

ImageNomer

Developing an interactive graphical analysis tool for examining fMRI
and omics data

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Outline

1 Background on fMRI and omics

2 Introduction to ImageNomer

- Objective
- Architecture

3 Validation study on race confound in fMRI

- Dataset and methods
- Results: fMRI data predicts race, not intelligence
- Discussion

4 Conclusion



Background on fMRI and omics



fMRI Background

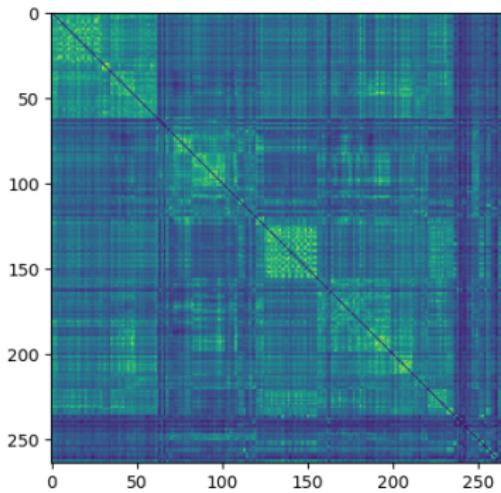
- fMRI is an endophenotype that has been used to predict age, sex, intelligence¹ and disease status, such as pre-clinical Alzheimer's disease²
- The most common way to interpret fMRI for prediction is through functional connectivity (FC)
- FC is the Pearson correlation between the BOLD signal of different brain regions (Equation 1)

$$\rho_{xy} = \frac{\sigma_{xy}^2}{\sqrt{\sigma_{xx}^2 \sigma_{yy}^2}} \quad (1)$$

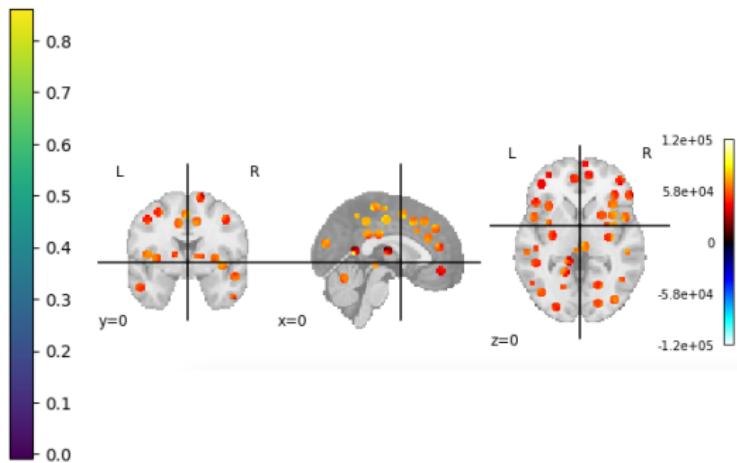
¹ Qu et al. 2021 10.1109/TBME.2021.3077875

² Millar et al. 2022 10.1016/j.neuroimage.2022.119228

Functional connectivity



mean FC of subjects in dataset



using 264 region Power template



Challenges: large cohort size and high dimensionality

- Both FC and genomic data contain up to tens of thousands of features
- Small effect size: SZ has more than 2,000 associated genes
- Only 23% of SZ variance can be explained by SNPs³
- Likewise, the effect size of a single functional connectivity (FC) feature may be very small⁴
- fMRI datasets may range in size from small (<100 subjects), to large (PNC <2,000 subjects), to huge (UKBB 50,000 subjects)

³Lee et al. 2012 10.1038/ng.1108

⁴Orlichenko et al. 2022 10.1109/TBME.2022.3232964

Introduction to ImageNomer



ImageNomer objective

Problem 1: Quality Control

In large datasets, a researcher may not even look at every FC matrix (or other type of data)

Problem 2: Dataset Familiarity

How to find relationships, explore data, and get basic statistics on a dataset?

Our solution

Exploration

We create a browser-based tool to visualize subjects and get statistics about a dataset

Correlation

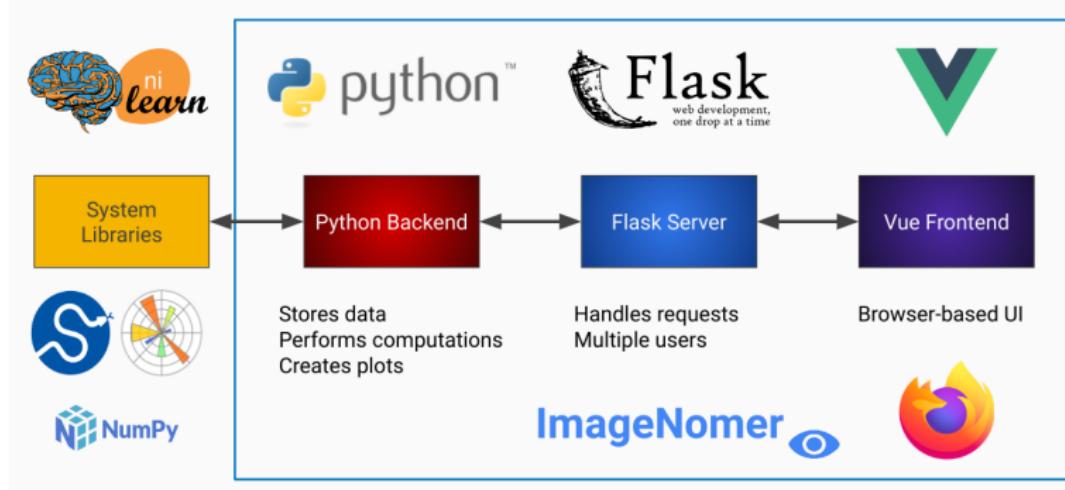
Quickly find correlations between images, phenotypes, and genomics data

Analysis

Summarize and get distribution of weights from machine learning models



ImageNomer architecture



ImageNomer capabilities

- Functional (FC) and partial correlation (PC) connectivity views
- Correlation analysis
- p-value maps for correlations
- Image math
- FC decompositions (such as PCA)
- Visualize weights from machine learning models



ImageNomer screenshot

Screenshot of functional connectivity view in ImageNomer

ImageNomer

test cohort: [Upload Data](#) [All Cohorts](#)

[GitHub](#) [Bugs](#) [Settings](#) Logged in: [Anton](#) [Sign out](#)

Subjects

830 subjects (0 selected)

- 600009963128
- 600018902293
- 60020927179
- 60031697545
- 60038720566
- 60039015048

[Filter Subjects](#)

Groups

Create groups based on phenotypes e.g., "age > 180" or "sex == F" and age < ..

Group Query [CREATE](#)

All (830)

Phenotypes

age: min: 103.0 mean: 180.9 max: 271.0 (n=830)
 pvt_cr: min: 2.0 mean: 11.1 max: 15.0 (n=827)
 race_EA: 407 AA: 326 EAAA: 19 OT: 16 AAHH + AA: 11... (24 others) (n = 830)
 sex_male: 382 female: 448 (n=830)

PHENOTYPES [FC](#) [PC](#) [SNPs](#) [DECOMPOSITION](#) [CORRELATION](#) [WEIGHTS](#) [IMAGE MATH](#)

Display Options

Task [rest](#) ID Task age pvt_cr race sex wrat

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | ... | 47 | > |
|------|---|---|--|--|--|---|---|---|---|---|---|
| rest | age: 116 pvt_cr: 14 race_EA: 9 sex_F: 114 wrat: 114 | rest age: 187 pvt_cr: 13 race_EA: 9 sex_F: 114 wrat: 145 | rest age: 190 pvt_cr: 12 race_EA: 9 sex_F: 114 wrat: 93 | rest age: 242 pvt_cr: 12 race_AA: 9 sex_M: 103 wrat: 10 | rest age: 137 pvt_cr: 11 race_EA,AA: 9 sex_F: 100 wrat: 100 | rest age: 139 pvt_cr: 11 race_EA,AA+AA: 9 sex_M: 101 wrat: 101 | rest age: 113 pvt_cr: 9 race_EA: 9 sex_M: 112 wrat: 112 | rest age: 210 pvt_cr: 12 race_EA: 9 sex_F: 95 wrat: 125 | rest age: 183 pvt_cr: 12 race_EA: 9 sex_F: 95 wrat: 125 | rest age: 115 pvt_cr: 13 race_EA: 9 sex_F: 103 wrat: 133 | |
| rest | age: 223 pvt_cr: 13 race_AA: 9 sex_M: 95 wrat: 95 | rest age: 190 pvt_cr: 12 race_EA: 9 sex_F: 100 wrat: 98 | rest age: 197 pvt_cr: 13 race_EA: 9 sex_F: 100 wrat: 91 | rest age: 145 pvt_cr: 13 race_AA: 9 sex_M: 99 wrat: 91 | rest age: 148 pvt_cr: 9 race_AA: 9 sex_F: 98 wrat: 88 | rest age: 142 pvt_cr: 7 race_AA: 9 sex_F: 103 wrat: 103 | rest age: 176 pvt_cr: 14 race_EA: 9 sex_M: 108 wrat: 108 | |

Create summary image: [MEAN](#) [STANDARD DEVIATION](#)

ImageNomer subjects panel

ImageNomer

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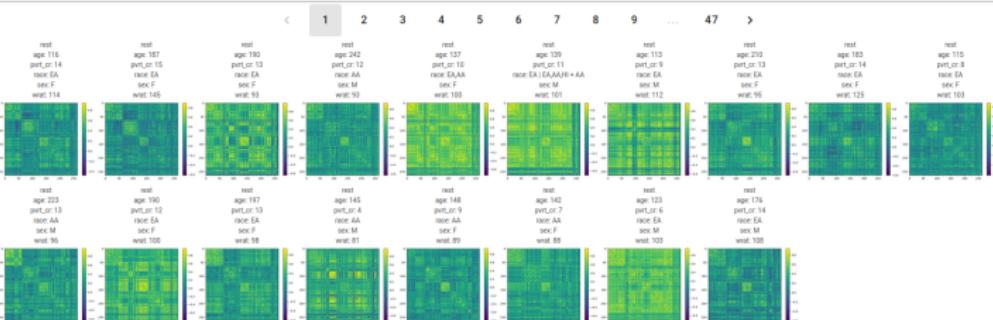
age

pvt_cr

race

sex

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ImageNomer groups panel

ImageNomer

test cohort Upload Data All Cohorts

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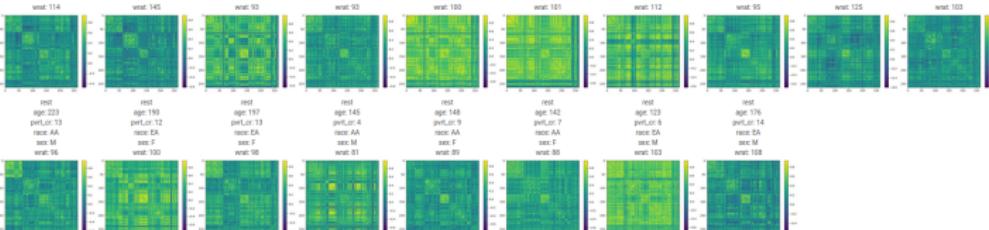
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Create summary image:

MEAN **STANDARD DEVIATION**



ImageNomer phenotypes panel

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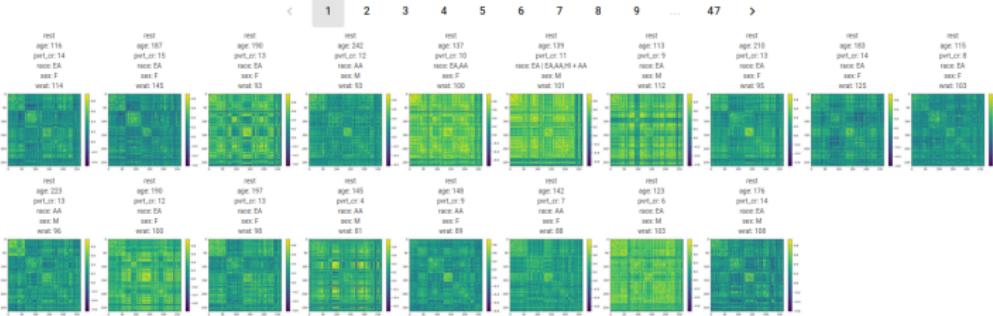
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ImageNomer tabs

ImageNomer

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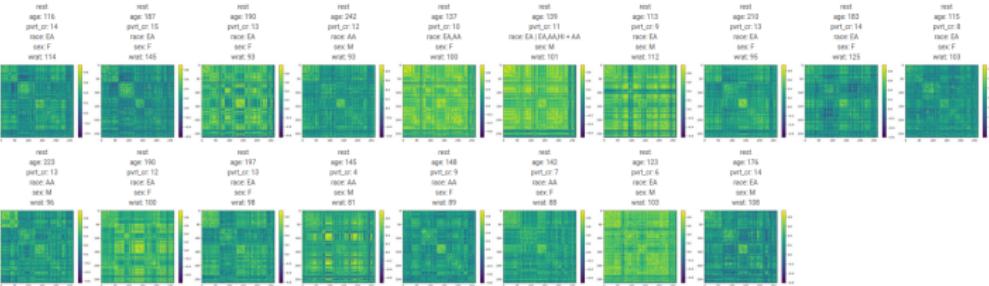
age

pvt_cr

race

sex

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Create summary image:

MEAN STANDARD DEVIATION



ImageNomer FC explorer view

ImageNomer

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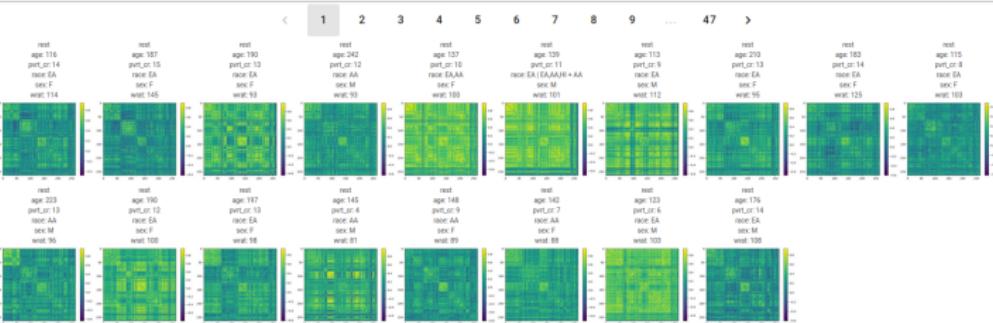
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Create summary image:

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[STANDARD DEVIATION](#)



ImageNomer summary image

ImageNomer

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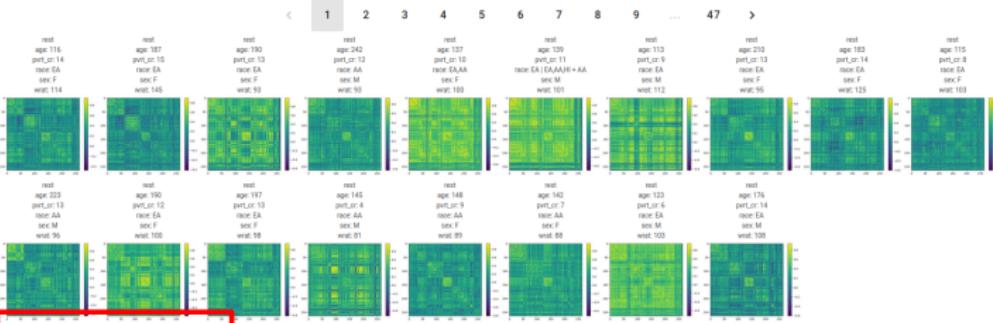
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Create summary image:

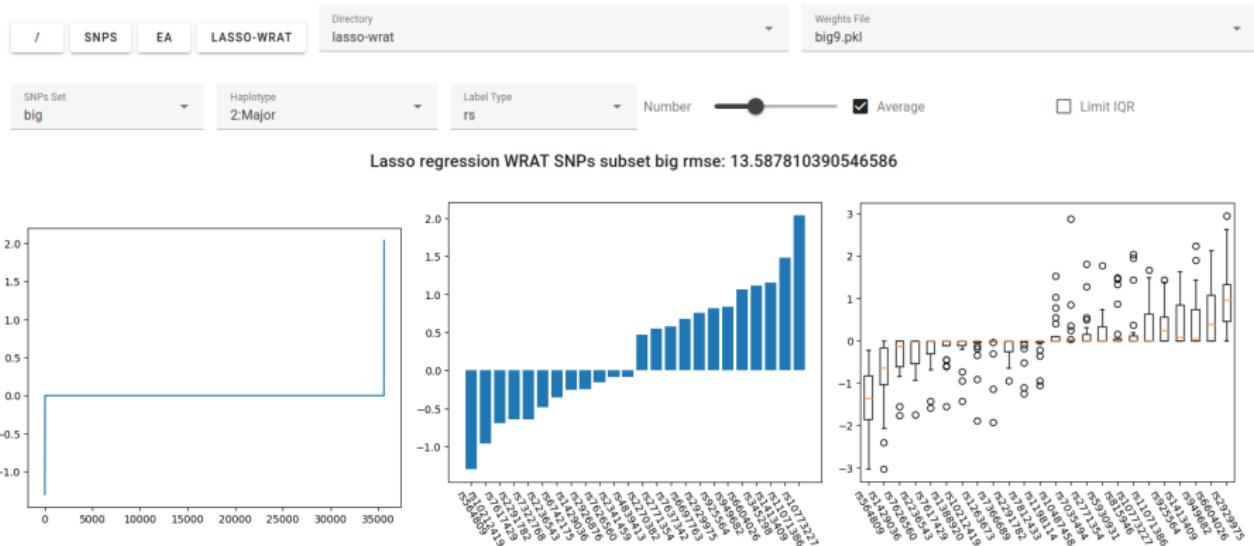


ImageNomer and model weights

Weights

Compare model weights from analysis runs

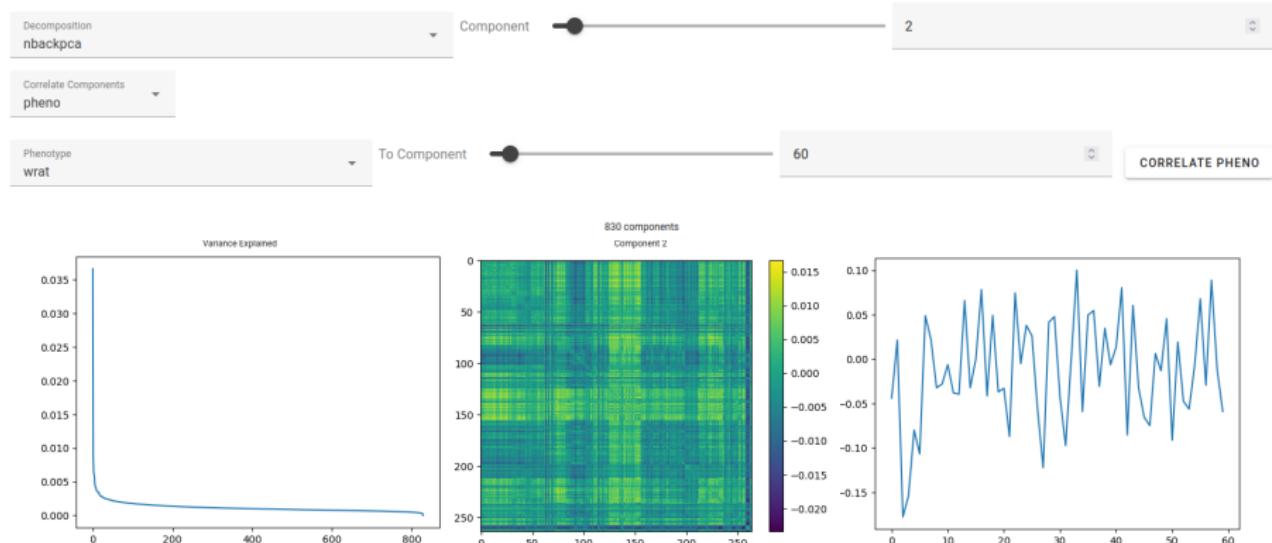
FC/PARTIAL SNPS



ImageNomer and decomposition

Decomposition

Decomposition of FC, PC, and SNPs into lower-dimensional representations



Validation study on race confound in fMRI



Previous studies potentially confounded by race

- Previous studies (by the authors and others) have identified small effects of FC on intelligence
- Other studies have found that dynamic connectivity predicts which social group subjects identify with⁵
 - 80 adolescent males
 - No attempt was made to control for ethnicity



⁵ Schmalzle et al. 2017 10.1073/pnas.1616130114

Preview of validation study findings

FC can legitimately predict age and sex

- FC explains 35% of variance in age, and only 10 features can explain up to 15%
- Sex prediction accuracy is 78%

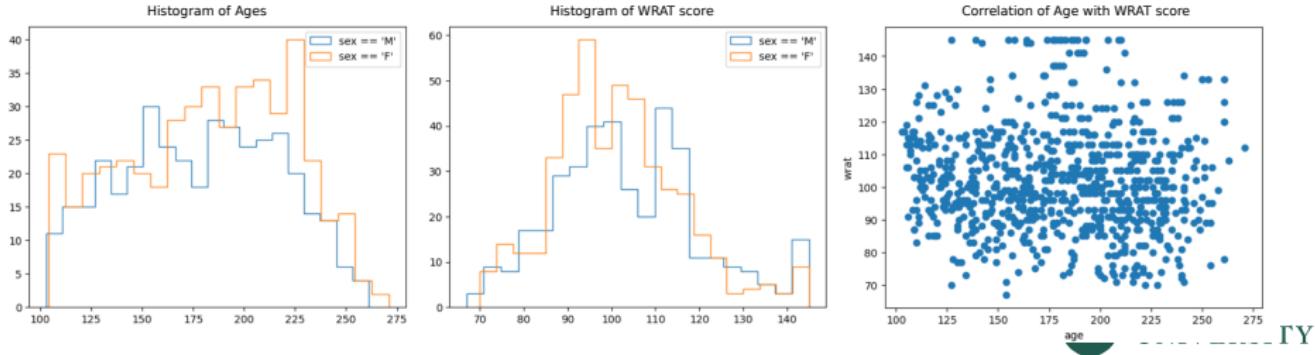
FC predicts race, not intelligence

- FC explains 10% of variance in intelligence, as measured by cognitive battery
- Race prediction accuracy is 85%
- Controlling for race removes any ability to predict intelligence



Dataset: Philadelphia Neurodevelopmental Cohort

- fMRI scans for 1,445 healthy adolescents and SNP data for more than 9,267
- 8-23 years old
- Used 830-subject subset with 3 scanner tasks
- Dataset enriched for European (EA) and African (AA) ancestry
- Intelligence measured by WRAT = Wide Range Achievement Test (effect of age regressed out)



Methods

- Parcellation into 264-region Power atlas, followed by calculation of FC
- Set of 1,185,051 SNPs reduced to 35,621 that were found in at least 50 subjects
- We predict age, sex, intelligence (WRAT score), and race from FC and SNP data via Ridge and Logistic Regression
- We select 10 best features using model weights, LASSO weights, correlation, and greedy selection



Results

| Prediction | Modality | Metric | Null Model | Best Full Model | Best 10 Features |
|-------------------|----------|------------------|------------|-----------------|------------------|
| Age | FC | RMSE, months | 38.4 | 26 | 32.2 |
| Intelligence | FC | RMSE, WRAT score | 15.1 | 13.6 | 15.1 |
| Intelligence | SNPs | RMSE, WRAT score | 15.1 | 14 | - |
| Intelligence (AA) | FC | RMSE, WRAT score | 13.9 | 13.8 | 13.9 |
| Intelligence (AA) | SNPs | RMSE, WRAT score | 13.9 | 13.4 | - |
| Intelligence (EA) | FC | RMSE, WRAT score | 14 | 14.1 | 14 |
| Intelligence (EA) | SNPs | RMSE, WRAT score | 14 | 13.6 | - |
| Race | FC | Accuracy | 58% | 85% | 72% |
| Sex | FC | Accuracy | 51% | 78% | 62% |

Small ability to predict intelligence disappears when controlling for race.
Significant results in blue.



Race confound

Group Selection Panel

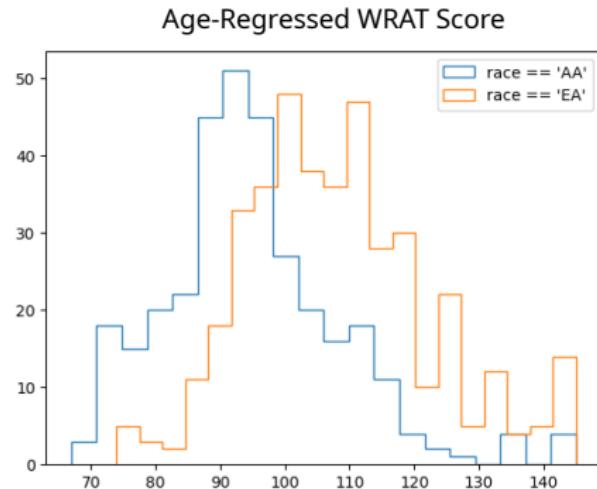
Groups

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Group Query
`sex == 'F'`

CREATE

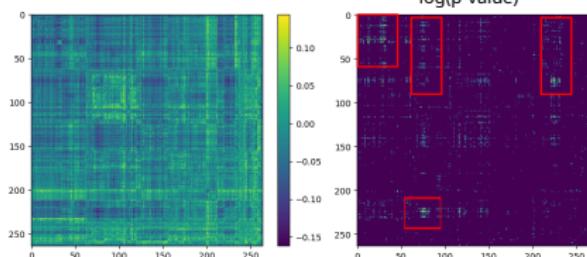
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- age < 160 (265)
- age > 160 (559)
- race == 'AA' (326)
- race == 'EA' (407)
- sex == 'M' (382)
- sex == 'F' (448)



Correlation analysis identifies problem

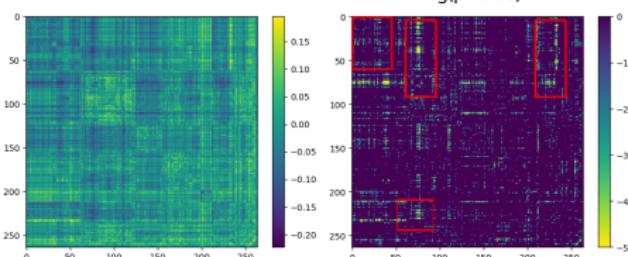
FC Correlation with WRAT Score

/analysis/corr/fc?cohort=test&query=All&field=wrat&fcType=fcl&remap



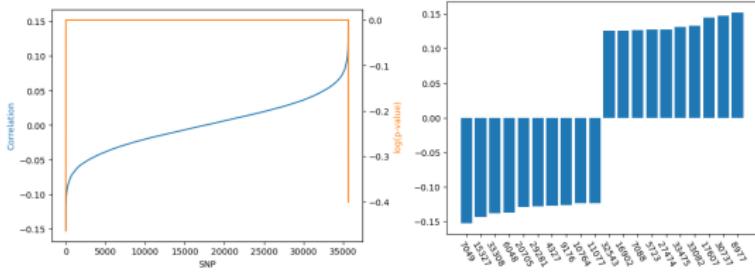
FC Correlation with European Ancestry

/analysis/corr/fc?cohort=test&query=All&field=race&fcType=fcl&remap&cat=EA

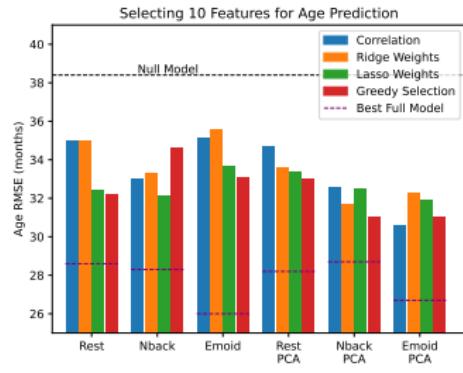


SNP Correlation with Age

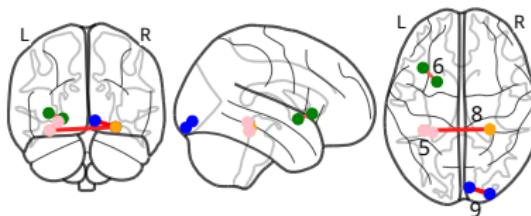
/analysis/con/snps?cohort=test&query>All&field=age&set=big&n=10&hap=2&labType=index



FC features legitimately predict age



Times in Top 10 Connections (Out of 12)



10 features selected in any manner can achieve 50% of full model variance explained

Conclusion



Conclusion

- We develop an easy to use visualization and analysis software for fMRI and omics data
- We perform correlation and machine learning analysis on the PNC dataset
- Age connectivity features are largely interchangeable, but the most predictive are either bilaterally symmetric or regionally proximal
- FC is not predictive of intelligence, but, surprisingly, is predictive of race
- Race prediction (85%) is more accurate than sex prediction (78%)
- All but 2 figures were created with ImageNomer



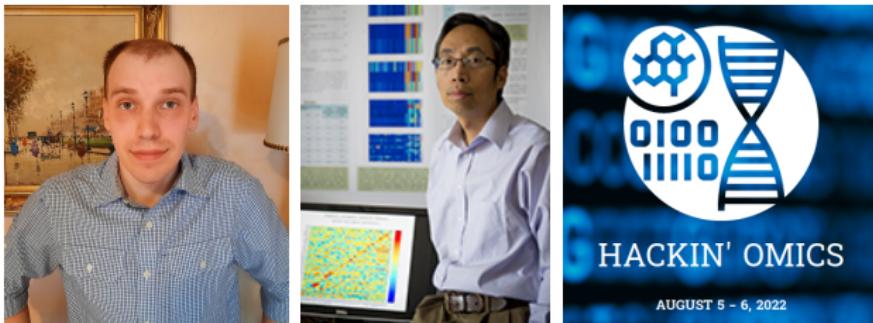
Future goals

- Apply ImageNomer to very large datasets (UKBB)
- Recruit developers and testers
 - Expand omics visualizations
- Identify biases and separate from true cognitive signal⁶
- <https://github.com/TulaneMBB/ImageNomer/>
- <mailto:aorlichenko@tulane.edu>



⁶ Tang et al. 2022 10.1101/2022.09.29.509744

Acknowledgements



- The authors would like acknowledge the NIH (grants R01 GM109068, R01 MH104680, R01 MH107354, P20 GM103472, R01 REB020407, R01 EB006841, R56MH124925) and NSF (#1539067) for partial funding support
- MRI, SNP, and phenotype data came from the Neurodevelopmental Genomics: Trajectories of Complex Phenotypes database of genotypes and phenotypes repository, dbGaP Study Accession ID phs000607.v3.p2
- Part of the software was developed at the 2022 University of Alabama at Birmingham UBRITE Multiomics Hackathon.⁷



⁷ <https://hackathon.ubrite.org/>