Extensive Benchmark Calculations Based on "Gold Standard"

Systematic Quantification of Relationships Between Functional and Anatomical Connectivity in Macaque Monkeys

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18-02-2014

Motivation

Central Theme: how functional connectivity quantification influences its relationships to structural connectivity in macaque monkeys?

anatomy

functional

"Gold Standard" (AC):
a weighted and directed interareal connectivity matrix for macaque cerebral cortex based on retrograde tracer injections

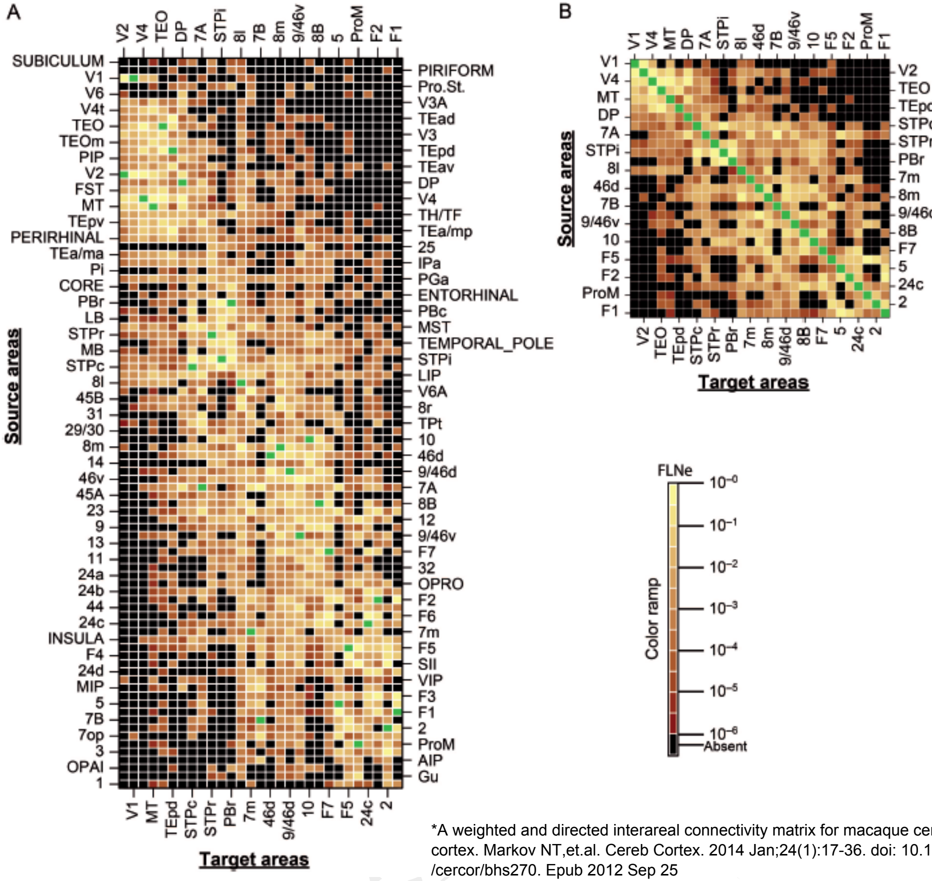
rsfMRI: functional connectivity (FC)

“Gold Standard”

- Retrograde tracer injections in 29 of the 91 areas of the macaque cerebral cortex
- A weighted and directed interareal connectivity matrix for macaque cerebral cortex

- A weight index determined for each area-to-area pathway
    - FLNe : extrinsic fraction of labeled neurons

*



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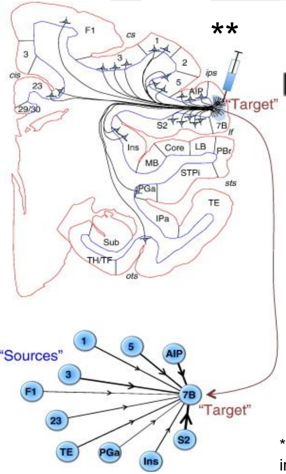
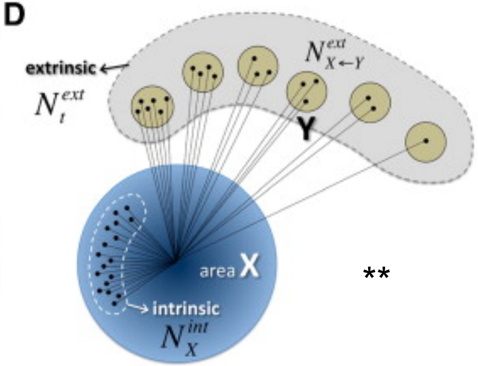


$$\text{FLN\% value Area X} = \frac{\text{Nb of neurons in area X projecting to target Area}}{\text{Total Nb of neurons projecting on target Area}}$$



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**Why data coherence and quality is critical for understanding interareal cortical networks. Kennedy H et.al. Neuroimage. 2013 Oct 15;80:37-45. doi: 10.1016/j.neuroimage. 2013.04.031. Epub 2013 Apr 18.

*A weighted and directed interareal connectivity matrix for macaque cerebral cortex. Markov NT,et.al. Cereb Cortex. 2014 Jan;24(1):17-36. doi: 10.1093 /cercor/bhs270. Epub 2012 Sep 25

Overview of Benchmark Calculation

Input: single subject (one macaque monkey M5) with two sessions, 298 volumes in each session

Preprocessing:

Regressors = {compcor}+{motion par}

rm {1-3} vols

motion cor

slice timing cor

physiological noise correction by GLM

bandpass filter

smoothing

coregistration

segmentation

Noise mask in compcor (noise ROI)
1. WM
2. CSF
3. WM&CSF
4. High temporal standard deviation (tSTD)

normalization

FC:

session cmb?

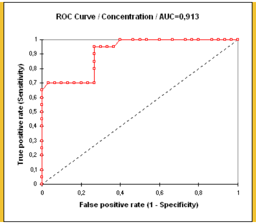
Full/partial correlation

AC: gold standard

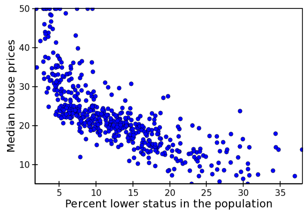
29 ⋯ 91
[0,1]

Result rendering:

1. AC as true labeling, FC as test result → ROC curve



2. Scatter plot to find relationships {AC, FC}



Noise Mask & GLM

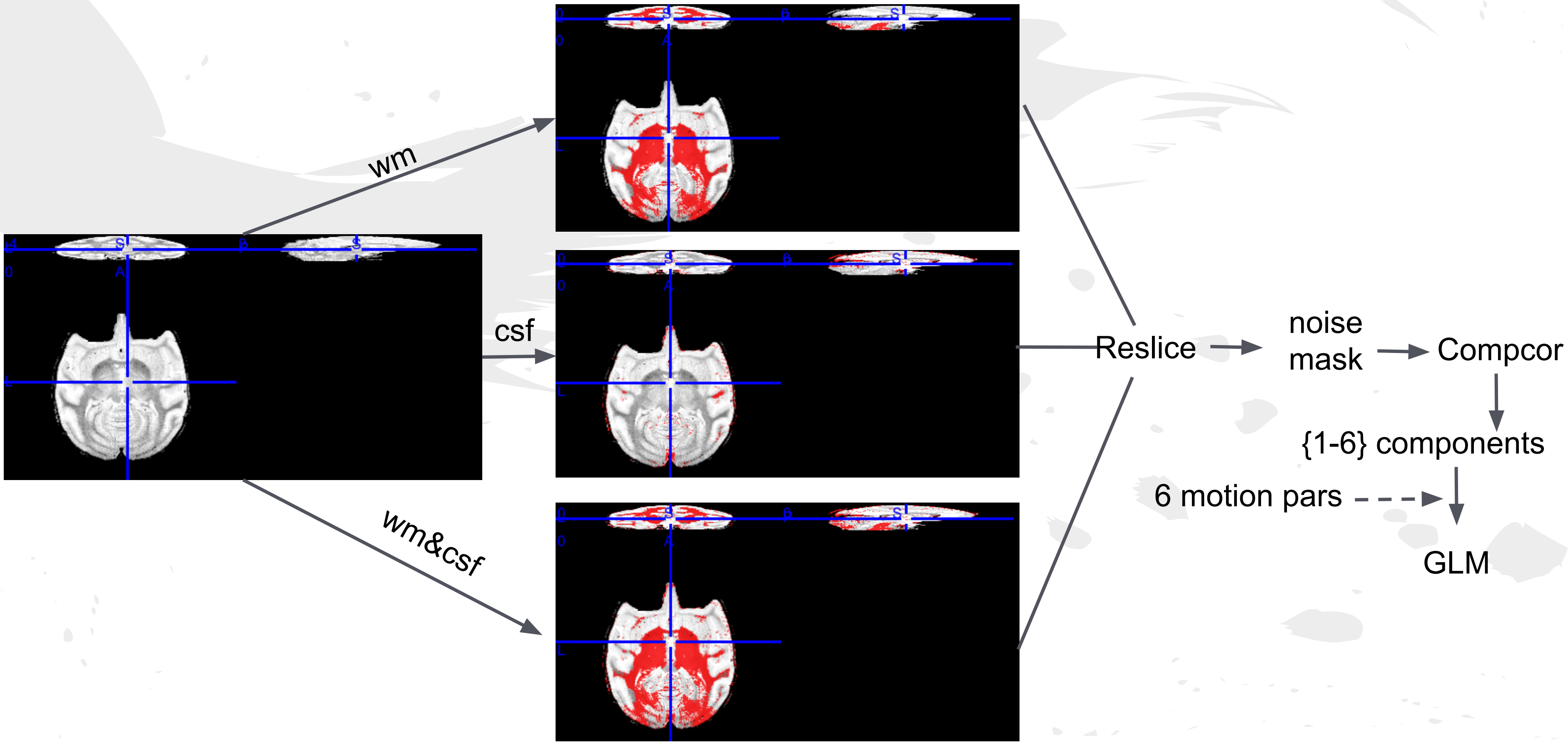
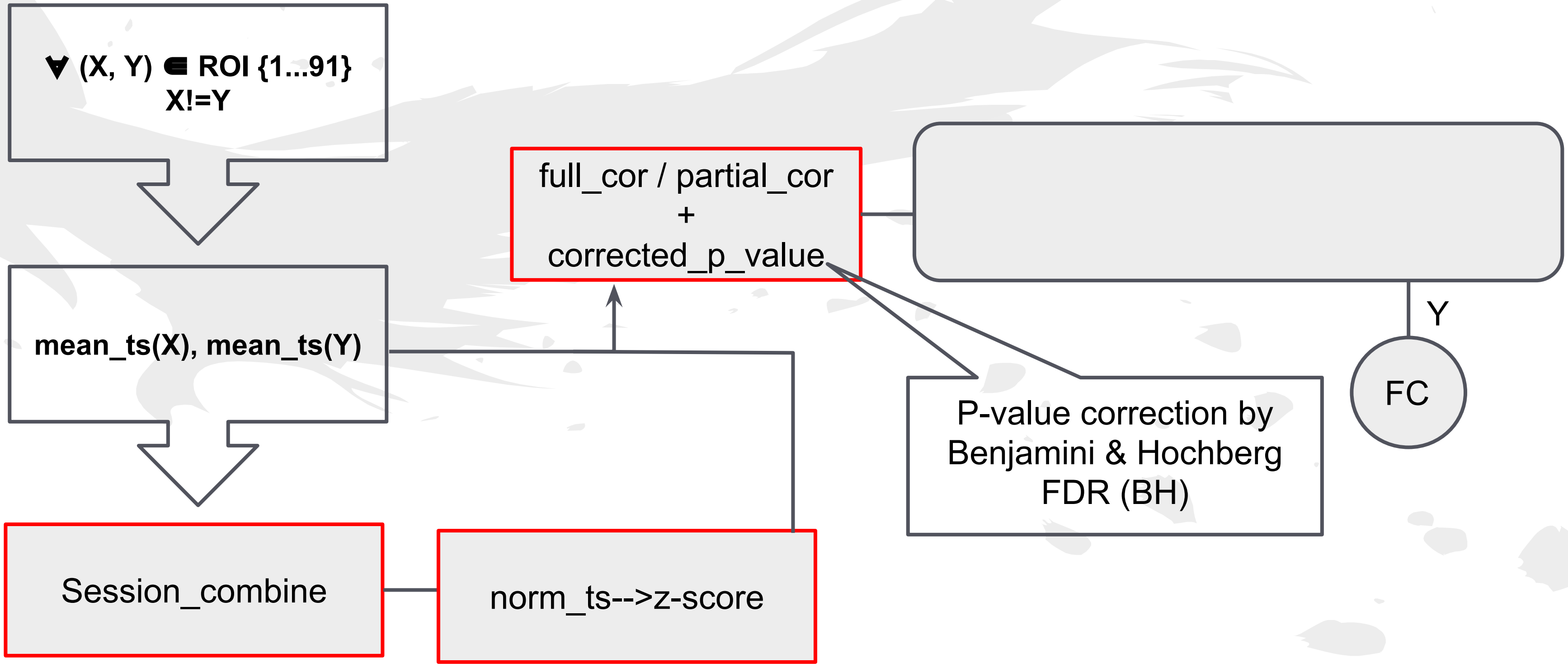
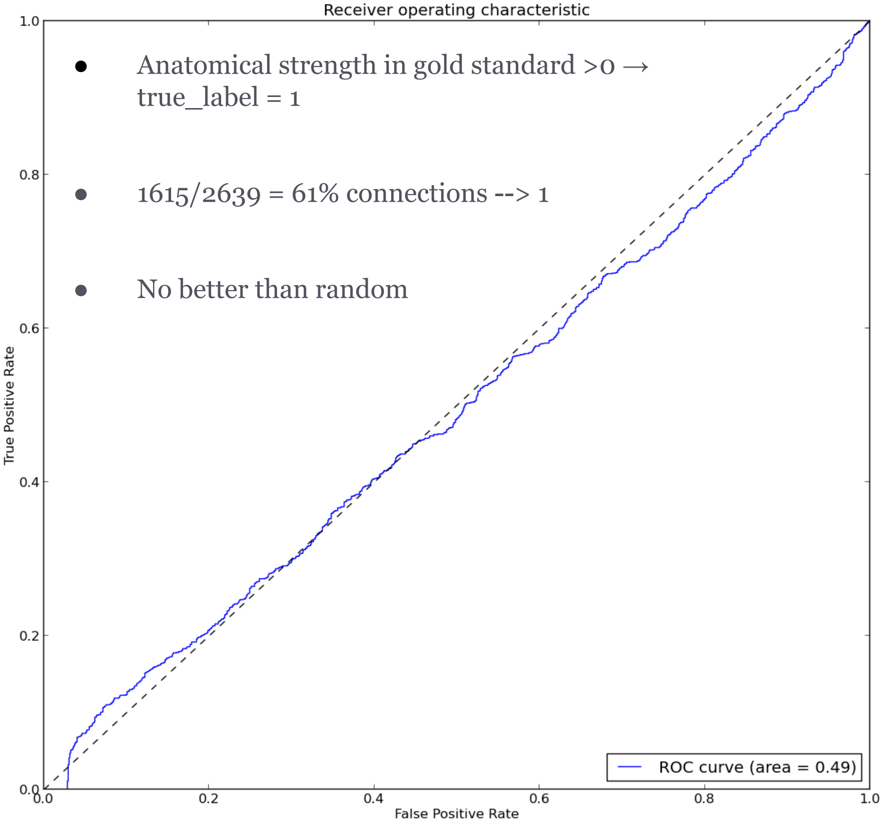


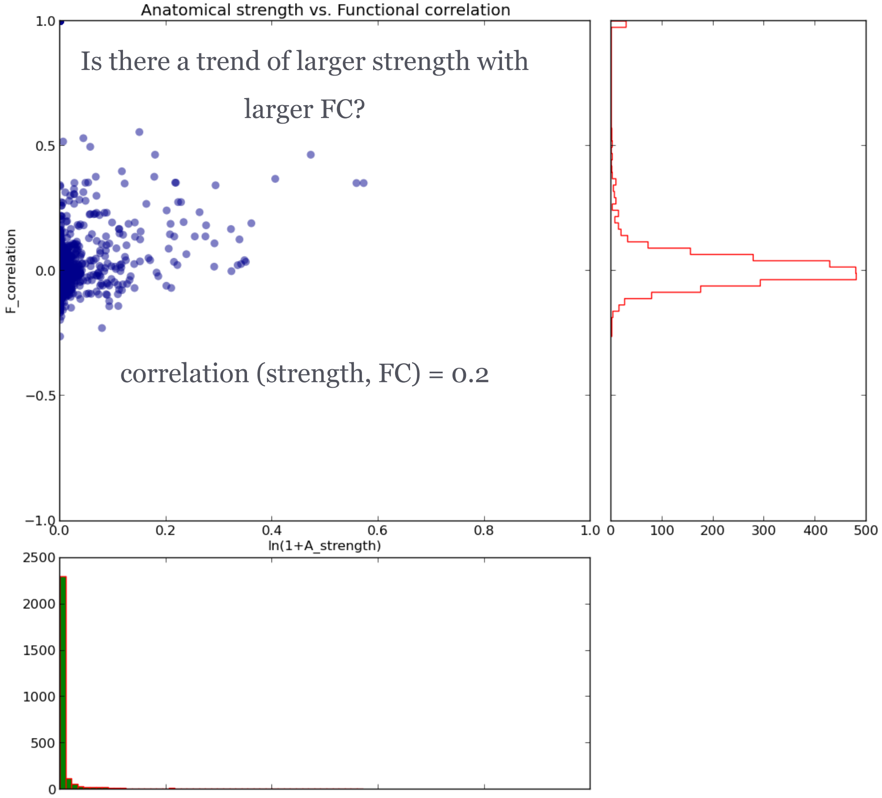
Diagram of FC Quantification



Exemplary Output Rendering

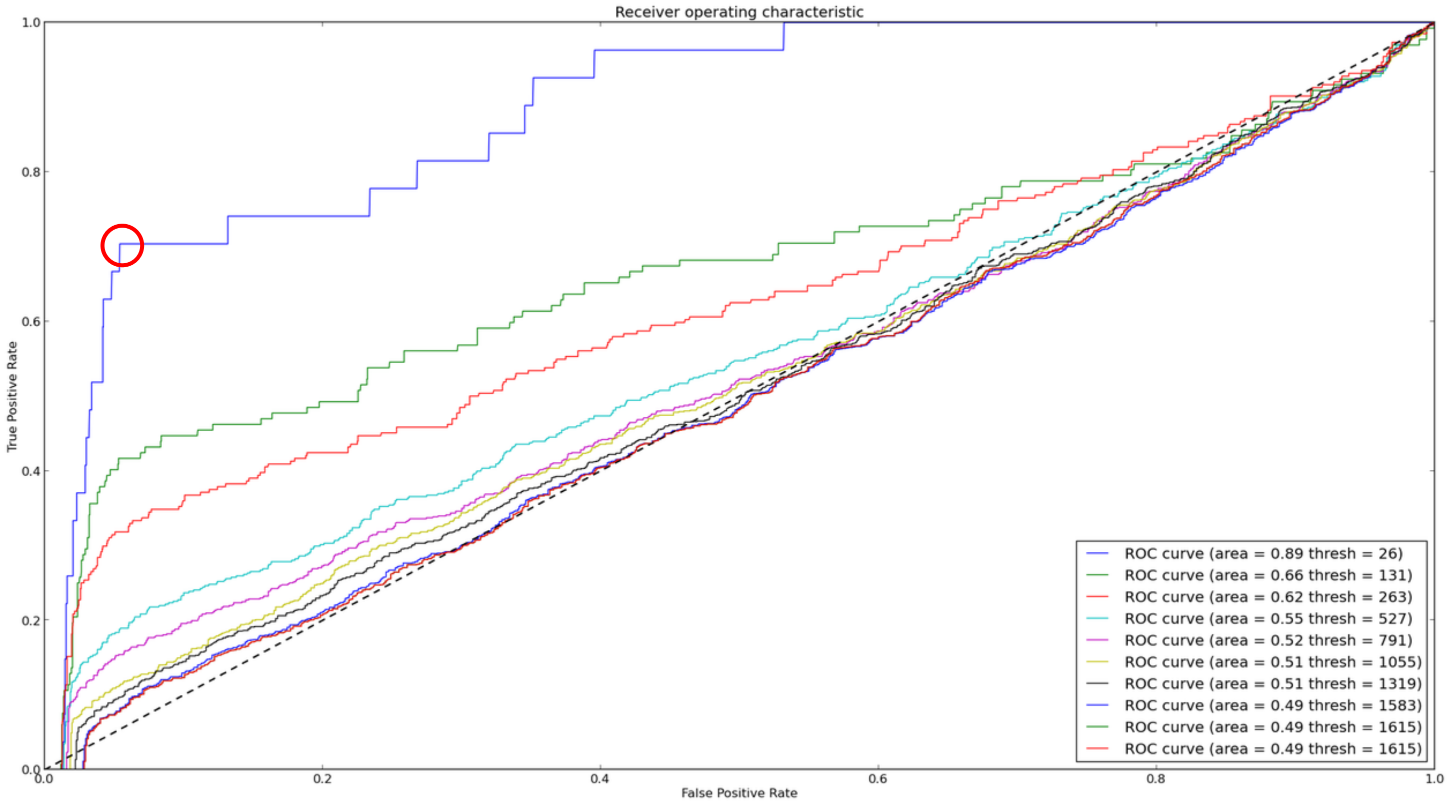
- wmcsf_partial_cmb scenario (AUC = 0.49)





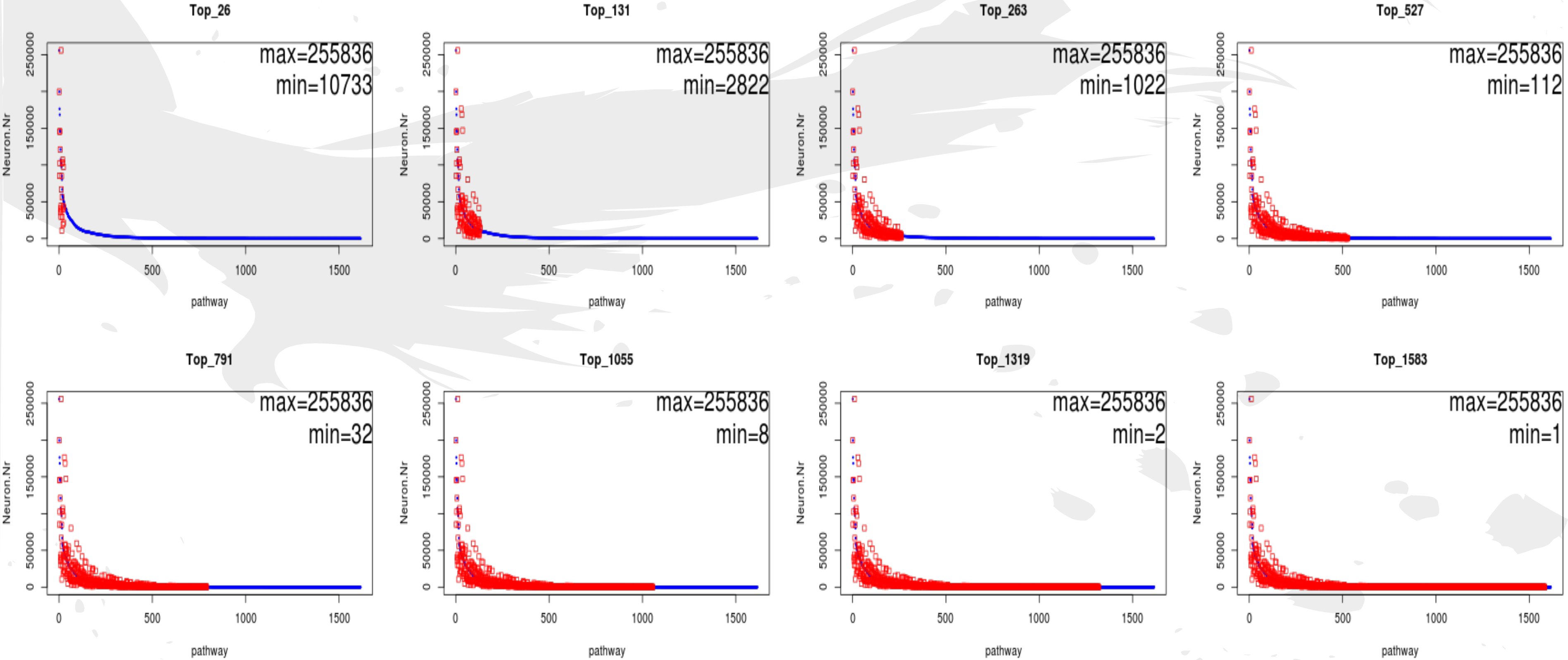
AUC Trends With Anatomical Strengths

- wmcsf_partial_cmb scenario (AUC = 0.49)

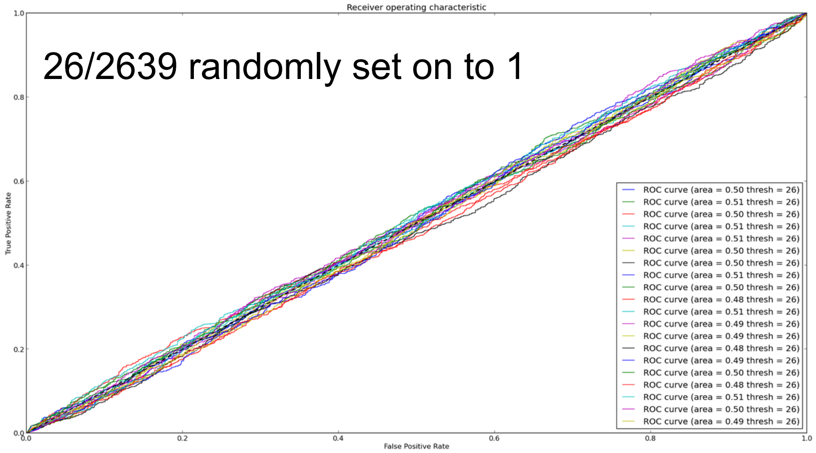


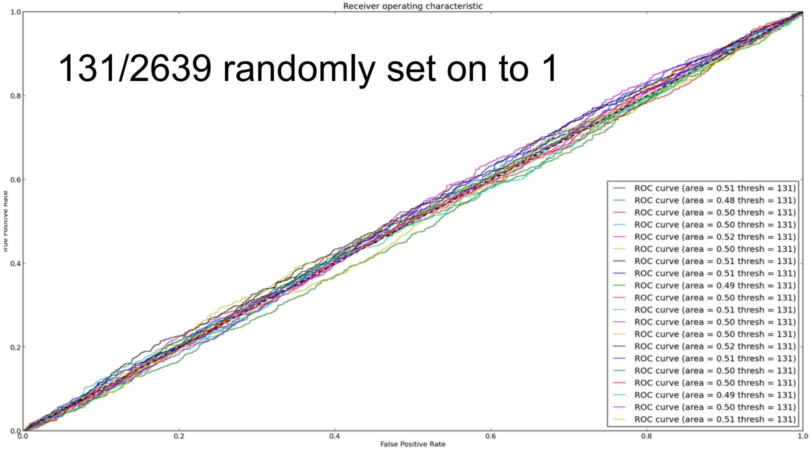
fpr(1-specificity)	tpr (sensi-tivity)	T
0.01	0	0.56
0.01	0.04	0.47
0.02	0.22	0.35
0.02	0.33	0.26
0.03	0.37	0.2
0.05	0.7	0.11
0.14	0.74	0.06
0.35	0.93	0.02

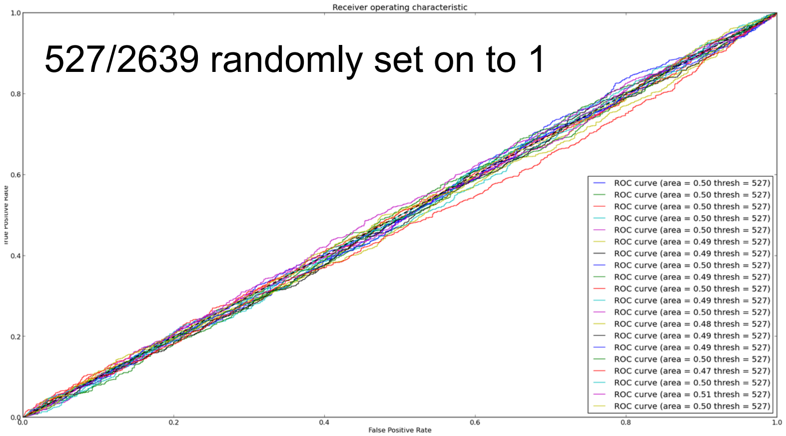
Neuron Number Distribution

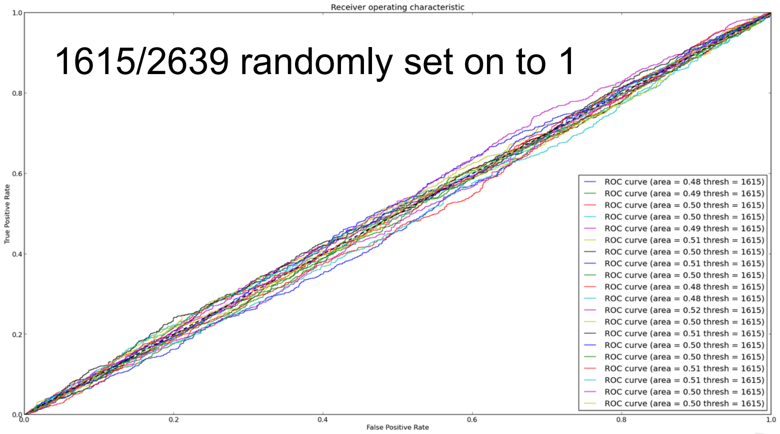


Permutation Runs on AUC Trends With Strength Thresholds



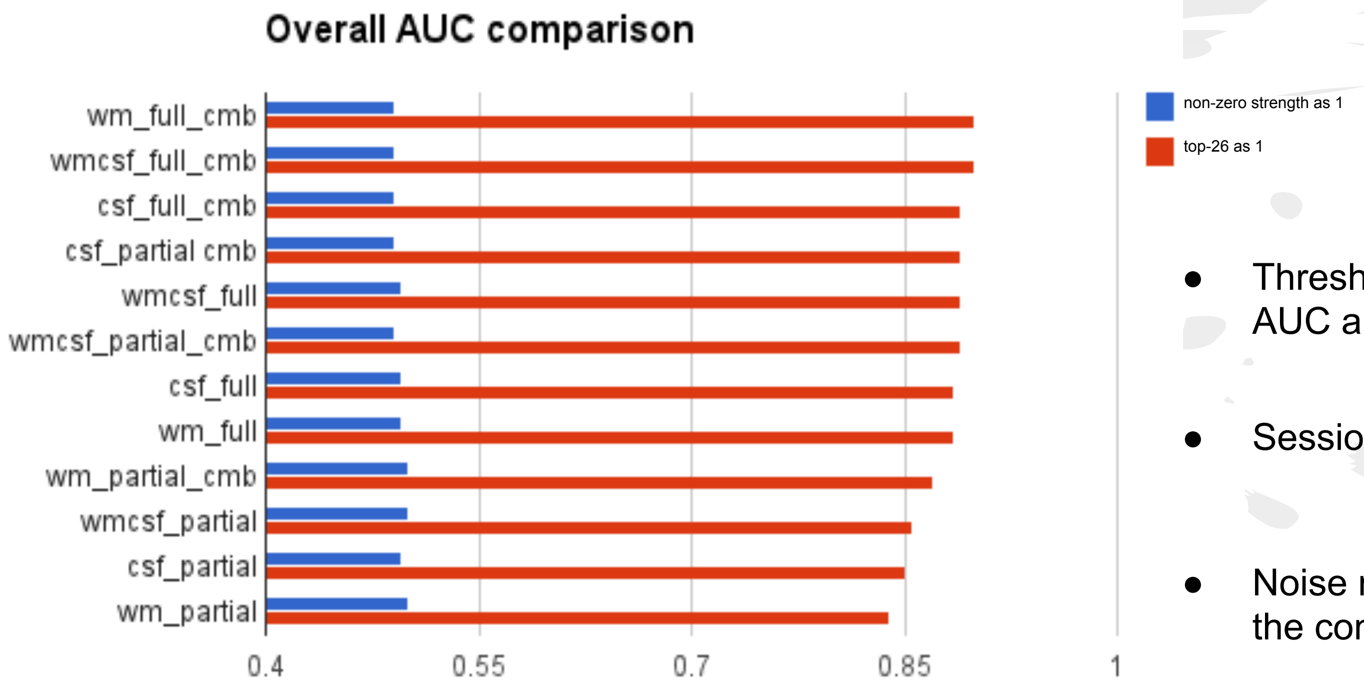






Overall Comparisons Under Strong Connections

Noise mask (wm, csf, wmcsf) | Full/partial correlation | Session combine/separation



- Thresholding on strength increases AUC a lot
- Session combine + full correlation
- Noise mask is not so differentiated in the comparisons

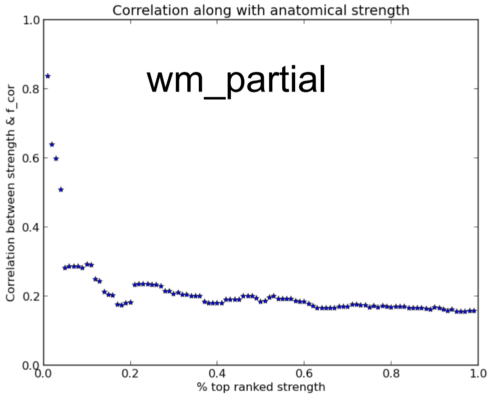
Correlation Trends With Anatomical Strengths

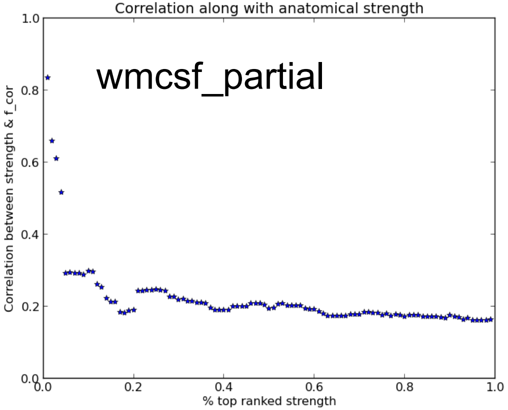
wm

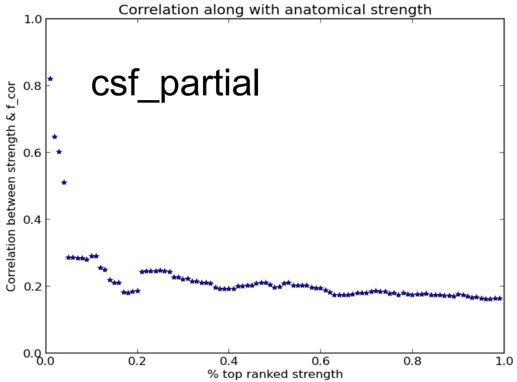
wmcsf

csf

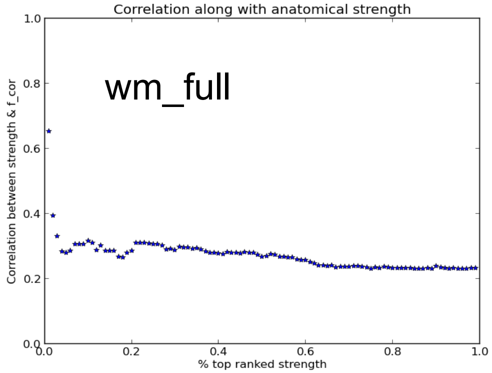
Partial

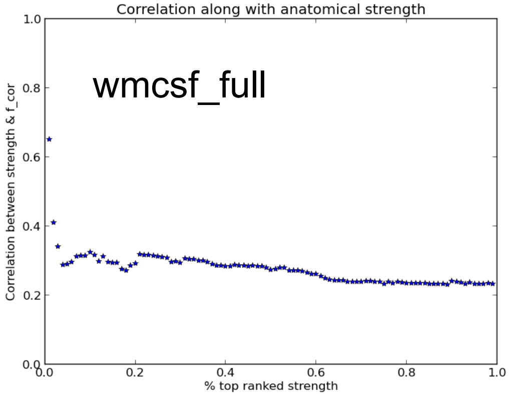


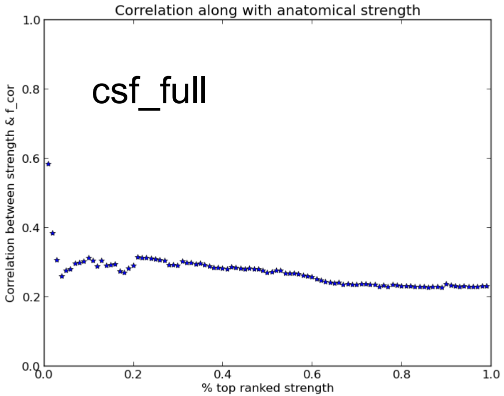




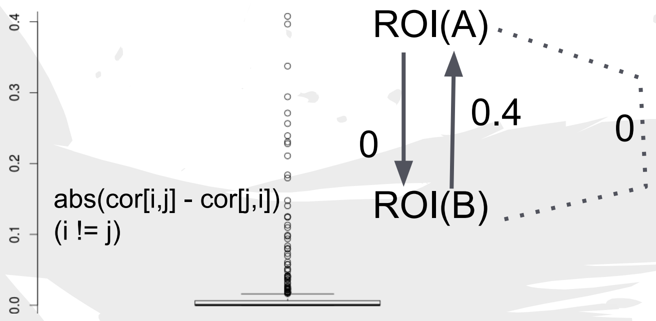
Full







Effect of Directed Connections in Gold Standard

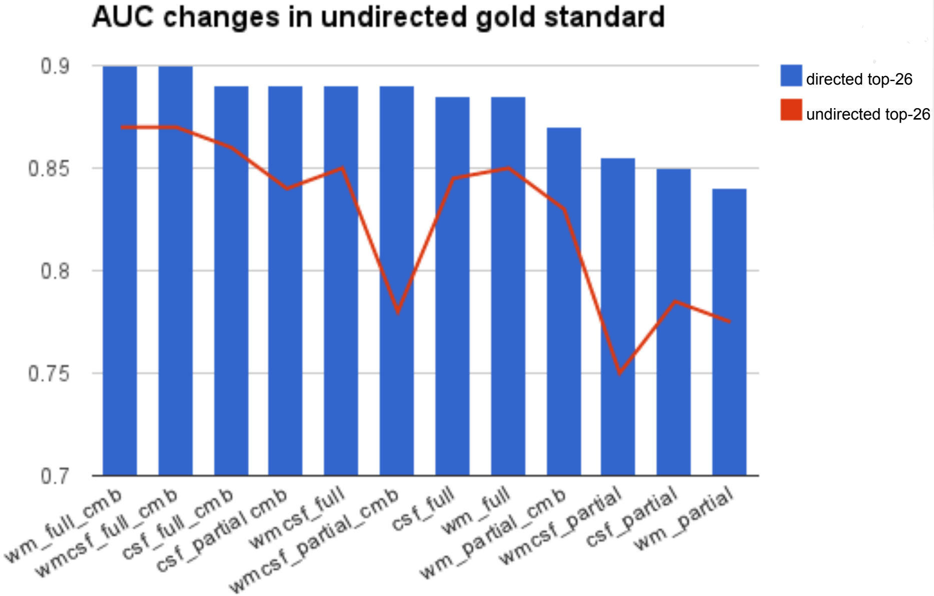


Directed graph to undirected graph of Gold Standard

ROI(A) $\underset{v2}{\overset{v1}{\rightleftarrows}}$ ROI(B) (directed connection)

avg(v1,v2) max(v1,v2)

ROI(A) $\overset{v'}{\text{———}}$ ROI(B) (undirected connection)



29 * 91 = 2639

{0-->1} = 108

108/2639 = 4%

Summary

- A pipeline to benchmark FC based on gold standard
- Not significant effect of directed connections in gold standard
- Taking strong strengths as ACs improves AUC & correlation a lot
- TODO list
    - Use first component instead of the average time series
    - Consider global signal regression in the preprocessing
    - Autocorrelation issue
    - ...

THANKS

Dr. Daniel S. Margulies

Dr. Alexandros Goulas

Dr. Chris Gorgolewski

THANKS

Multiple Testing Correction

	H0 True	H0 False
Not reject H0	TN	FN (type-2 error)
Reject H0	FP (type-1 error)	TP

Bonferroni: rejects any hypothesis with p-value <= a/m

- belong to family-wise error rate control strategy (FWER)
- the general H0 is rarely of interest
- high prob of type-2 errors
- type-1 error = overdiagnosis
- type-2 error = miss the early diagnosis

False discovery rate (FDR)

- Control the % of FP among the set of rejected hypotheses
- Benjamini and Hochberg FDR (BH)

* Benjamini and Hochberg FDR

- To control FDR at level δ:

1. Order the unadjusted p-values: $p_1 \leq p_2 \leq \ldots \leq p_m$
2. Then find the test with the highest rank, j, for which the p value, p_j, is less than or equal to (j/m) x δ
3. Declare the tests of rank 1, 2, …, j as significant

$$p(j) \leq \delta \frac{j}{m}$$

*http://www.gs.washington.edu/academics/courses/akey/56008/lecture/lecture10.pdf

Regression Error Characteristic Curves

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Abstract

Receiver Operating Characteristic (ROC) curves provide a powerful tool for visualizing and comparing classification results. Regression Error Characteristic (REC) curves generalize ROC curves to regression. REC curves plot the error tolerance on the x-axis versus the percentage of points predicted within the tolerance on the y-axis. The resulting curve estimates the cumulative distribution function of the error. The REC curve visually presents commonly-used statistics. The area-over-the-curve (AOC) is a biased estimate of the expected error. The R^2 value can be estimated using the ratio of the AOC for a given model to the AOC for the null model. Users can quickly assess the relative merits of many regression functions by examining the relative position of their REC curves. The shape of the curve reveals additional information that can be used to guide modeling.

1. Introduction

Receiver Operating Characteristic (ROC) curves have proven to be a valuable way to evaluate the quality of a discriminant function for classification problems (Egan, 1975; Swets et al., 2000; Fawcett, 2003). ROC curves address many of the limitations of comparing algorithms based on a single misclassification cost measure (Provost et al., 1998). An ROC curve characterizes the performance of a binary classification model across all possible trade-offs between the false negative and false positive classification rates. An ROC graph allows the performance of multiple classification functions to be visualized and compared simultaneously. ROC curves can be used to evaluate both expected accuracy and variance information. ROC curves are consistent for a given problem even if the distribution of positive and negative instances is highly skewed. The area under the ROC curve (AUC) represents the expected performance as a single scalar. The AUC has a known statistical meaning: it is equivalent to the Wilcoxon test of ranks. Fundamentals of interpreting ROC curves are easily grasped. ROC curves are effective tools for visualizing results for non-experts as well as experts and help them make more valid conclusions. For example, a non-expert can see that two functions have similar ROC curves and can conclude that there is no significant difference between the functions even though one may have a larger classification cost. Currently ROC curves are limited to classification problems.

The goal of this paper is to devise a methodology for regression problems with similar benefits to those of ROC curves. Our solution, the Regression Error Characteristic (REC) curve, plots the error tolerance on the x-axis versus the percentage of points predicted within the tolerance on the y-axis. The resulting curve estimates the cumulative distribution function (CDF) of the *error*. The *error* here is defined as the difference between the predicted value $f(\mathbf{x})$ and actual value y of response for any point $(\mathbf{x}, y)$. It could be the squared residual $(y - f(\mathbf{x}))^2$ or absolute deviation $|y - f(\mathbf{x})|$ depending on the error metric employed. Figure 1 provides an example of REC curves generated for industrial data. See Section 3 for more details.

REC curves behave much like ROC curves.

- REC curves facilitate visual comparison of regression functions with each other and the null model.
- The curve area provides a valid measure of the expected performance of the regression model. The REC curve estimates CDF of the error. The area **over** the curve (AOC) is a biased estimate of the expected error.
- The REC curve is largely qualitatively invariant to choices of error metrics and scaling of the resid-

Proceedings of the Twentieth International Conference on Machine Learning (ICML-2003), Washington DC, 2003.