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New York State Psychiatric Institute

A Hierarchical Feature Extraction Pipeline using Resting-state fMRI for Autism Classification

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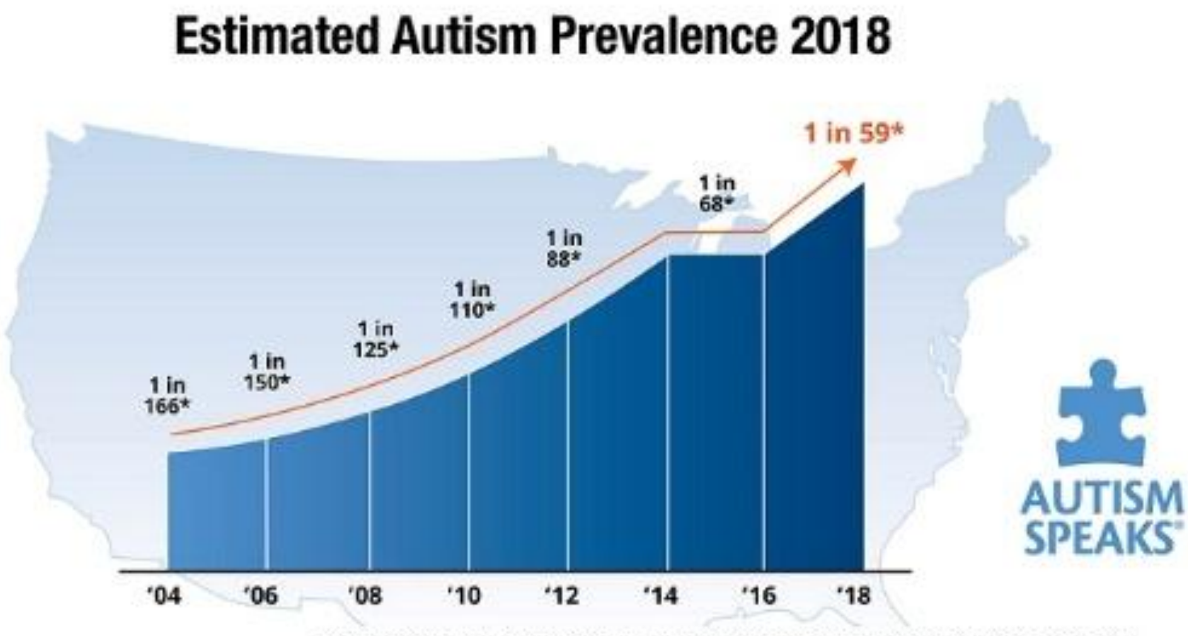
What is Autism Spectrum Disorder?

- Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder with core deficits in social communication and interaction as well as stereotypic behaviors.
- Prevalence: 1 in 59 children had a diagnosis of ASD by age 8 in 2014 (estimates are for 4 years prior to the report date)



Picture from https://www.autismspeaks.org/science-news/cdc-increases-estimate-autisms-prevalence-15-percent-1-59-children

Diagnosis of ASD

- Diagnostic and Statistical Manual for Mental Disorders (DSM), published by the American Psychiatric Association (APA). The first version (DSM-I) was published in 1952 and the most recent version (DSM-5) was published in 2013.
- "According to the DSM-5, a guide created by the APA used to diagnose mental disorders, people with ASD have:
  – Difficulty with communication and interaction with other people
  – Restricted interests and repetitive behaviors
  – Symptoms that hurt the person's ability to function properly in school, work, and other areas of life"

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5th Edition Washington, D.C.: American Psychiatric Association; 2013

Challenges of diagnosis of mental disorders

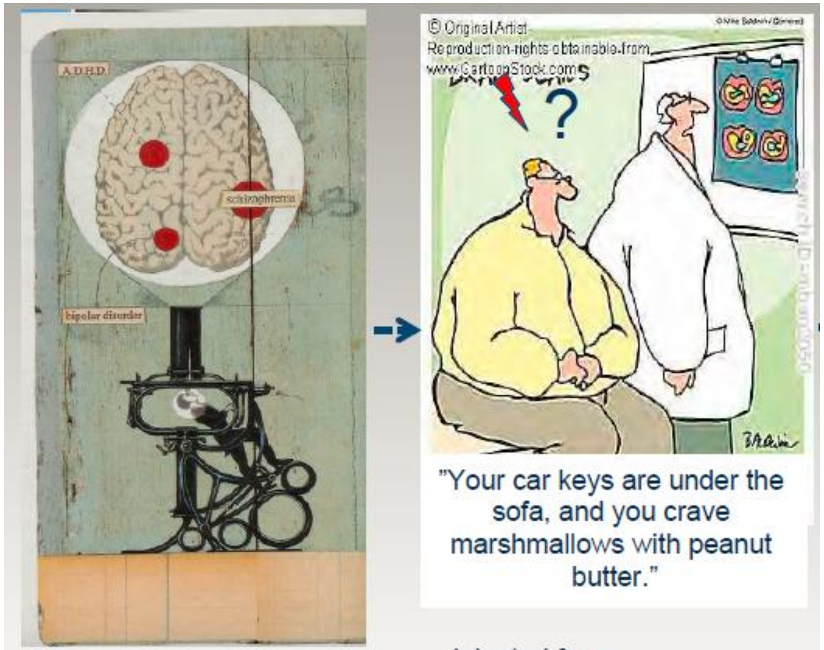
- Subjective: highly depends on assessments and psychiatrists experience

- Sensitivity (true positive rate) and specificity (true negative rate)

Can we objectively diagnose patients with mental disorders?

- All medical conditions except mental disorders can be objectively diagnosed by instruments
  - e.g., heart disease can be diagnosed by electrocardiograms (ECG/EKG). Similarly, blood sugar levels can be used for diagnosing patients with diabetes.
- Can a patient with mental disorders be objectively diagnosed by brain scans?
  - Not yet!

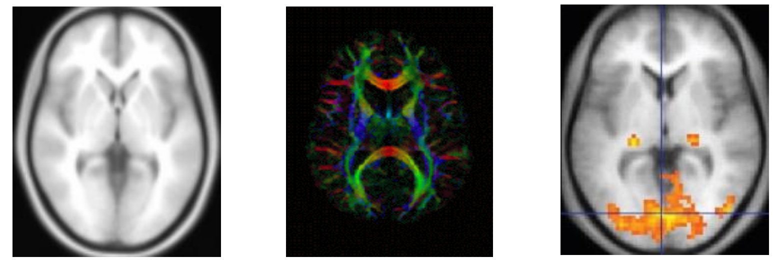
Brain scans



The Therapeutic Mind Scan (SPECT, fMRI, MRS) NYT, Feb. 20, 2005

Adapted from www.CartoonStock.com

Brain scans are usually used to identify brain biomarkers which would be used for differentiating healthy controls from patients, e.g., abnormal activity in motor cortex can be linked to ADHD patients.



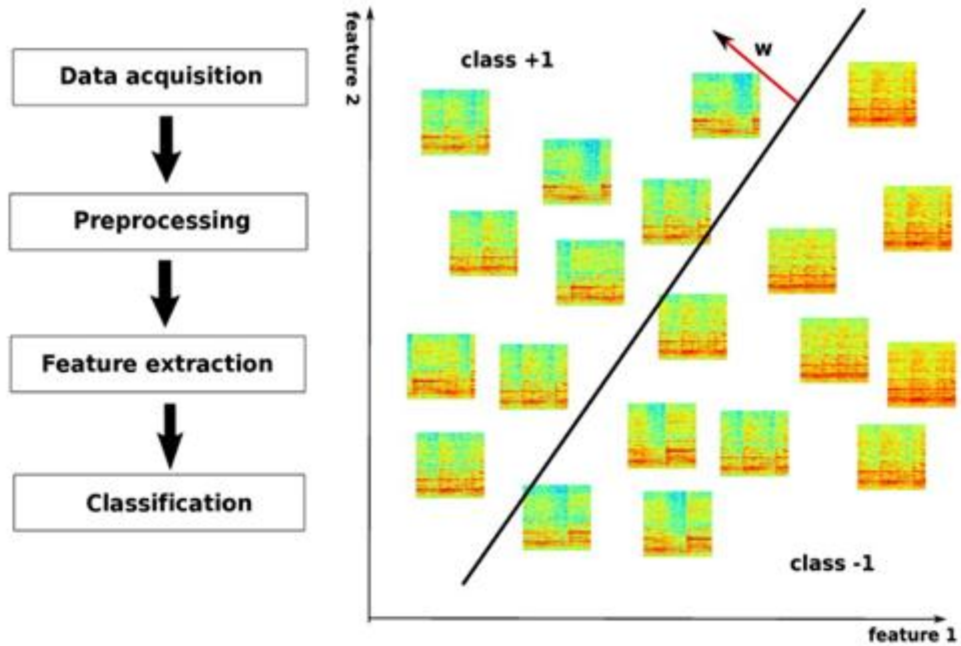
T1 weighed   DTI   task-fMRI

- Structural MRI (sMRI)
- Diffusion Tensor Imaging (DTI)
- Functional MRI (fMRI)
  - task fMRI (t-fMRI)
  - Resting state fMRI (rs-fMRI)
- …

ADHD: attention-deficit/hyperactivity disorder   Adapt from Stefan Posse, Real-Time Functional MRI, 2012

Classical methods for mental disorder classification

- Statistical methods
  - e.g., identify abnormal brain regions in ASD, such as thalamus and amygdala (Wee et al. 2014)
  - Problems: heterogeneity of ASD, Comorbidity in ASD (Masi et al. 2017)
- Machine Learning methods
  - Data-driven, such as logistic regression, SVM, Random Forest etc. (Abraham et al. 2014)
  - Limitations: Relatively small sample size (Wolfers et al. 2015). Also, impacted by the complex non-linear changes in volumetric (Courchesne et al. 2011a), morphometric (Ecker et al. 2014), and connectivity (Betzl et al. 2014) measures across the lifespan.



Workflow for classification of brain imaging data

[Adapted from https://ars.els-cdn.com/content/image/1-s2.0-S1053811910014163-gr1.jpg](https://ars.els-cdn.com/content/image/1-s2.0-S1053811910014163-gr1.jpg)

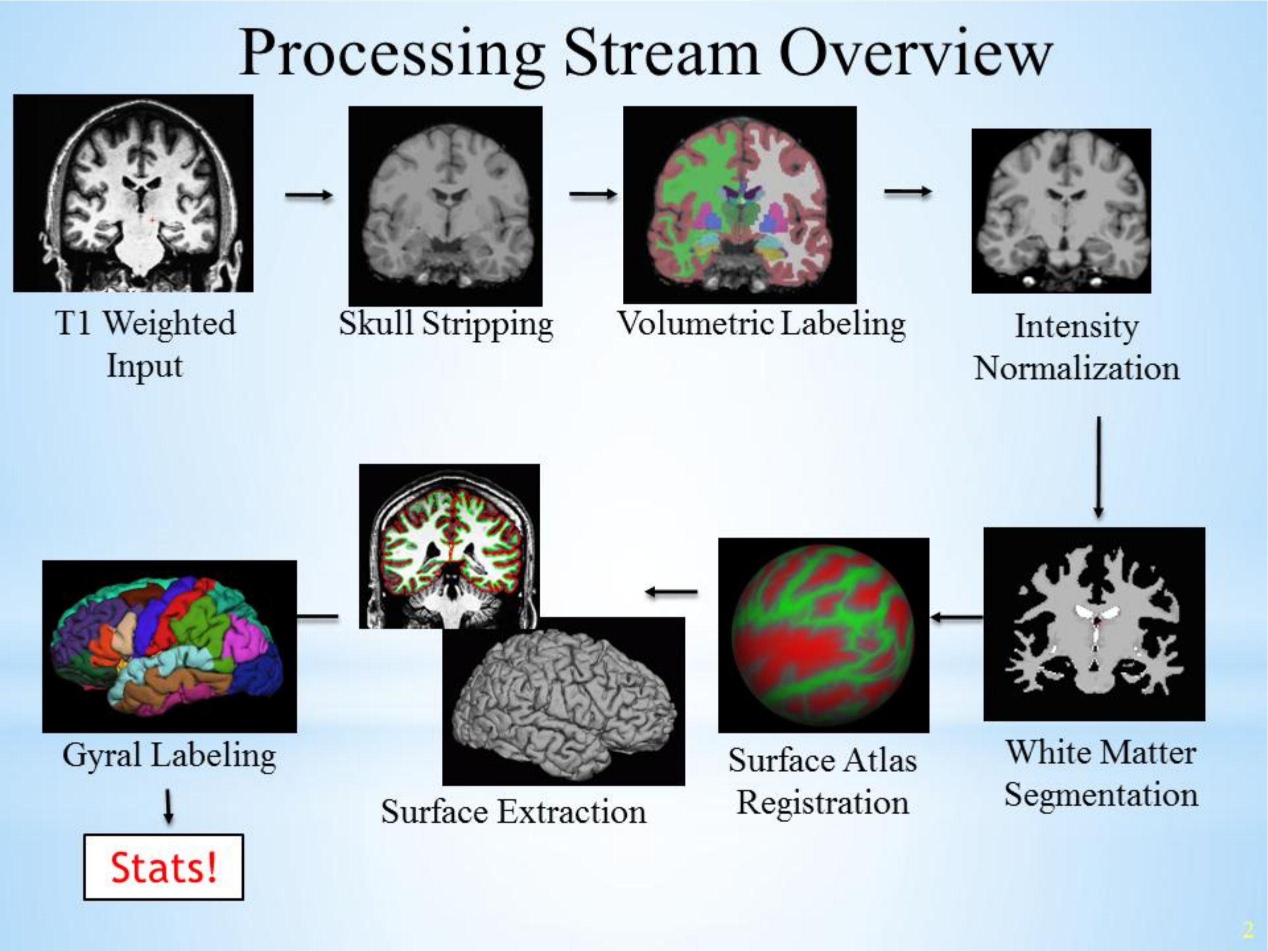
Our method: preprocessing

- Structural MRI (sMRI) data: a set of structural features have been extracted for each subject with normalized brain volume computed using subcortical segmentation, and cortical thickness and area for right and left hemisphere of Freesurfer output.
- Resting State functional MRI (rs-fMRI) data: create a functional connectivity map for each subject from the rs-fMRI signals based on different brain atlases, such as bootstrap analysis of stable clusters (BASC) parcellations (Bellec 2010), Ncuts parcellations (Craddock 2012) and Power atlas (Power 2011).

Mr. Jongwoo Choi

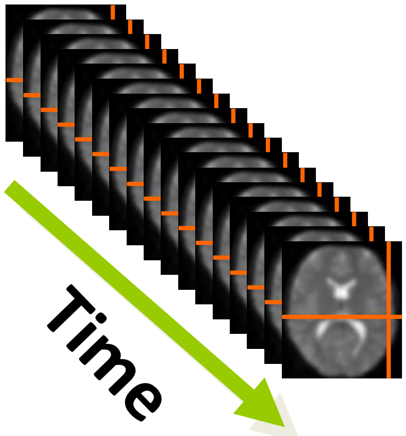
http://nbviewer.jupyter.org/github/ramp-kits/autism/blob/master/autism_starting_kit.ipynb

Structural MRI data preprocessing

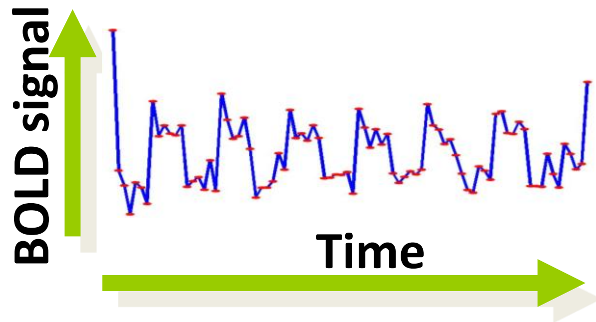


http://surfer.nmr.mgh.harvard.edu/fswiki/Tutorials

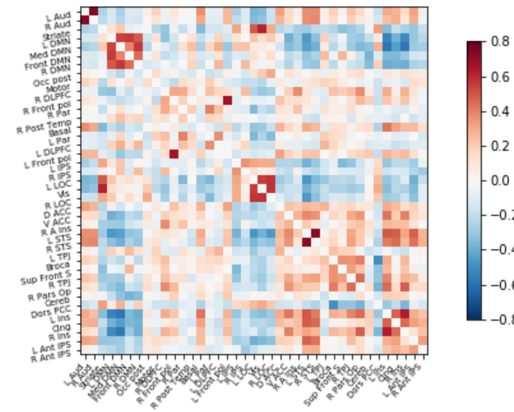
Rs-fMRI data preprocessing



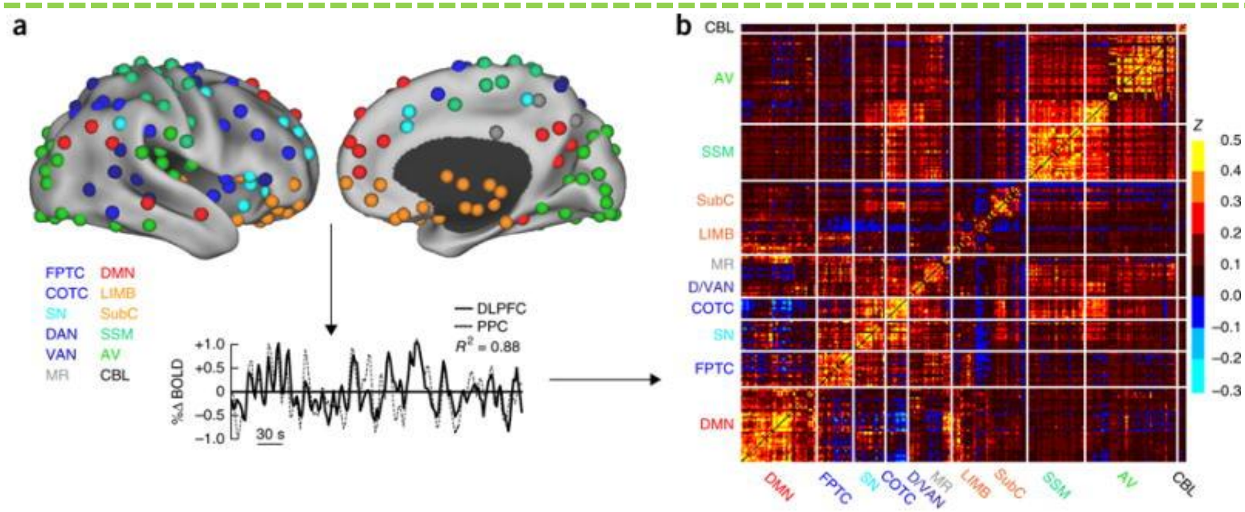
single voxel time series



Time series Extraction



Correlation Matrix



ROIs distributed across the cortex and subcortical structures with Power atlas (264 ROIs)

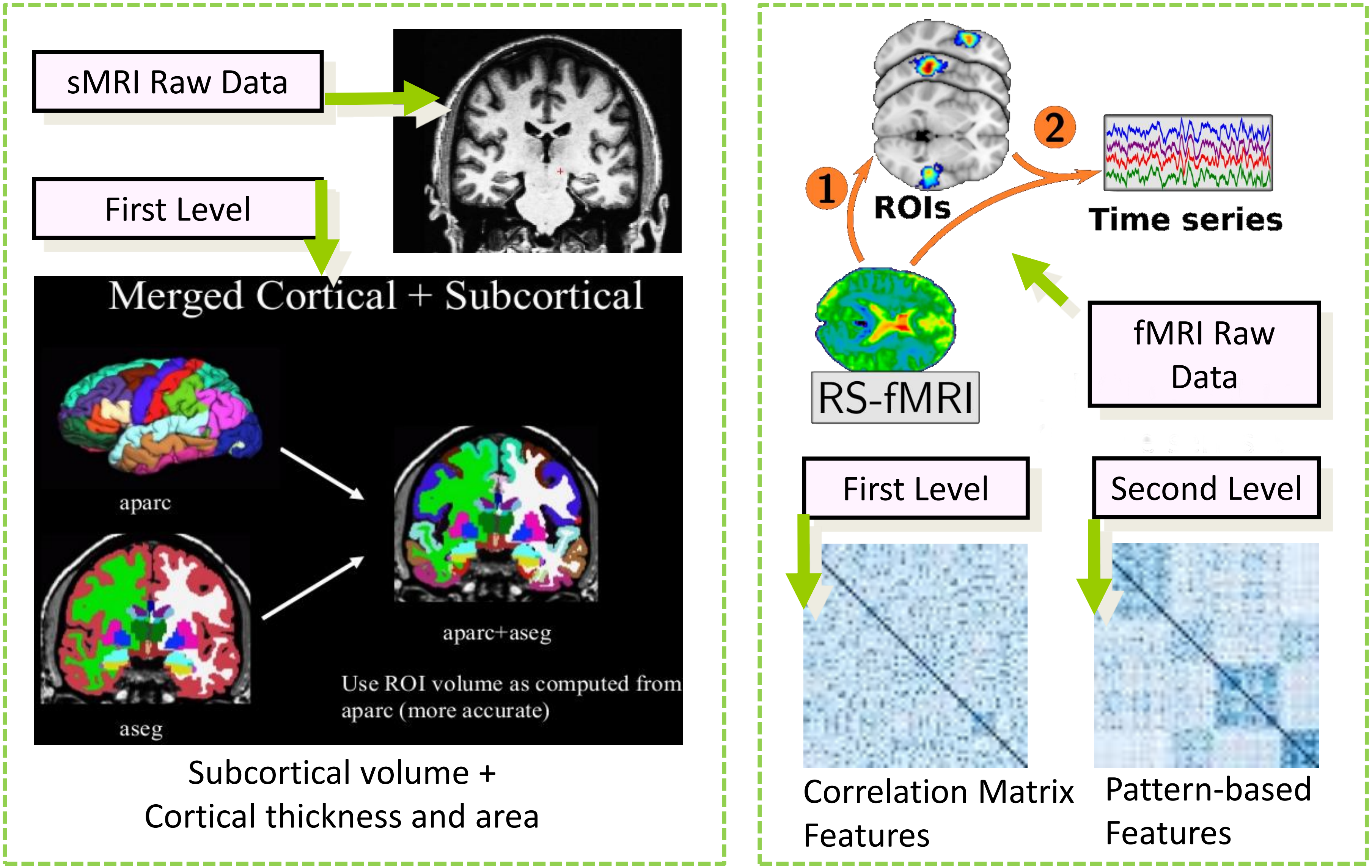
http://nilearn.github.io/auto_examples/ https://www.fil.ion.ucl.ac.uk/spm/course/slides16oct/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5624035/figure/F1/

Our method: feature selection

Ms. Qian Wang

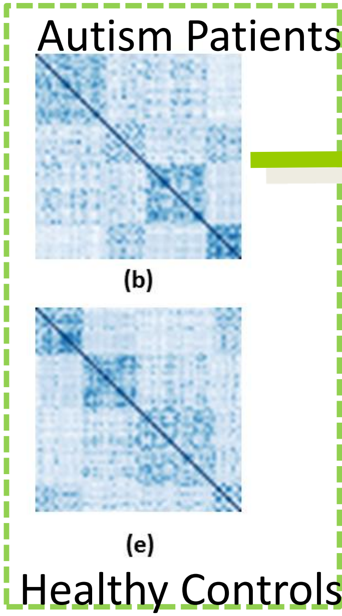
- Hierarchical feature selection pipeline consists of two steps: for the first level, the cortical thickness & area and sub-cortex volume features of sMRI and the functional connectivity features of rs-fMRI are extracted; for the second level, pattern-based features of functional connectivity are extracted from the first level features.
- Those hierarchical features are combined together and are put into random forest for feature selection, finally the top 205 features are extracted for classification.

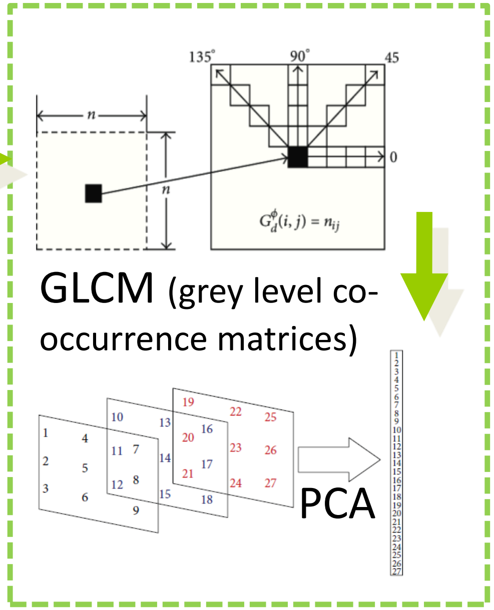
Hierarchical feature Extraction



http://nilearn.github.io/auto_examples/
http://nbviewer.jupyter.org/github/ramp-kits/autism/blob/master/autism_starting_kit.ipynb

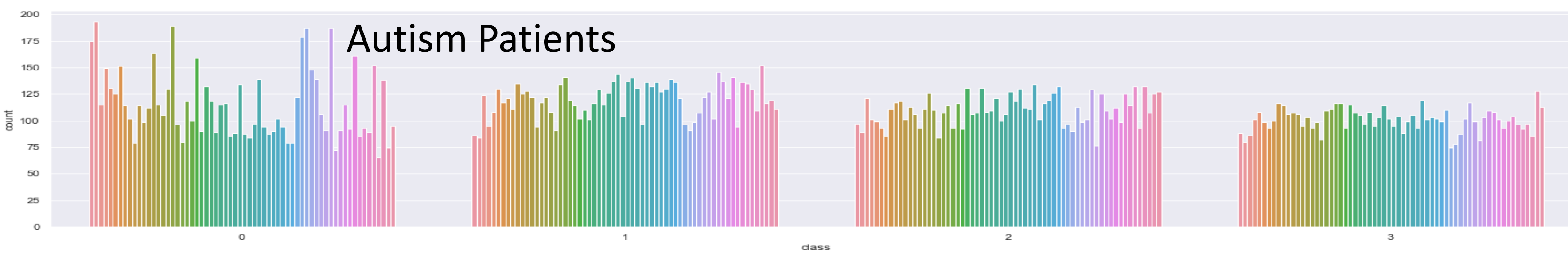
Pattern-based Features

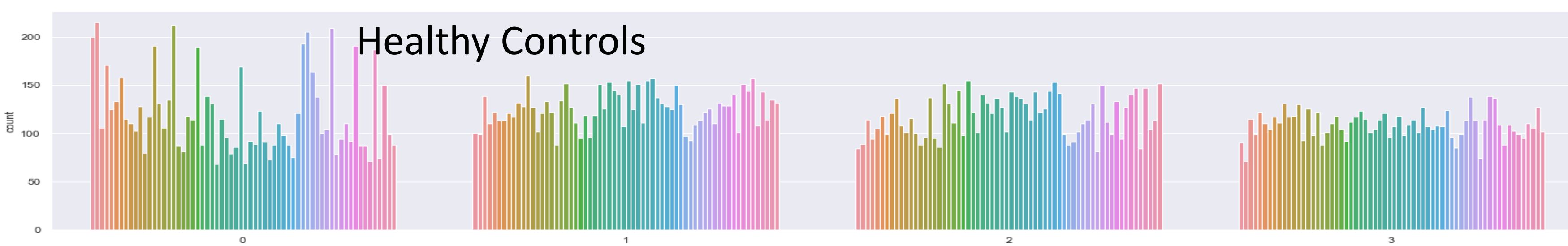




Spearman's correlation results of pattern-based features from Autism patients and Healthy controls:

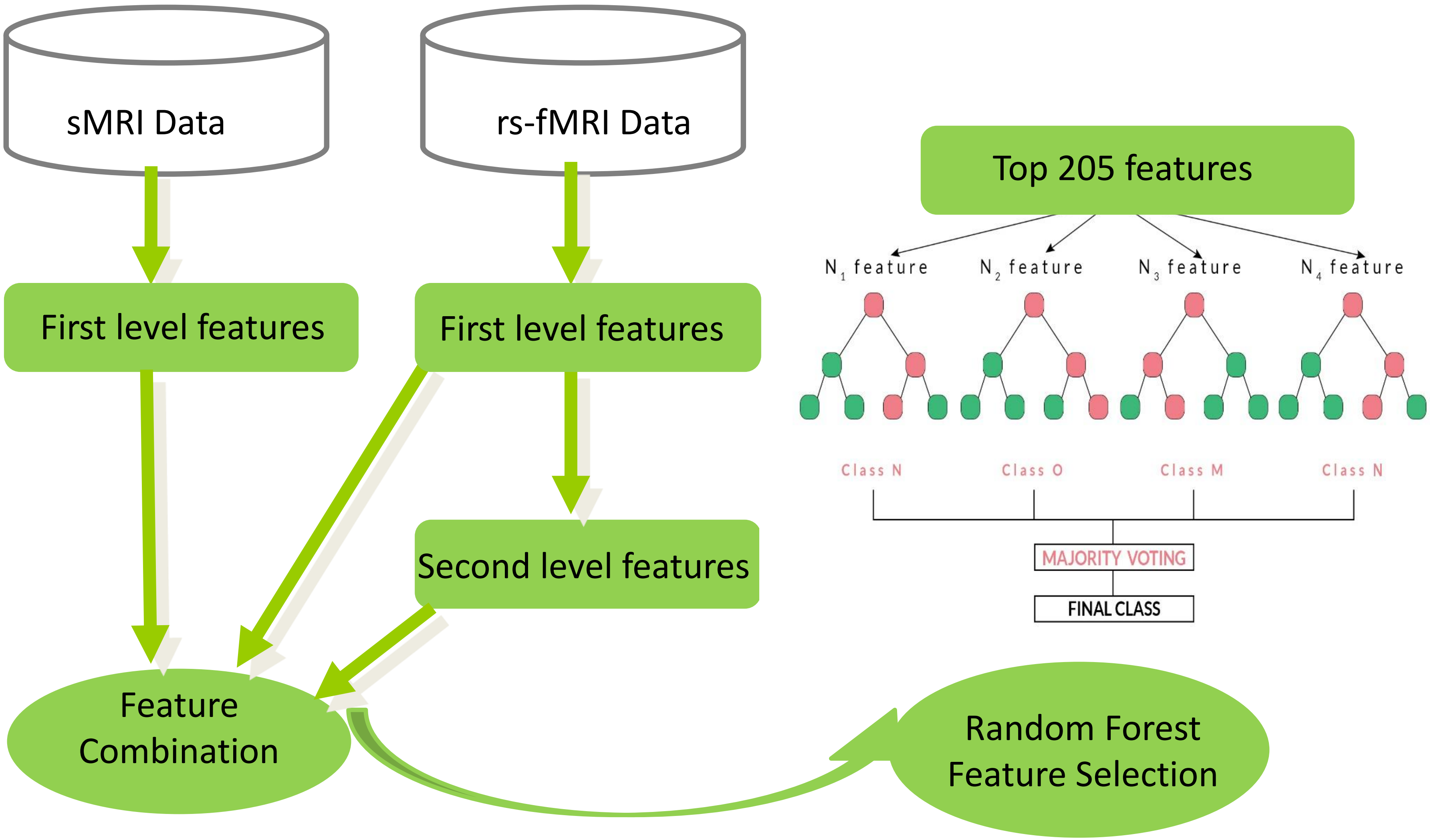
For class 0 : correlation=0.92, pvalue=4.5e-27
For class 1 : correlation=0.82, pvalue=1.6e-16
For class 2 : correlation=0.80, pvalue=1.1e-15
For class 3: correlation=0.69, pvalue=3.6e-10





GLCM illustration comes from https://www.researchgate.net/publication/277313083_638563

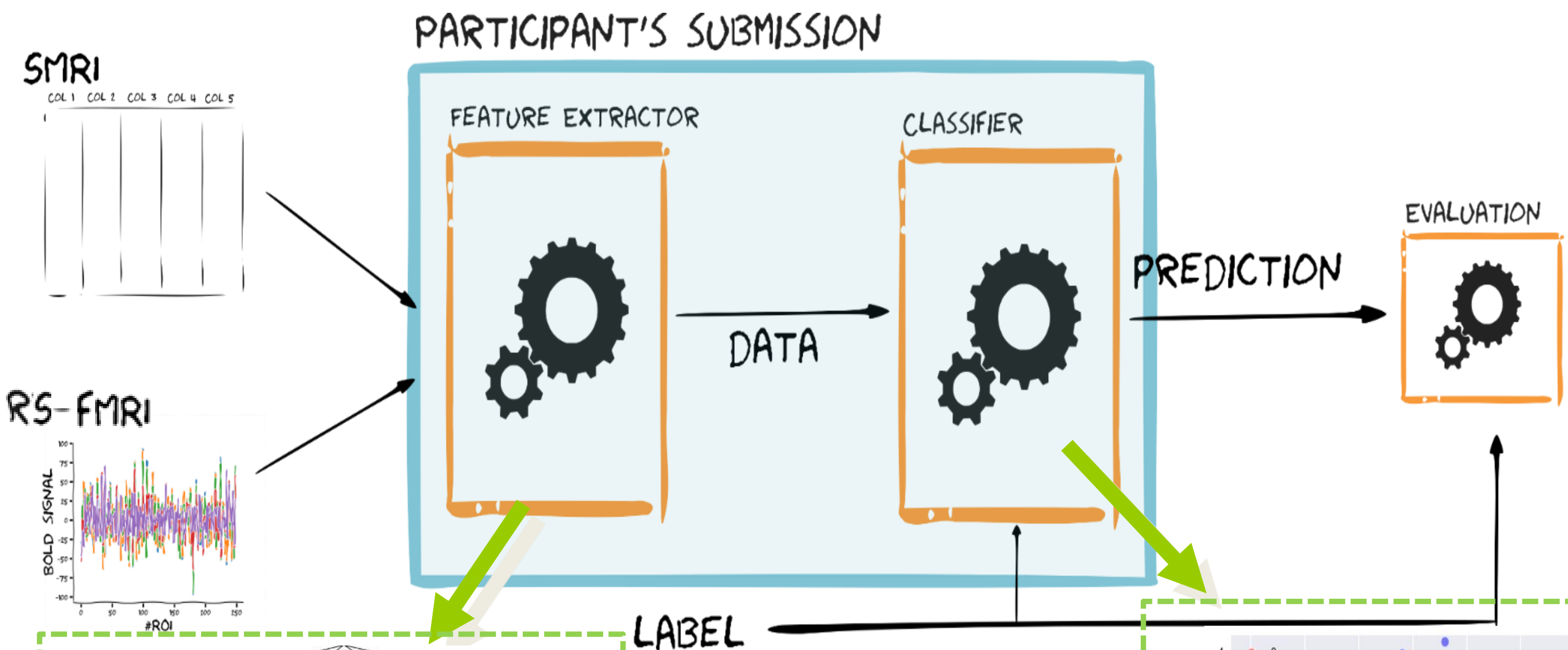
Hierarchical feature Selection

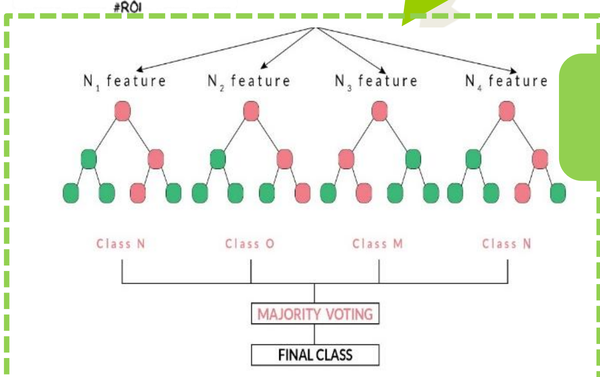


https://blog.quantinsti.com/random-forest-algorithm-in-python/

Our method: classification

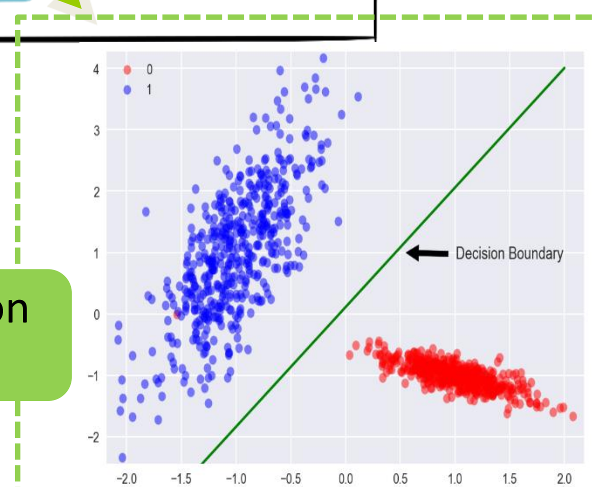
- Method1: Feature selection + classification





Random Forest Feature Selection

Logistic Regression Classifier

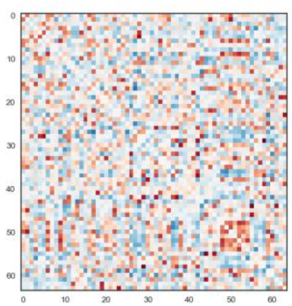


http://nbviewer.jupyter.org/github/ramp-kits/autism/blob/master/autism_starting_kit.ipynb

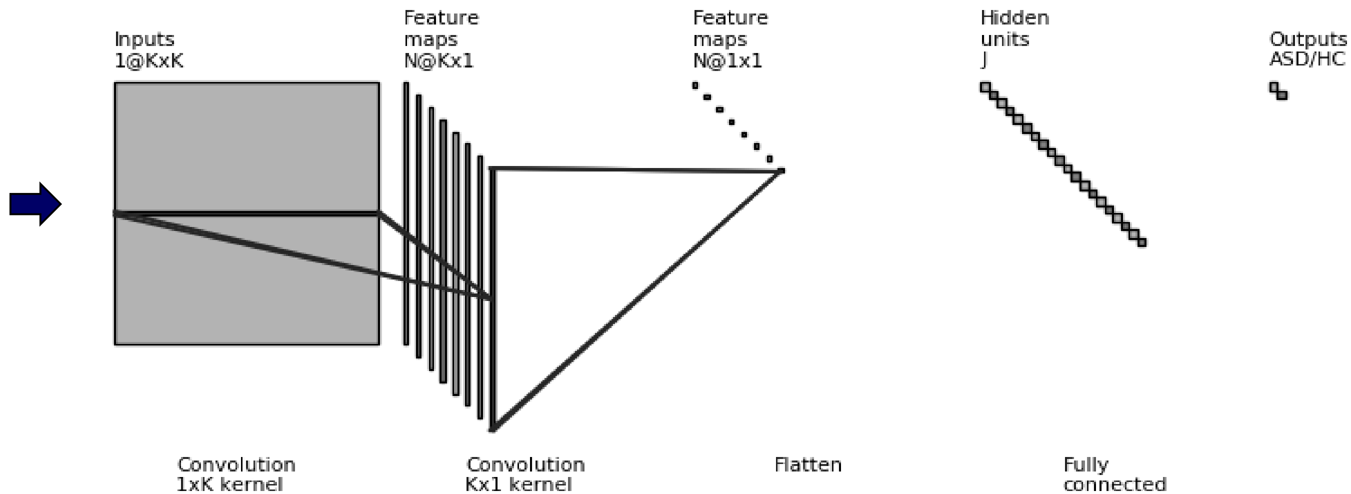
https://github.com/trekhleb/machine-learning-octave/tree/master/logistic-regression

Method2: Convolutional Neural Network

- We proposed a CNN model, where row-by-row and column-by-column filters form the first two convolution layers. We then added a fully connected layer followed by an output softmax layer that outputs probability of each class. For instance, for a functional connectivity matrix with size K*K (row *col), we used N filters with kernel size of 1*K and K*1.



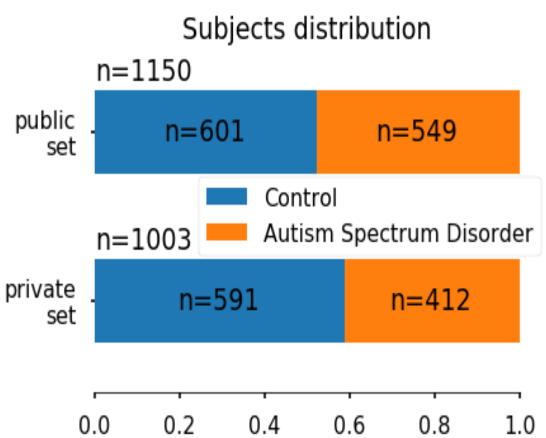
K*K correlation matrix

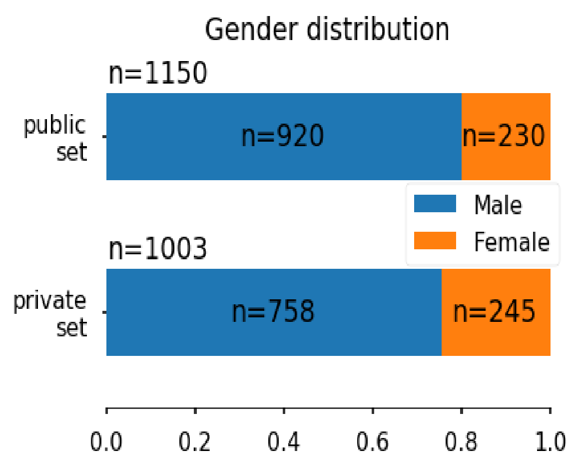


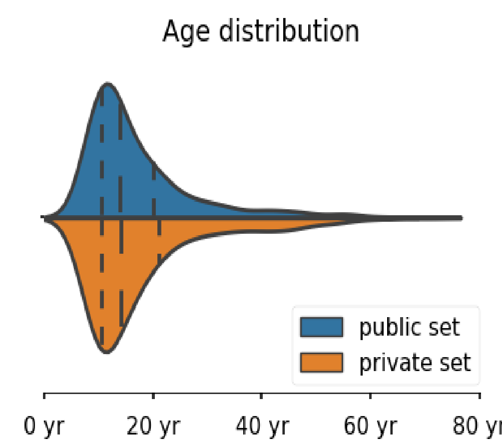
In the experiment, the parameters are set : K=(64, 122, 197 respectively). Please see details in our poster (Poster Session 2, Poster#5: Classification of Autism Spectrum Disorder Based on Brain Imaging Using Convolutional Neural Networks)

Datasets

- Data we used for this project is available at https://paris-saclay-cds.github.io/autism_challenge/ and initially published for competition: Imaging-psychiatry challenge: predicting autism (IMPAC). The data contained 1150 subjects (601 health controls and 549 ASD patients). Age range: 5~64.







Picture from https://paris-saclay-cds.github.io/autism_challenge/

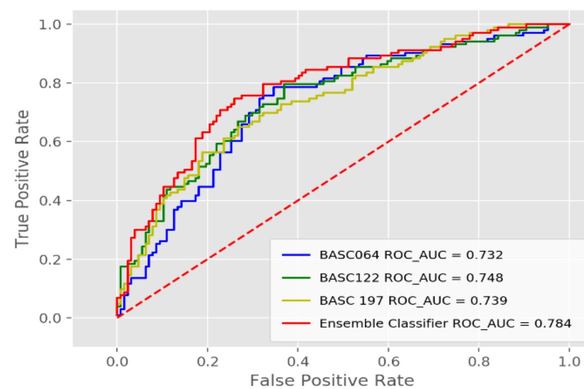
Results

- Method 1: Feature selection + classification (cv=8)

	Accuracy		AUC	
	First-level	First + Second level	First-level	First + Second level
Logistic Regression	**0.78**	0.75	0.85	0.83
SVM	0.58	**0.77**	0.62	0.86
Naïve Bayes	0.75	0.73	0.82	0.81
AdaBoost	0.72	0.71	0.81	0.80

- Method 2: We trained a classifier using the proposed CNN model for each BASC atlas separately and combined all three classifiers through majority vote (Ensemble). (Training 920 (80%) vs Testing 230 (20%))

	Accuracy	Sensitivity	Specificity	AUC
BASC 64	0.7	0.69	0.72	0.73
BASC 122	0.7	0.69	0.71	0.75
BASC 197	0.64	0.7	0.68	0.74
Combined	**0.72**	0.72	0.75	0.78



ROC curve for BASC 64, BASC 122, BASC 197 and Ensemble Classifier

Summary

- Challenges:
  - Small sample size (MRI is too expensive!)
  - Standardization of data acquisition, preprocessing, and atlas selection.
  - Test-retest reliability
- Future work
  - Unsupervised machine learning
  - Interpretable machine learning

Thank you!