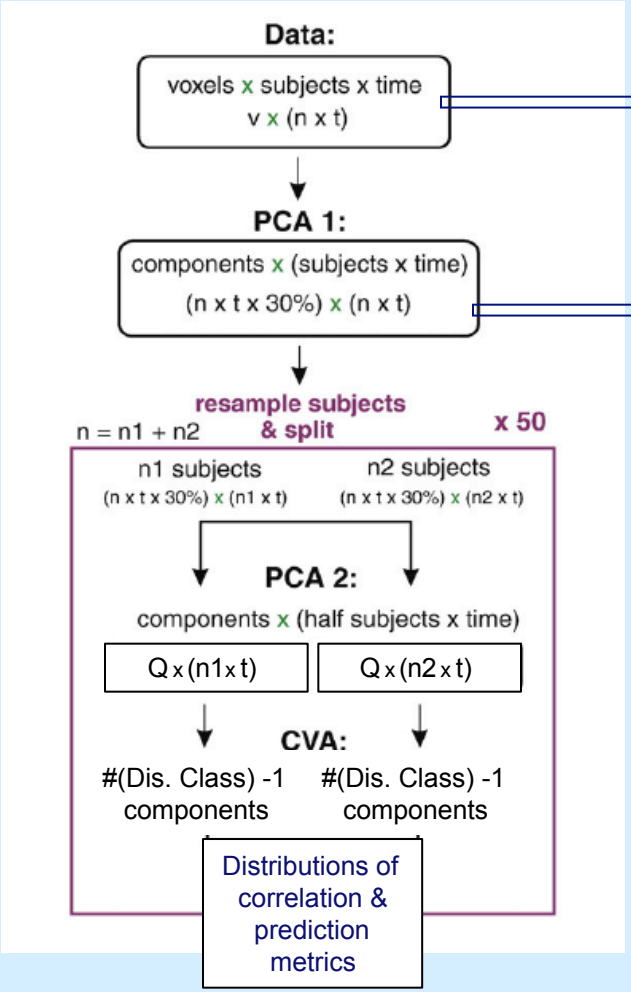
NPAIRS with CVA* on PCA Basis



Data: motor task data of 16 subjects x 187 scans

$X = v \times (n \times t) = [27843 \text{ voxels} \times 2992 \text{ scans}]$

Column centre X by column centering each subject's subblock

PCA 1: STEP DOWN variable selection

to 30% of principal components (PCs)

$X^* = (n \times t \times 30\%) \times (n \times t) = [898 \text{ PCs} \times 2992 \text{ scans}]$

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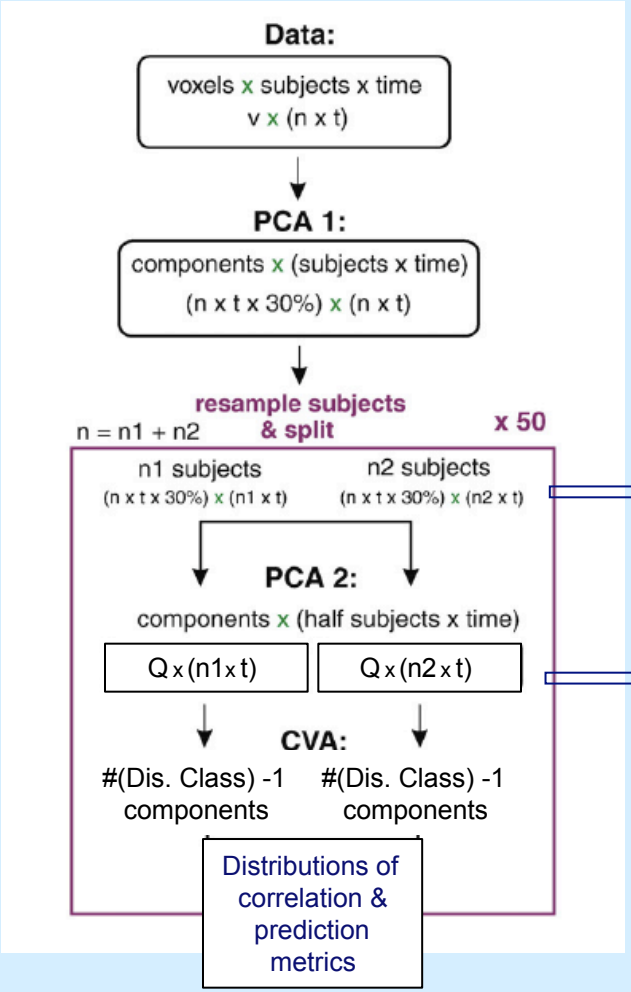
*Canonical Variates Analysis (CVA) = Linear Discriminant

- generalized eigensolution of $(\text{Within Class})^{-1}(\text{Between Class})$ covariances

NPAIRS with CVA* on PCA Basis



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$X^* = (n \times t \times 30\%) \times (n \times t)$ = [898 PCs x 2992 scans]

Each split-half data matrix (x 50)

$X^*_{½}$ = [898 PCs x 1496 scans]

PCA 2: STEP UP, 1:Q PC variable selection per split-half data matrix.

CVA* on 1:Q = 5:200 PCs from *svd*($X^*_{½}$)

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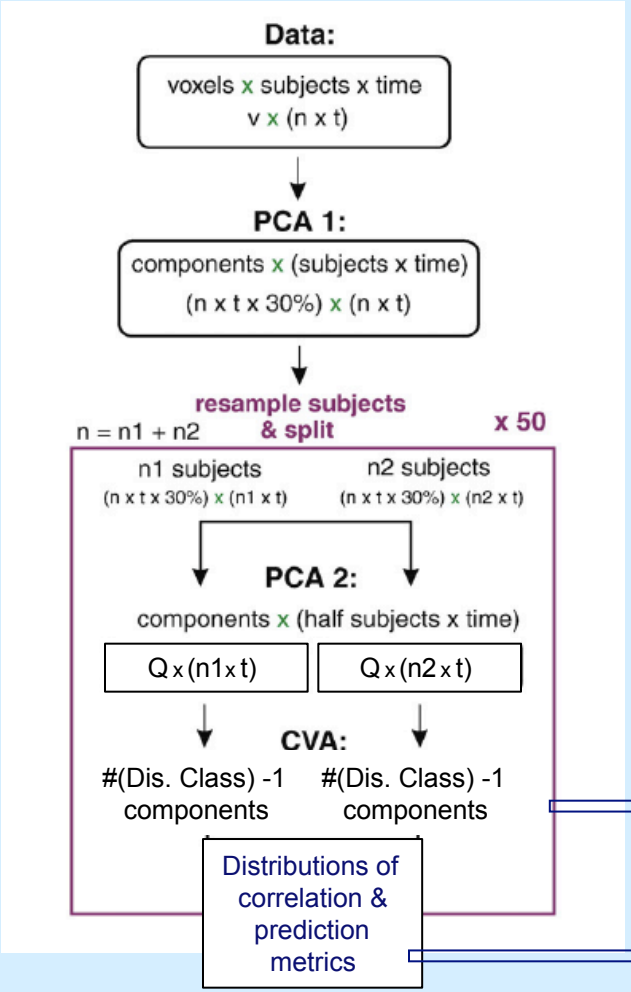

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Split-half CVA subspace matching

Restricted Procrustes: orthogonal rotation only

Plot medians of resampled split-half distributions

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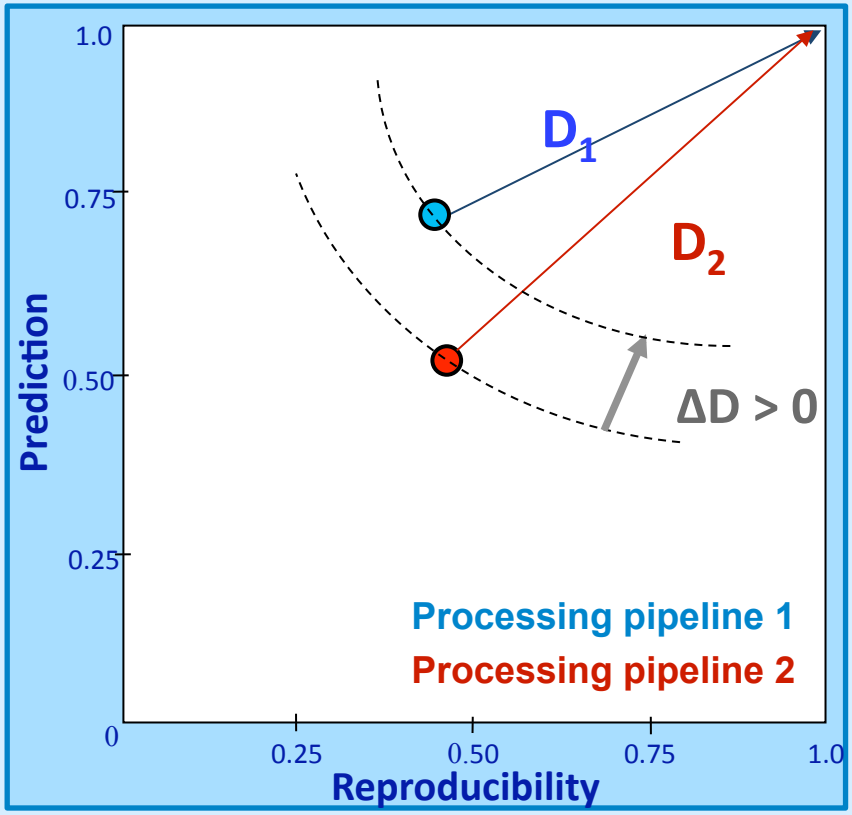
Measuring Pipeline Performance

- Use pseudo-ROC (p vs. r) measures

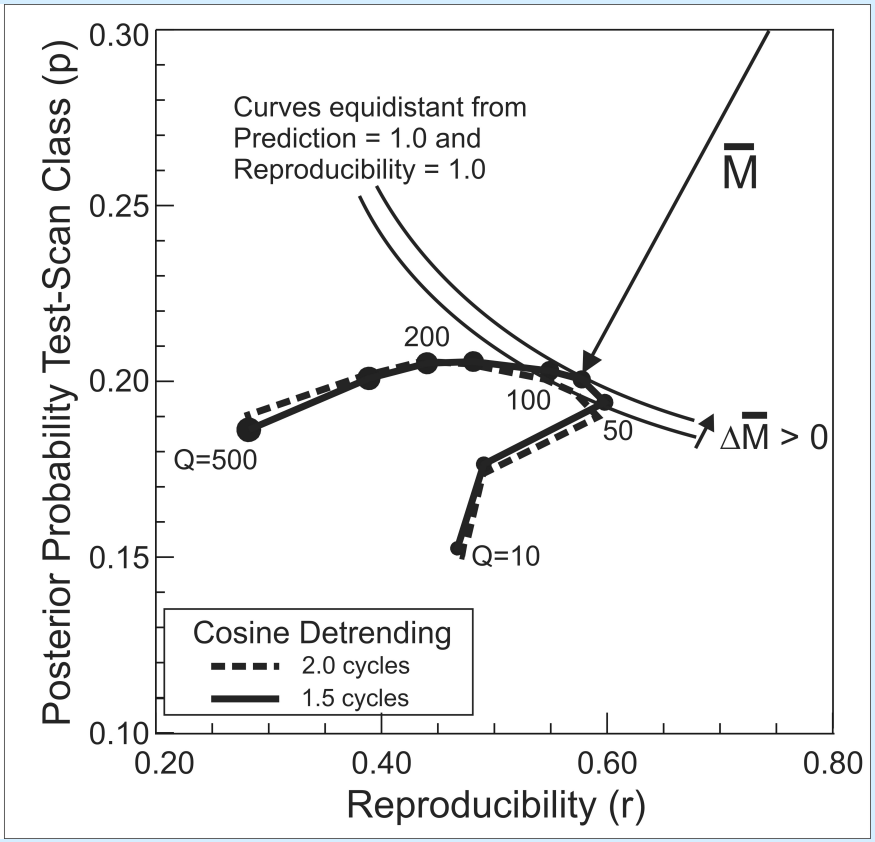
Define: relative performance by distance ***D*** from:

reproducibility = 1

prediction = 1



NPAIRS: Prediction vs. Reproducibility



- **16 subjects performing parametric, block static-force, task with BOLD fMRI**
  - group analysis (split-half = 8 subjs.)
  - 11-class CVA on PCA basis
  - include/exclude preprocessing steps
  - plot median (p,r) pairs for Q={10, 5, 50, 100, 150, 200, 300, 500}
- **Bias-variance tradeoff for CVA disciminant on PC basis**
  - model complexity increases (#PCs 10 →100)
  - hook-shaped curve with optimal prediction & reproducibility points

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Strother SC, et al. Neuroimage 23 Sup1:S196, 2004

Testing Pipelines with (p, r) Plots

Preprocessing steps		Data Analysis Model & Software	$\Delta\bar{M}$	Std. Dev.	p = [3]	$\Delta\bar{M}$ /(Std Dev)
1	Slice timing correction	GLM (NPAIRS)	-0.04	0.20	0.78	-0.21
		2c-CVA (NPAIRS)	0.07	0.20	0.14	0.36
2	Motion correction	GLM (NPAIRS)	-0.07	0.21	0.24	-0.34
		2c-CVA (NPAIRS)	0.08	0.094	**0.00**	**0.85**
3	**Spatial smoothing**	**GLM (NPAIRS)**	0.12	0.059	**0.00**	**2.03**
		2c-CVA (NPAIRS)	0.11	0.093	**0.00**	**1.18**
4	**Temporal detrending**	**GLM (NPAIRS)**	0.06	0.051	**0.00**	**1.18**
		2c-CVA (NPAIRS)	0.17	0.19	**0.03**	**0.90**
	High-pass filtering [1]	**GLM (FSL)**	0.04	0.049	**0.00**	**0.82**
	High-pass filtering [2]	**2c-CVA (NPAIRS)**	0.10	0.124	**0.01**	**0.81**
5	Global normalization	GLM (NPAIRS)	-0.00	0.020	0.55	-0.000
		2c-CVA (NPAIRS)	0.04	0.100	0.13	0.40

[1]Sliding window running means.
[2]Multi-Taper power spectrum
[3]Wilcoxin matched–pair rank sum test (N = 16)

Zhang et al., Neuromage 41:4:1242, 2008
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A Multi-Task Dataset as f(Age)

Encoding/recognition memory experiment

- Block design on 1.5T GE MRI (TR 2.5 s)
- 6 language/picture tasks/subject, 1 run/task
  - 4 Encoding Tasks – 80 scans/run/task
  - 2 Recognition Tasks – 160 scans/run/task
  - Grady et al., J. Cog. NSci, 2006

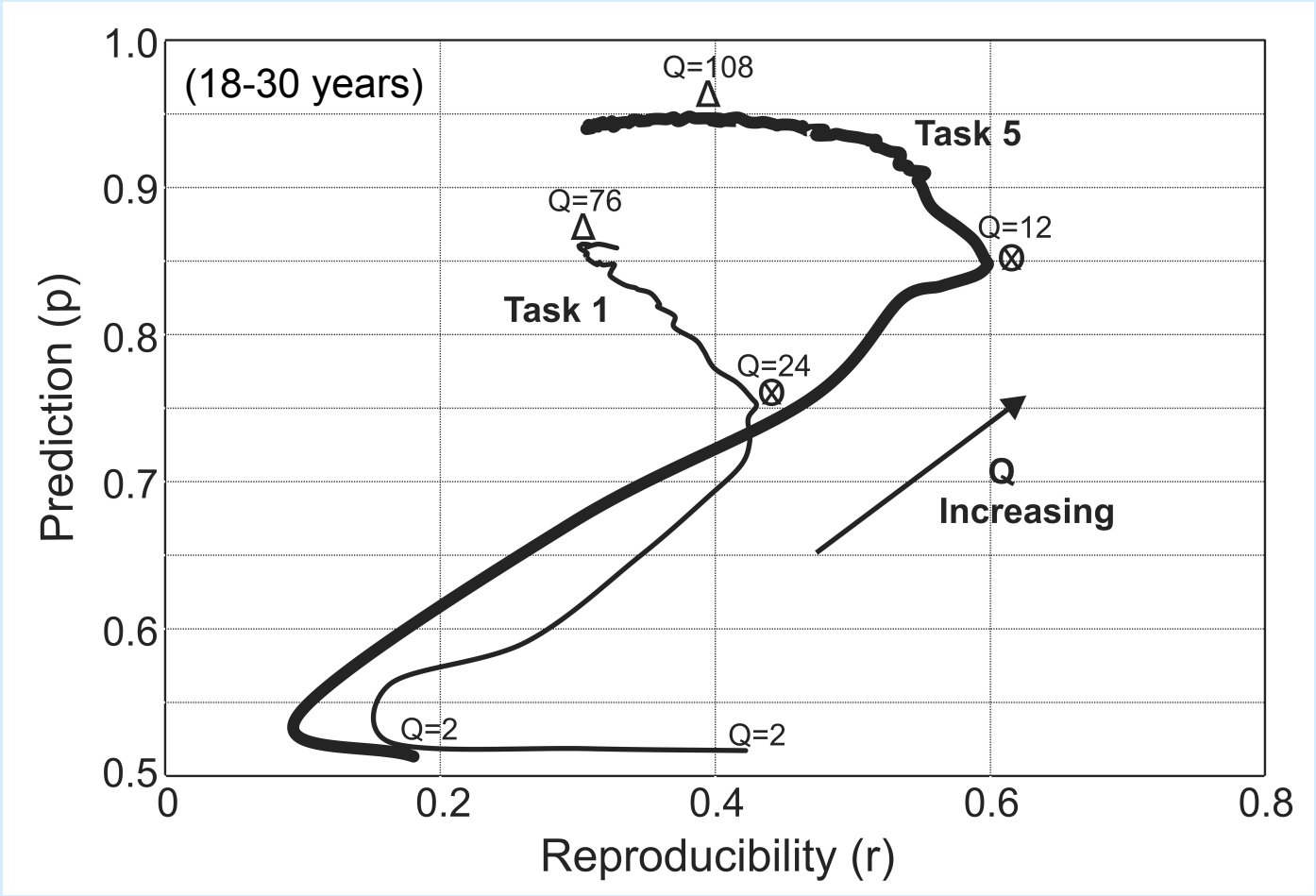
6 Tasks per Age Group analyzed separately

- 10 young (18-30 years)
- 10 middle-aged (40-60)
- 10 old (> 65 years)

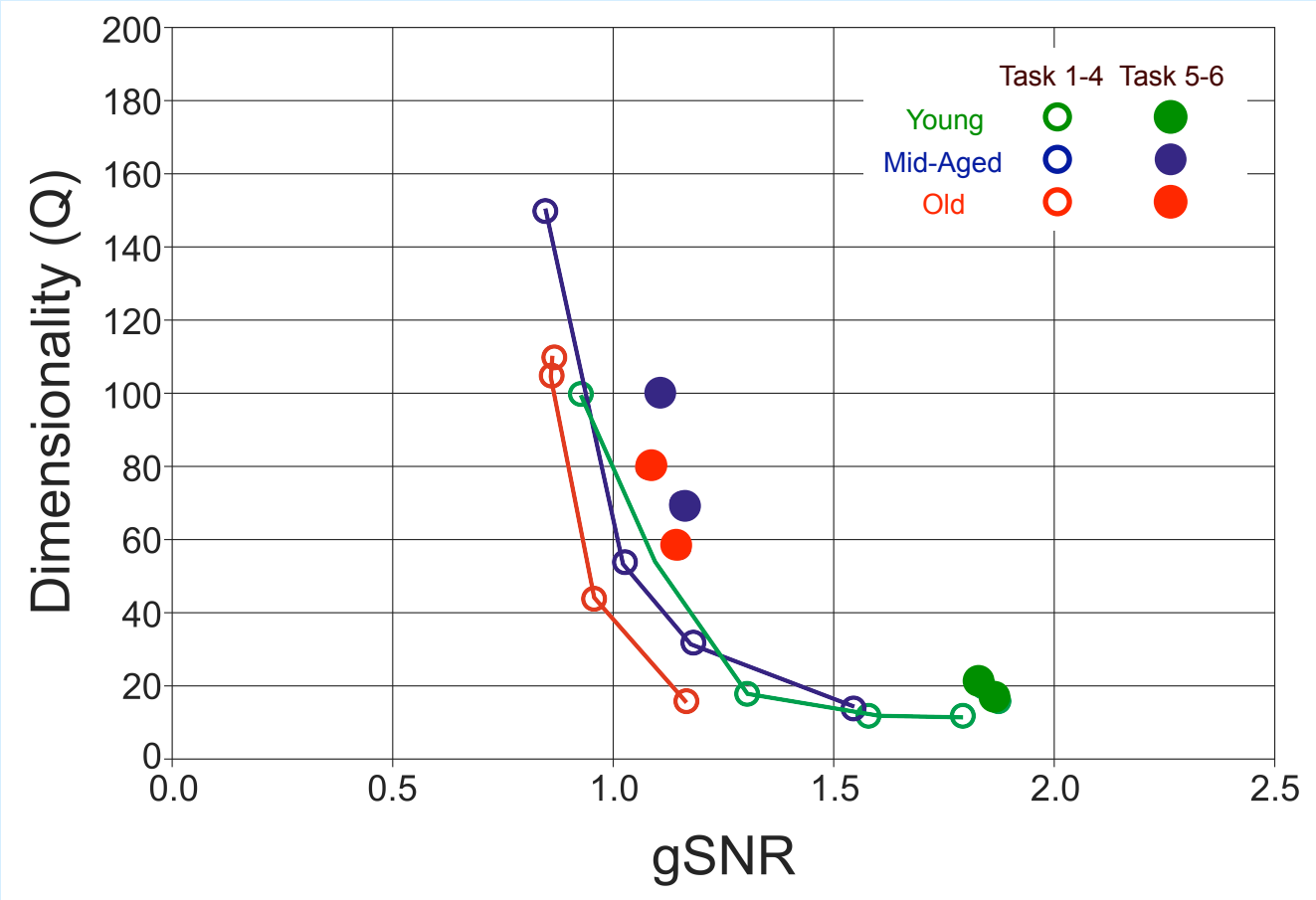
Processing & Analysis Pipelines/Task/Age Group

- **Pre-processing:** motion correction (AFNI); between-subject alignment (FSL); spatial smoothing (FWHM=6mm^2); linear detrending
- **Analysis Model:** two-class CVA on a PCA basis: a penalised discriminant (PDA)

Prediction vs. Reproducibility Curves



Maximum Reproducibility



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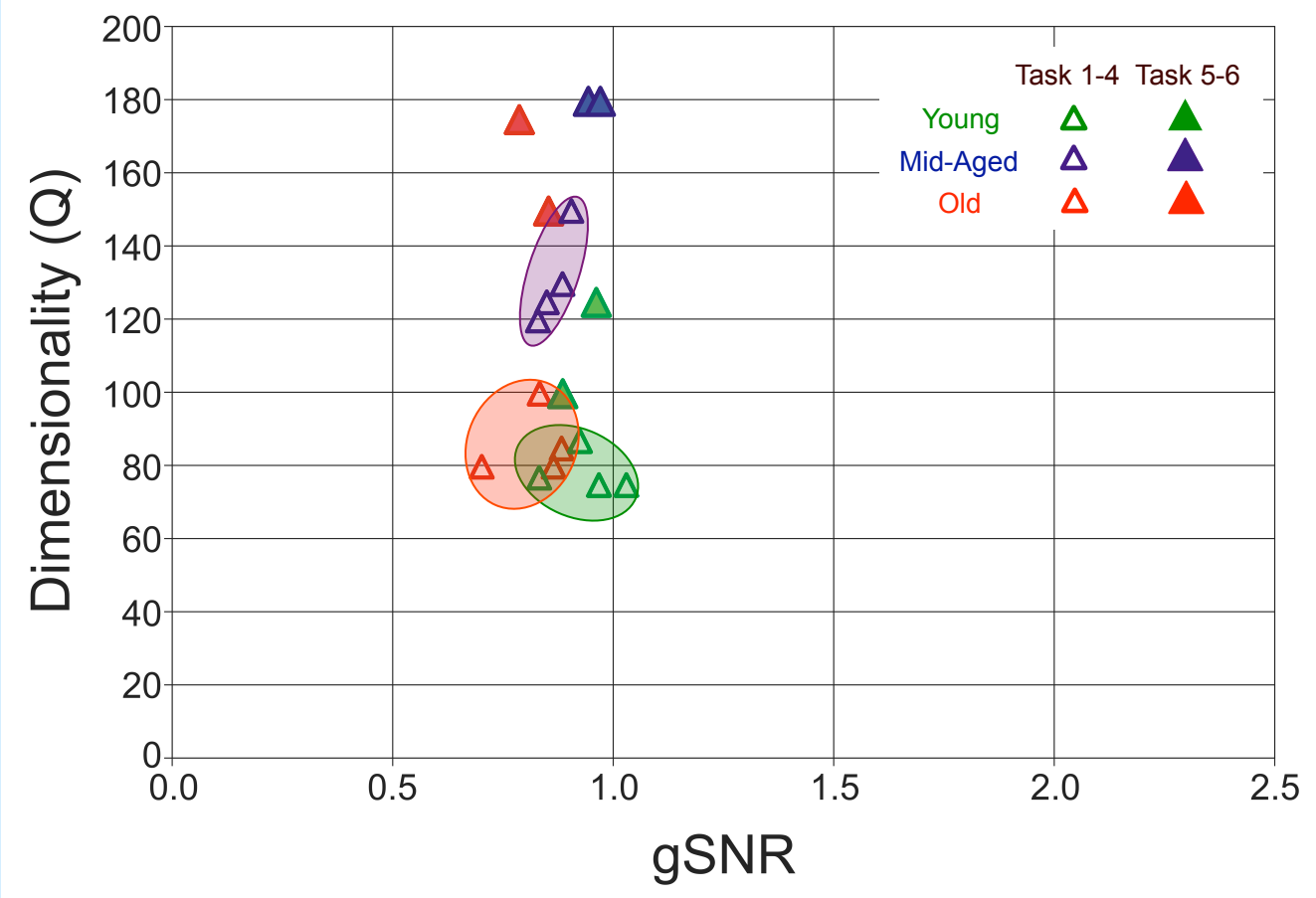
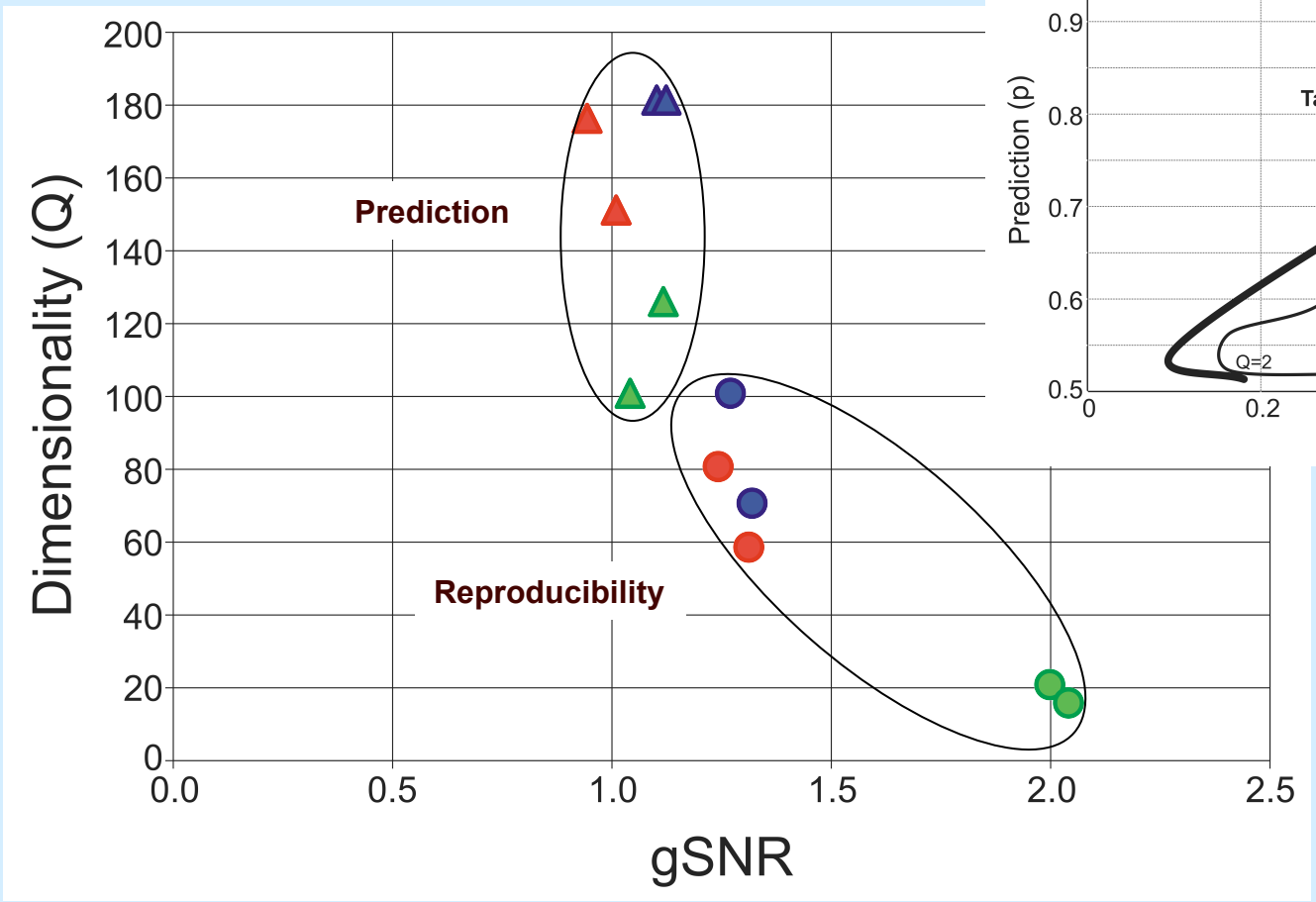
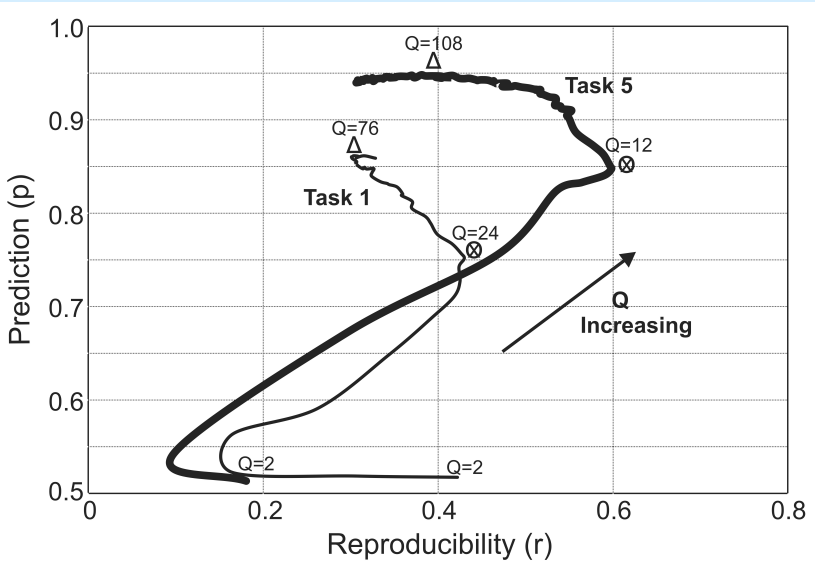
Yourganov G, et al. (minor revisions, Neuroimage).

Maximum Prediction



Stereotypical (p,r) Curve Structure





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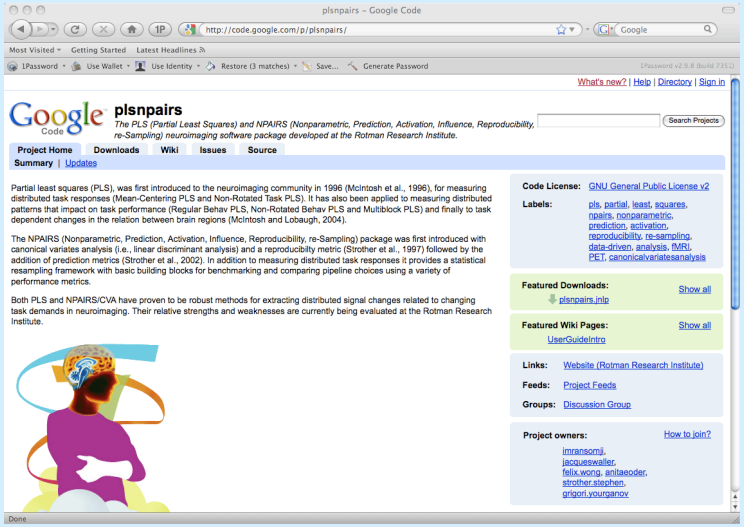
Practical Issues: Software & Other Uses

http://code.google.com/p/plsnpairs/



Non-standard uses of NPAIRS

- **Infrared Dermatology Imaging**
  - Sigurdsson S, et al. *IEEE Trans Biomed Eng* 51:1784-1793, 2004
- **Selection of Nonlinear, MCMC Bayes Models**
  - Jacobsen D, et al., *Neural Comput* 20:738, 2008
- **7T Acquisition Comparisons**
  - Barry RL, et al. *BSEC 2010 ORNL Biomed. Sci. & Eng. Conf. Biomed Res & Analysis in Neuroscience*, May 2010
- **Selection of Correlated Amino Acid Substitution Algorithms**
  - Brown CA, and Brown KS. *PLoS ONE*, 5(6):e10779, 2010

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Conclusions

- We do not adequately understand the pipeline choices that we make to produce & interpret BOLD fMRI results.
  - This is particularly true in cognitive studies as a function of age, and probably even more true as a funciton of disease & brain damage.
- NPAIRS-based (p,r) curves provide a systematic, data-analysis-model independent framework for such testing
- (p,r) curves show BOLD fMRI results are a function of:
  - CVA model regularization as function of PCA subspace size
  - preprocessing pipeline choices
  - subject age and experimental task
- (p,r) results for CVA on a PCA basis show that:
  - there is a hierarchical covariance structure in BOLD fMRI, perhaps reflectign age and task dependent brain networks
  - the middle-aged brain (40-65? years) may be unique in ways we have yet to understand.