Jointly Discriminative and Generative Recurrent Neural Networks for Learning from fMRI

Nicha C. Dvornek, Xiaoxiao Li, Juntang Zhuang, and James S. Duncan

MLMI 2019
Shenzhen, China
October 13, 2019

Yale SCHOOL OF MEDICINE

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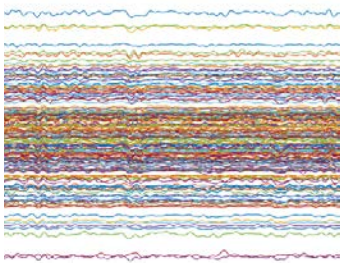
Investigate Neurological Disorders/Diseases with Functional MRI + Machine Learning

fMRI

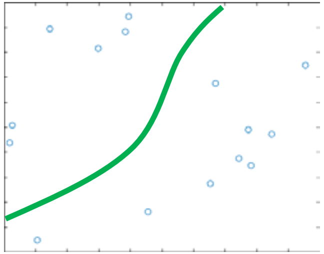
Brain Parcellation


[1]

fMRI ROI
Mean Time Series



Machine Learning
Algorithm



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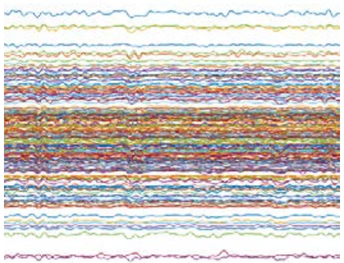

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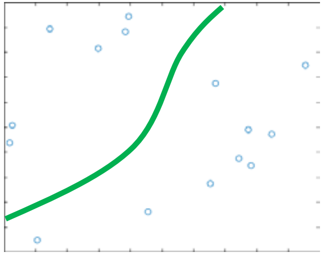

Example applications: Classify disease state
Identify biomarkers for disease

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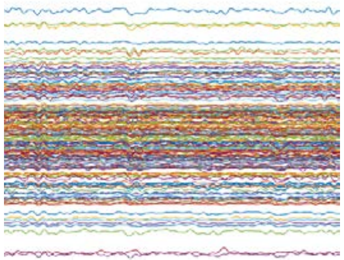

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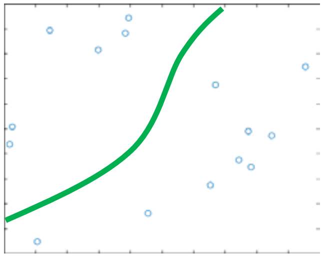

Recurrent Neural Network with Long Short-Term Memory (LSTM)

Example applications: Classify disease state
Identify biomarkers for disease

[1]Craddock et al., Nature Methods 2013

Challenge: How to Handle Limited Sample Size + Deep Learning from fMRI?

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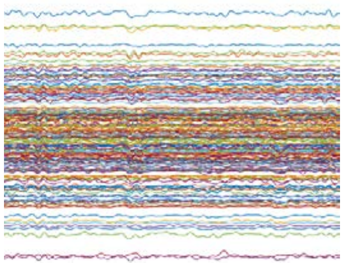

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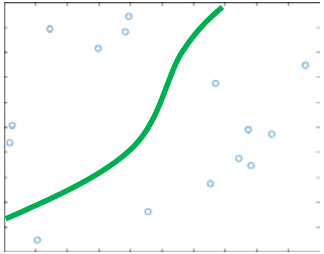


Recurrent Neural Network with
Long Short-Term Memory (LSTM)

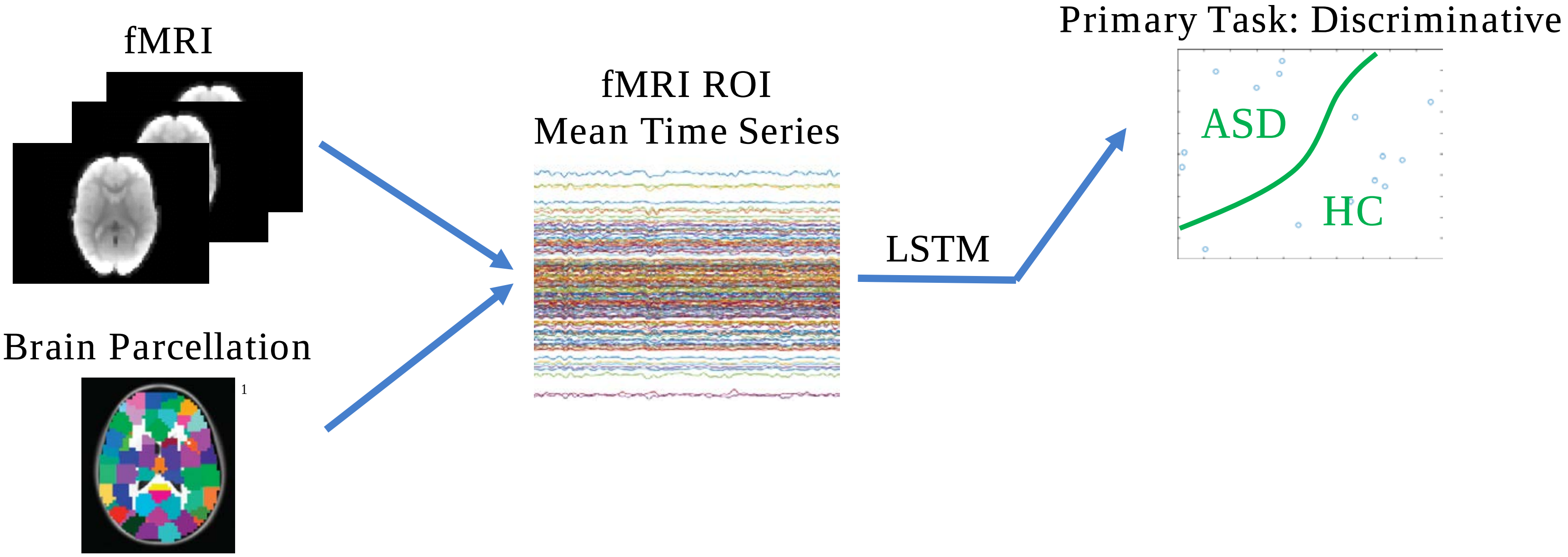
Difficulties in gathering large fMRI datasets

- Time and cost for acquisition, annotation
- Special cohorts: disease/disorder, treatment, children…

[1]Craddock et al., Nature Methods 2013

Our Solution: Make Full Use of All the Data with *Multitask Learning*

- Jointly learn shared information across related tasks



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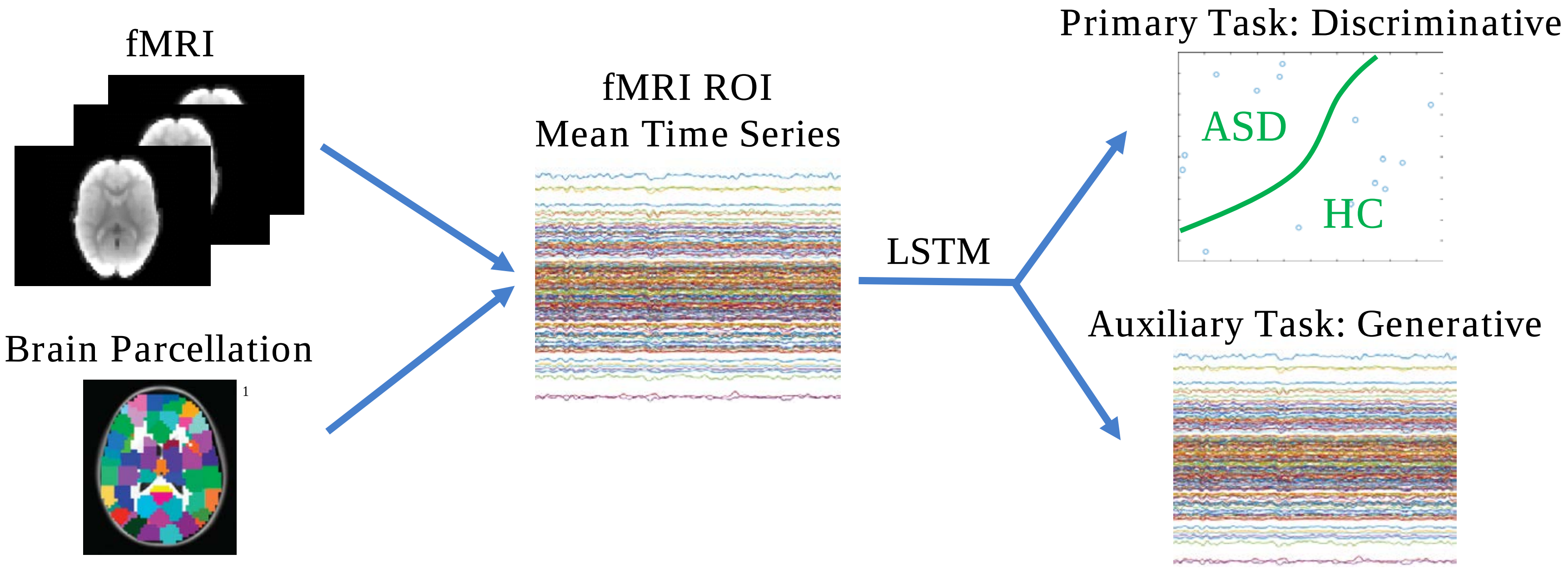

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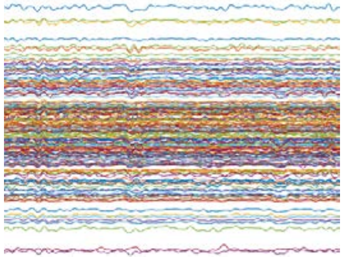
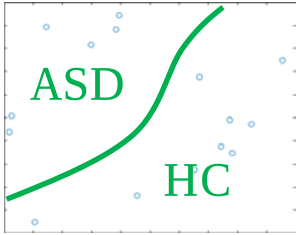
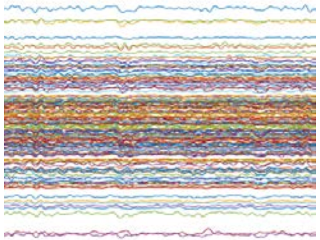


LSTM

Primary Task: Discriminative



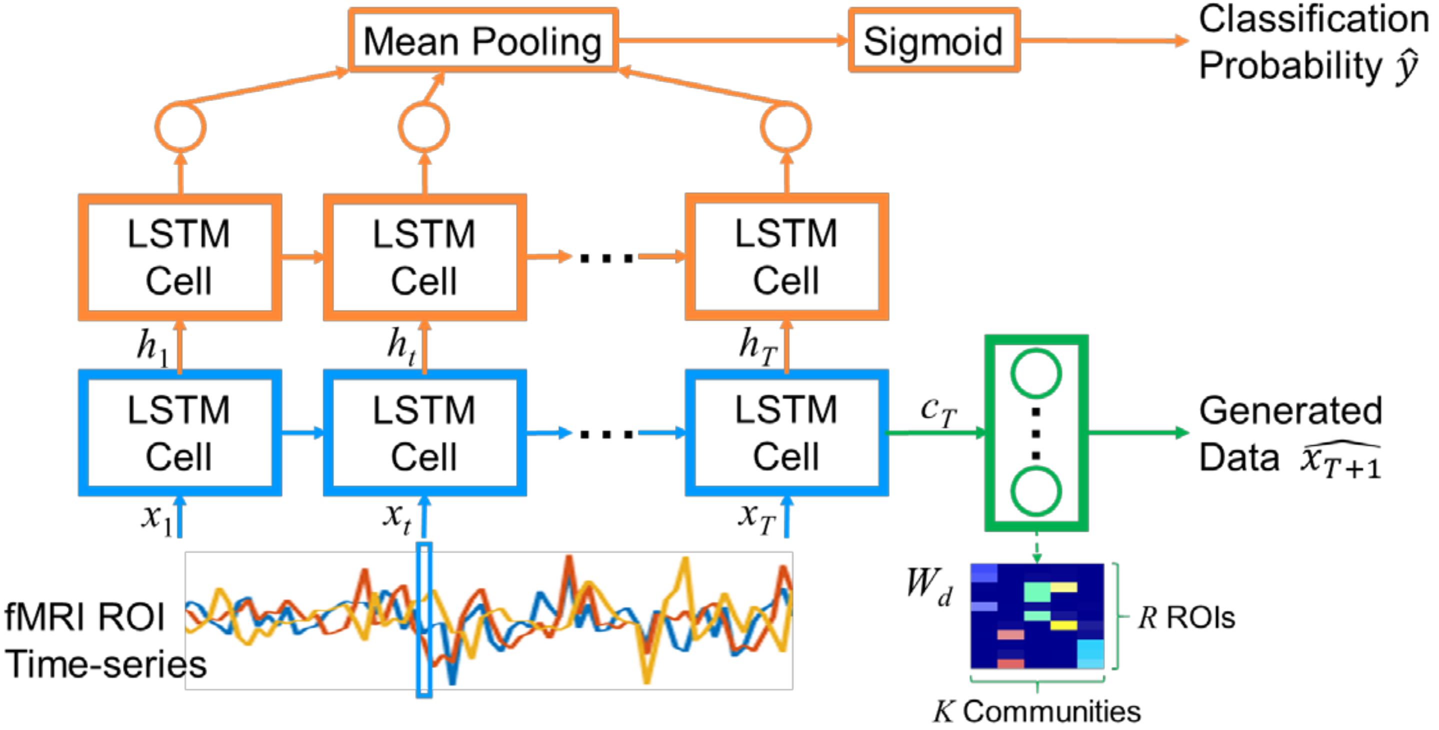
Auxiliary Task: Generative



+ No annotation required
+ Assist in interpreting discriminative model

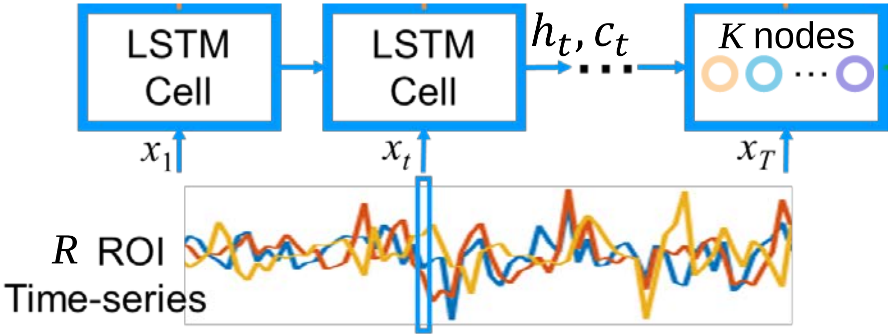
[1]Craddock et al., Nature Methods 2013

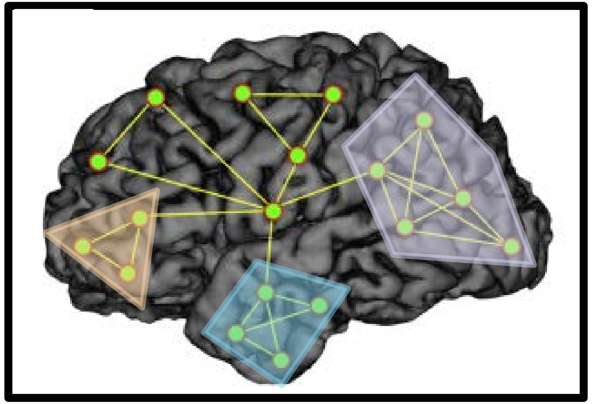
Jointly Discriminative and Generative RNN



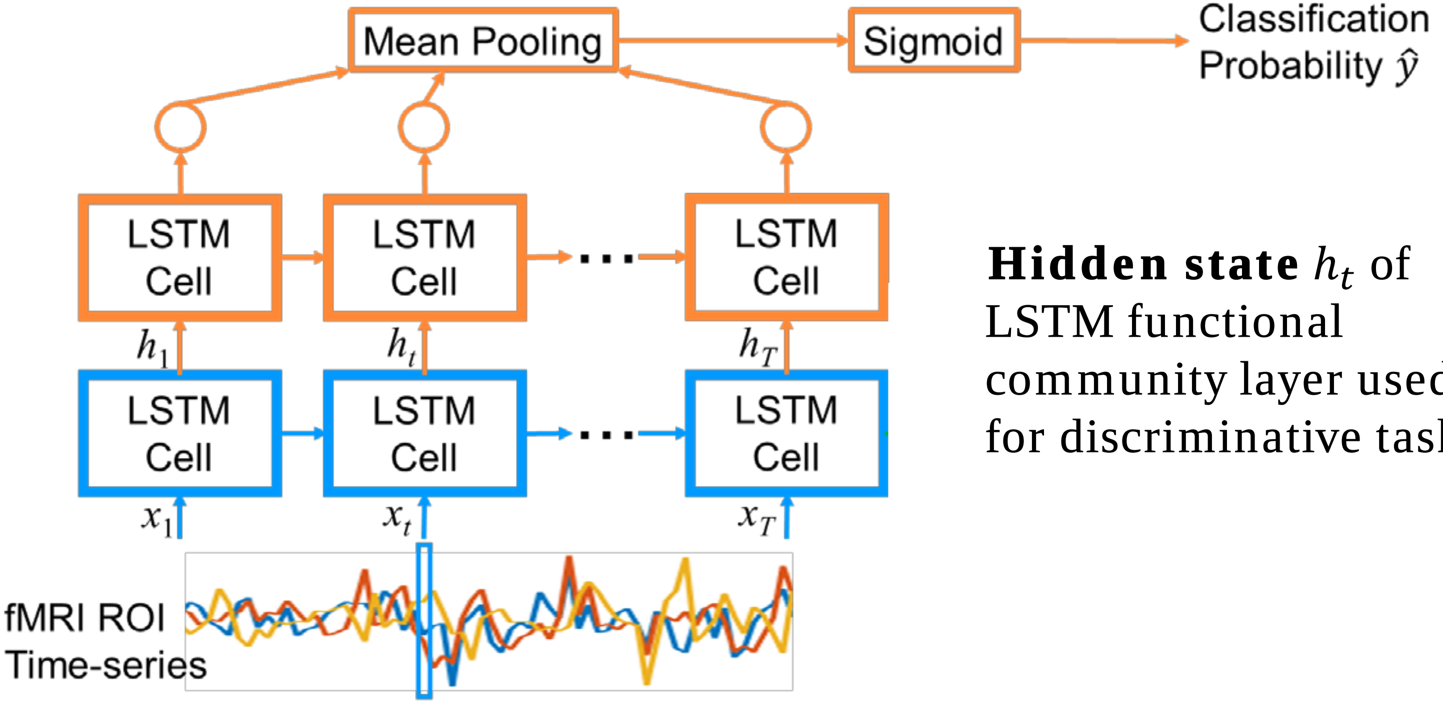
First LSTM Layer Models Interactions between Individual ROIs and *Functional Communities*

- Input ROI data $x_t \in \mathbb{R}^R$ into LSTM with K nodes
- Each LSTM node represents a functional community (group of ROIs that activate together)
- Community activity represented by hidden state $h_t \in \mathbb{R}^K$ and cell state $c_t \in \mathbb{R}^K$





Discriminative Path Learns ASD/HC Classification



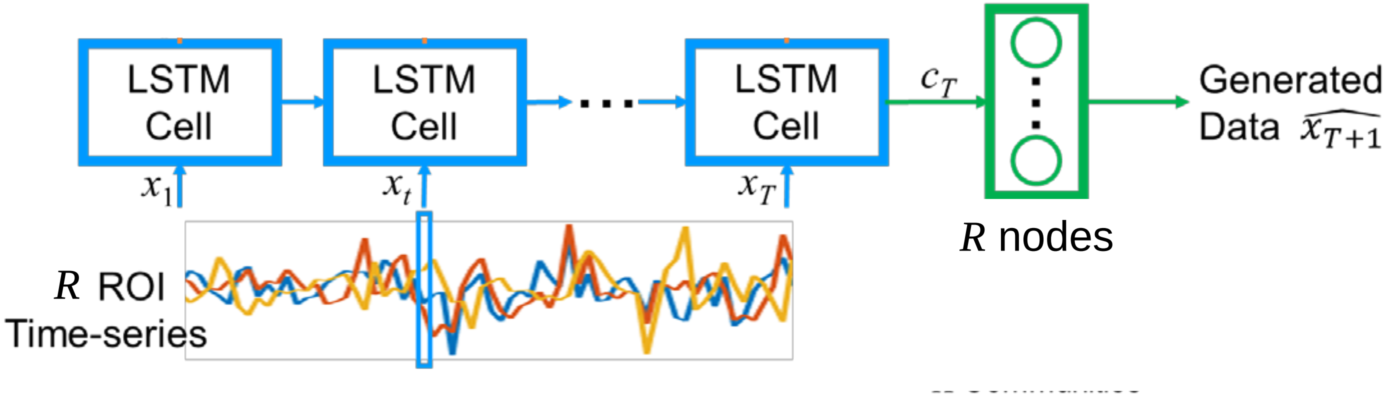
Hidden state h_t of LSTM functional community layer used for discriminative task

Generative Path Models fMRI ROI Time-Series

- **Cell state** c_T of LSTM functional community layer used to generate ROI data at time $T+1$

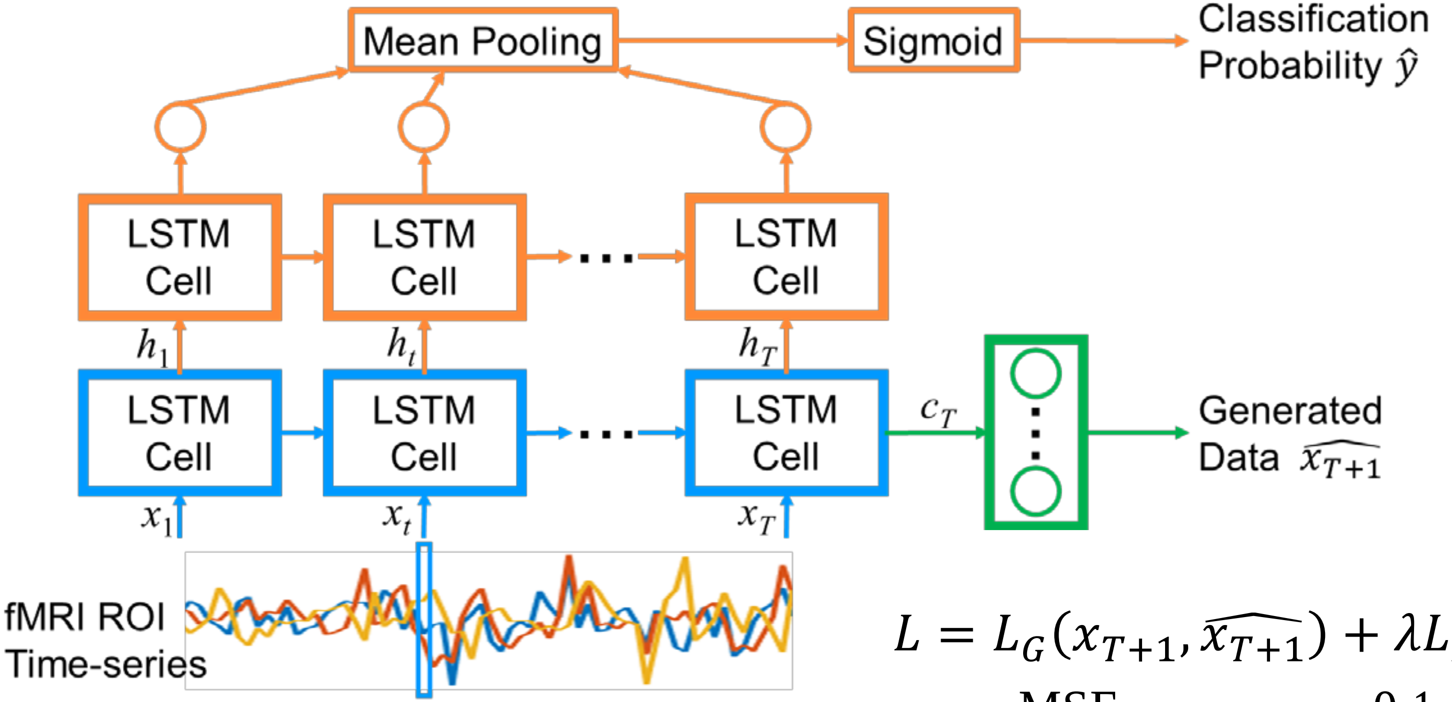
$$\widehat{x_{T+1}} = W_d c_T + b_d$$

- Constrain $W_d \geq 0$ to model only positive community influences



Graves A., "Generating Sequences With Recurrent Neural Networks," 2014

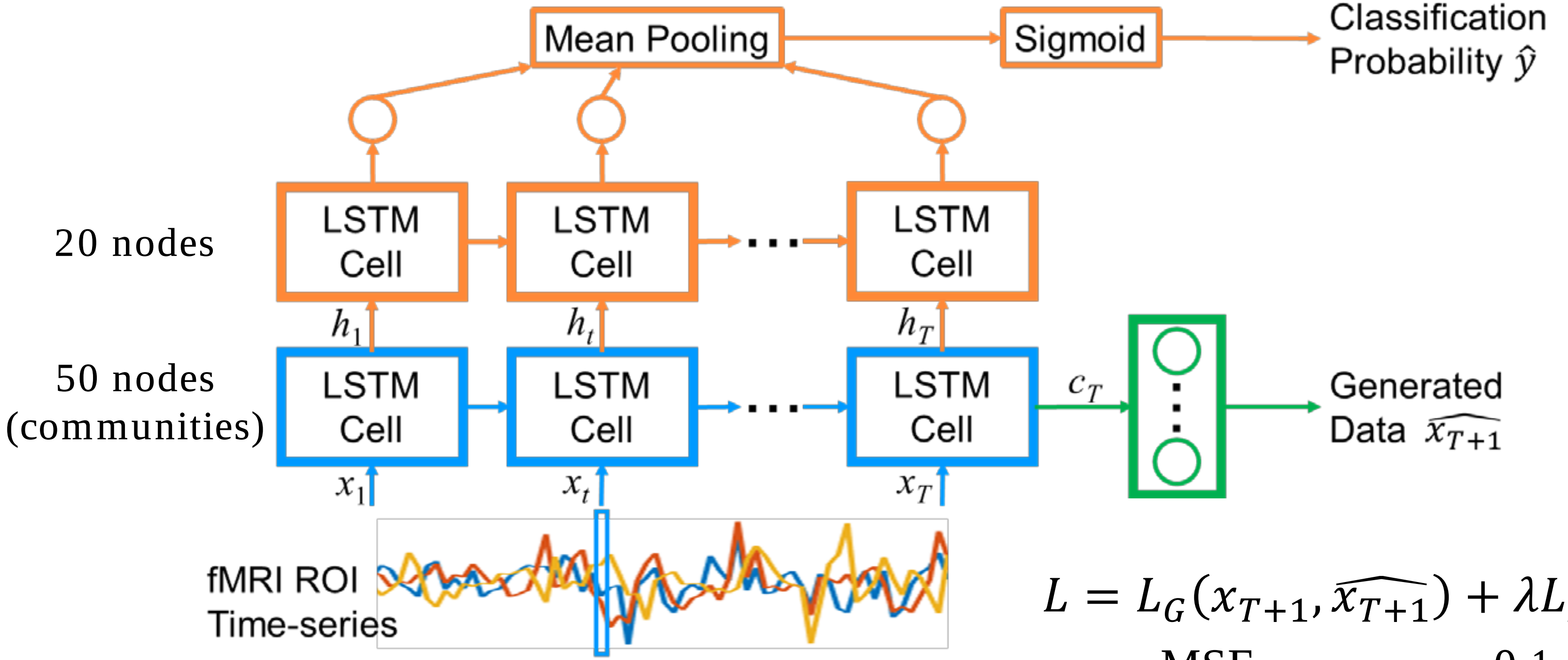
Training the Discriminative and Generative RNN



$$L = L_G(x_{T+1}, \widehat{x_{T+1}}) + \lambda L_D(y, \hat{y})$$

MSE 0.1 BCE

Training the Discriminative and Generative RNN



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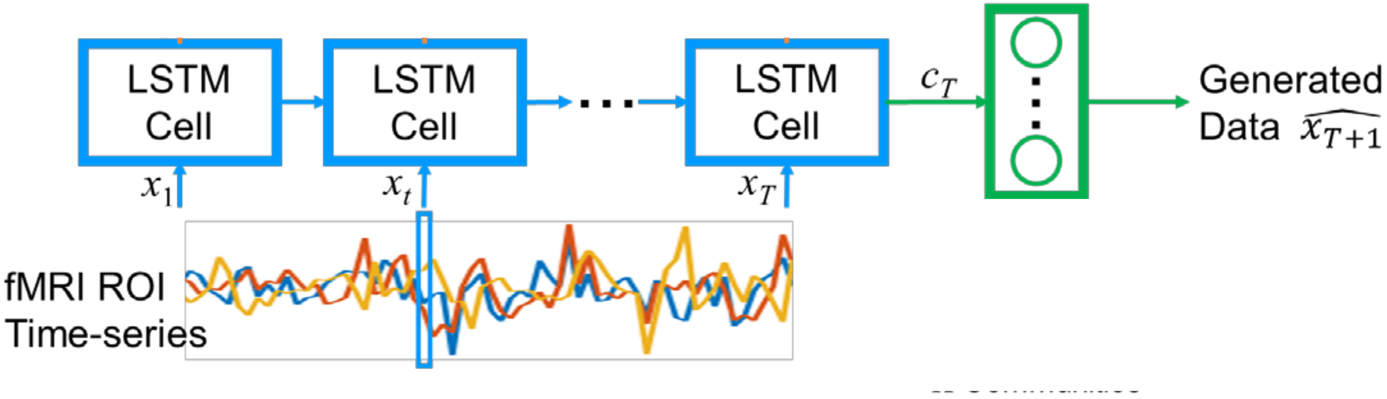
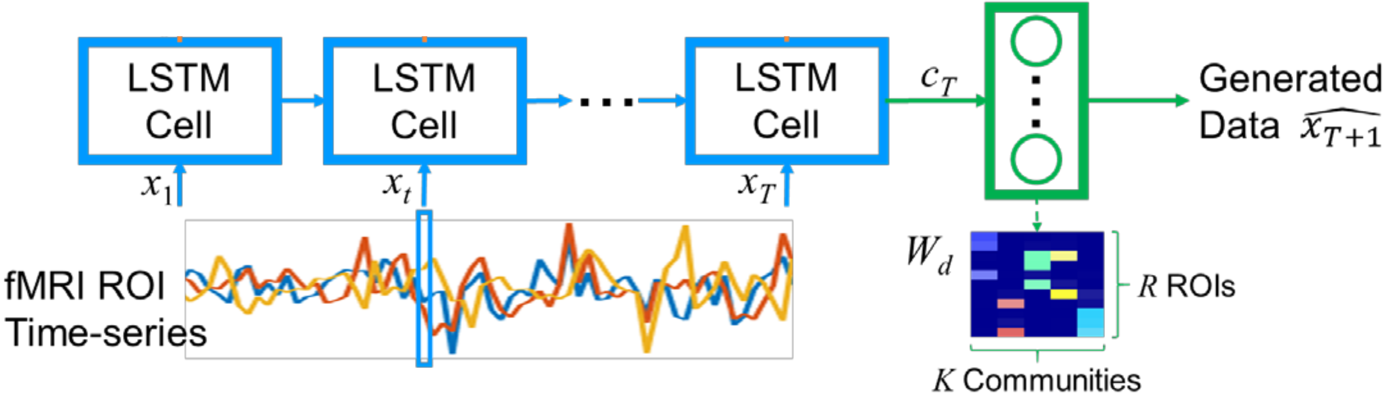
Extract Functional Communities Using Weights in Dense Layer of Generative Path

- What makes a community?
  - Community member strongly influenced by its community
  - Community strongly influenced by its members



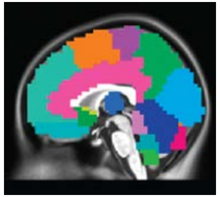
Extract Functional Communities Using Weights in Dense Layer of Generative Path

- What makes a community?
  - Community member strongly influenced by its community
  - Community strongly influenced by its members
- Assign ROI memberships to community k by K-means clustering of weights in column k of W_d



Datasets and Preprocessing

- 4 Sites from Autism Brain Imaging Data Exchange (ABIDE) I
  - NYU, UM, USM, UCLA (~100-200 subjects)
- Resting-state fMRI from Preprocessed Connectomes Project
  - Connectome Computation System pipeline
  - Automated Anatomical Labeling (AAL) atlas (R = 116 ROIs)
- Standardized ROI mean time-series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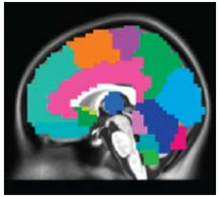
- Data augmented to ~14,000-38,000 samples/site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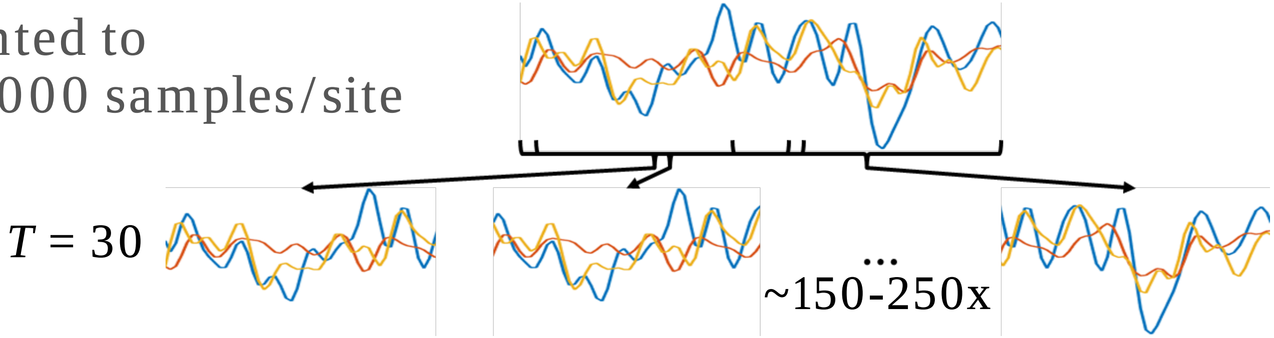

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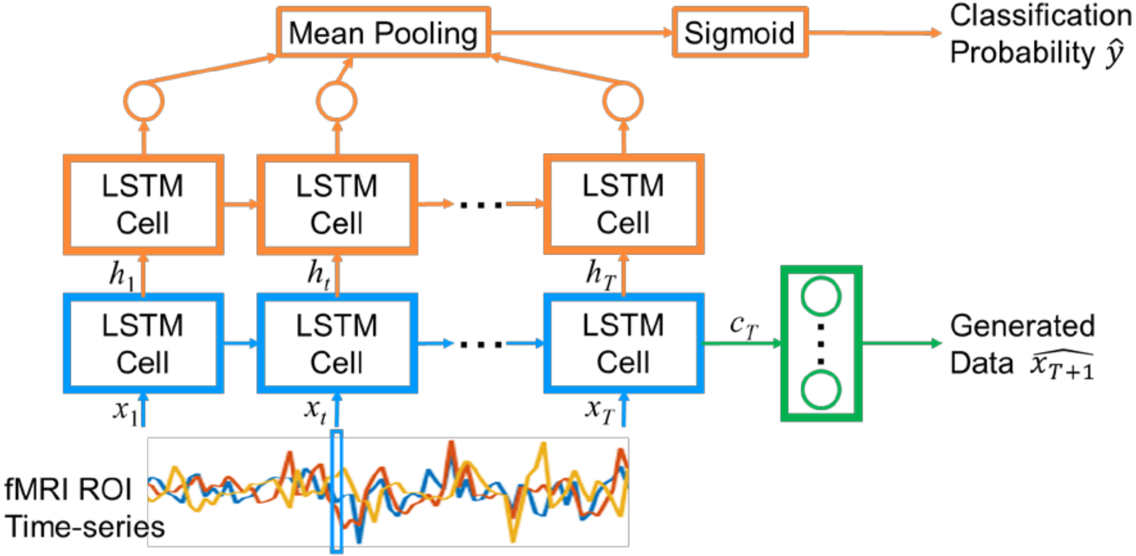
Experimental Methods: Compared Models Trained on Each Individual ABIDE Site

Model
LSTM-S [7]
FC-SVM [1]
HMM [11]
DTL [13]
LSTM-D
LSTM-H
LSTM-DG

Network Variations



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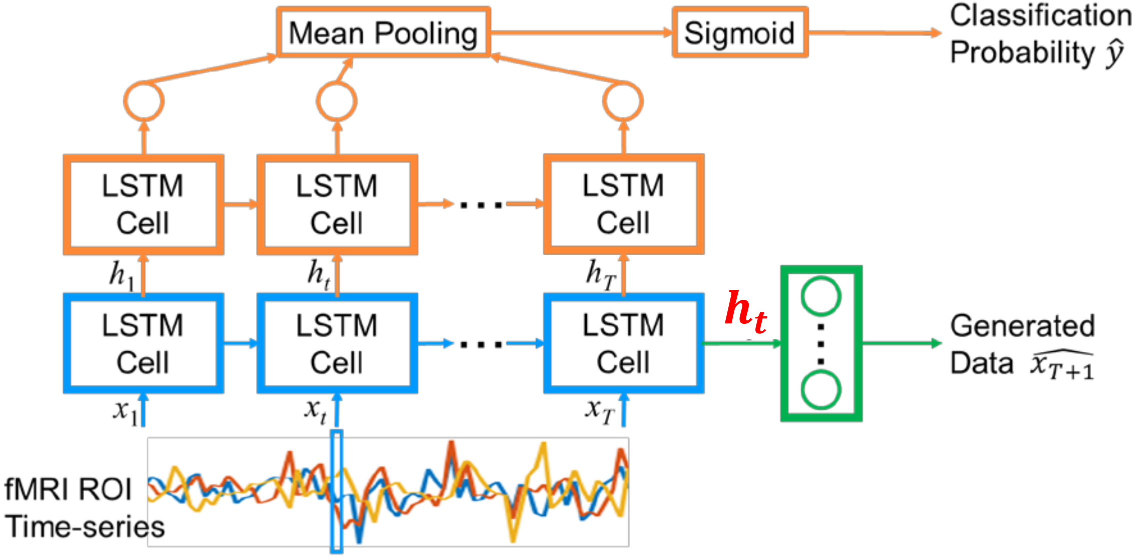

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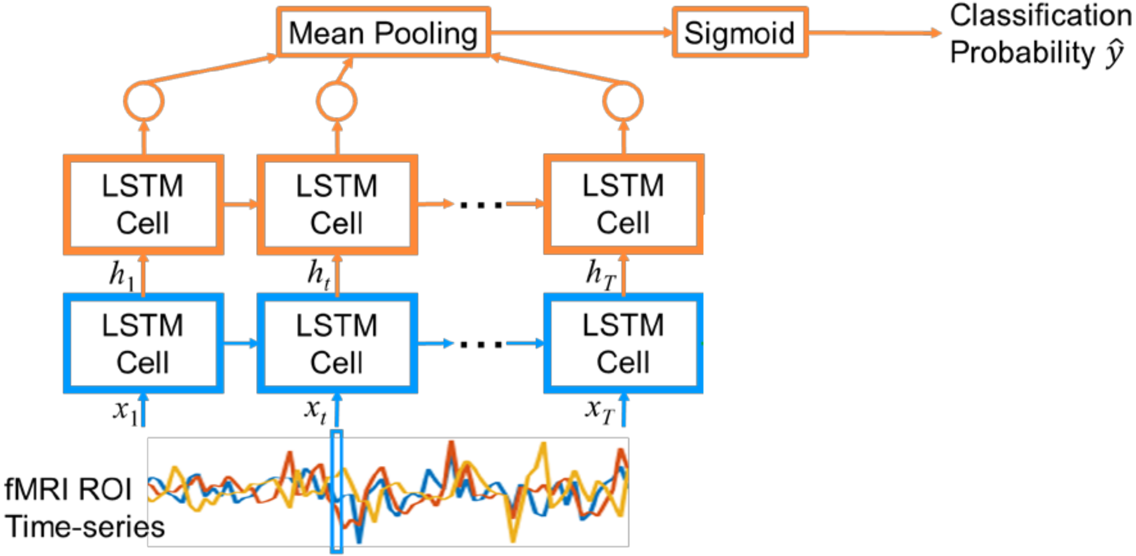

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Dvornek et al., MLMI 2017

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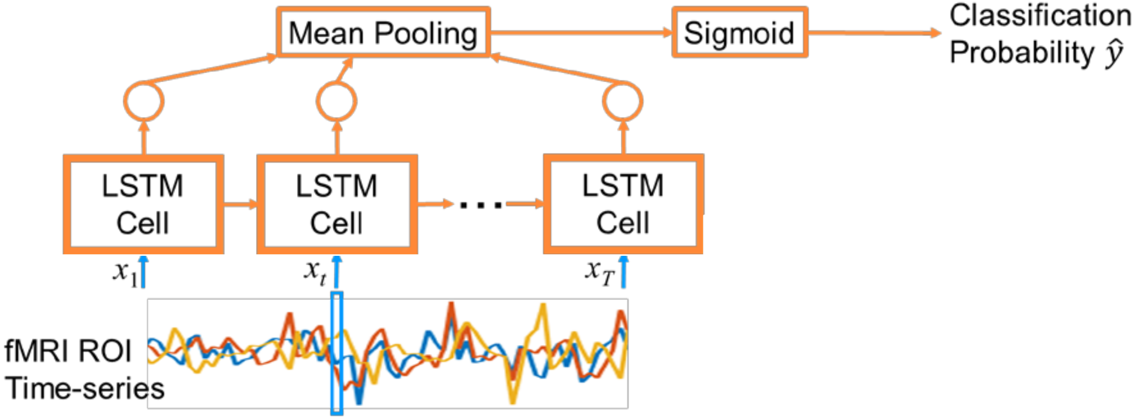

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Abraham et al., Neuroimage 2017

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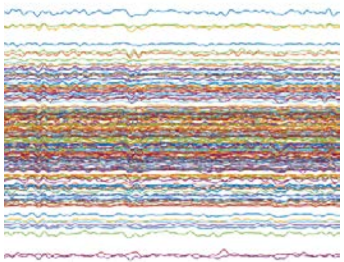
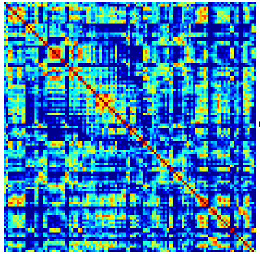
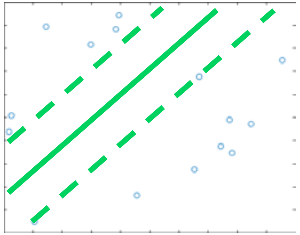


Connectivity Matrix



Linear SVM



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Jun et al., NeuroImage 2019

Li et al., Front. Neurosci. 2018

Hidden Markov Model

Stacked Autoencoders with Deep Transfer Learning

- Used same ABIDE site and AAL atlas
- Reported published values

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Evaluation of implemented models

- 10-fold cross validation
- Paired t-tests to compare all folds from all datasets

Our Joint Learning Method Produced Consistently Good Results Across 4 Datasets

Model	UM (143 subjects, 46.2% ASD)			
	Mean (Std) ACC (%)	Mean (Std) TPR (%)	Mean (Std) TNR (%)	AUC
LSTM-S [7]	69.8 (11.4)	56.7 (24.2)	74.0 (25.3)	0.740
FC-SVM [1]	69.2 (12.0)	46.7 (18.9)	89.8 (12.8)	0.713
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LSTM-H	69.2 (11.4)	57.9 (14.5)	78.7 (18.1)	0.777
LSTM-DG	**74.8 (10.0)**	**60.8 (12.8)**	**85.6 (14.5)**	**0.774**

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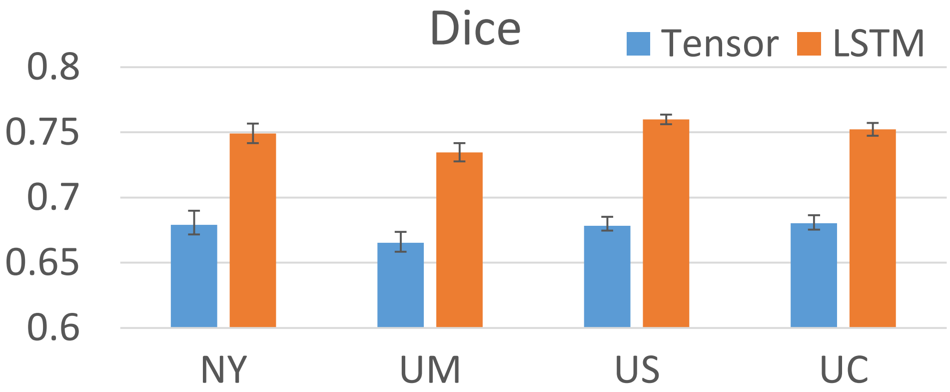
- Outperformed all non-generative models (ACC $p < 0.05$)
- Only method to outperform original LSTM fMRI classification model (ACC $p = 0.04$, TNR $p = 0.04$)

Our Communities are More Robust than Those Found by Tensor-Based Community Detection

- Compared the 50 communities found across CV folds



11% Increase in Dice

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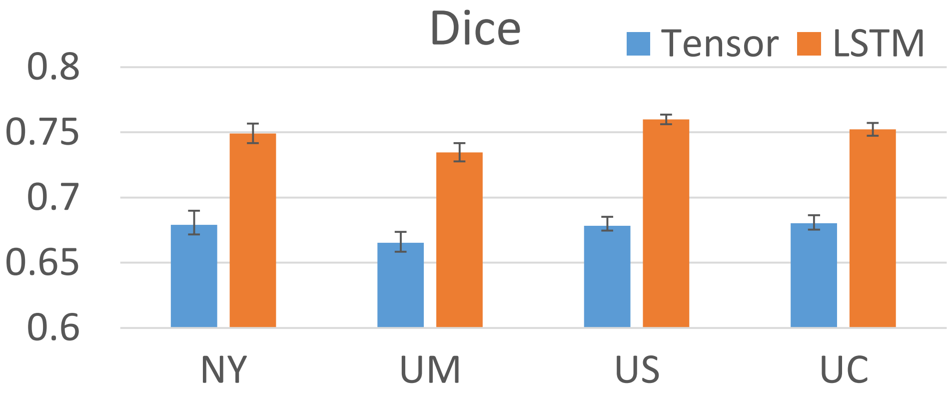
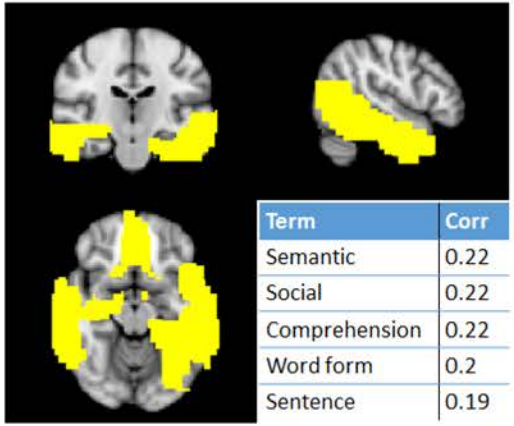


11% Increase in Dice

- More reliable functional communities → better for interpretation

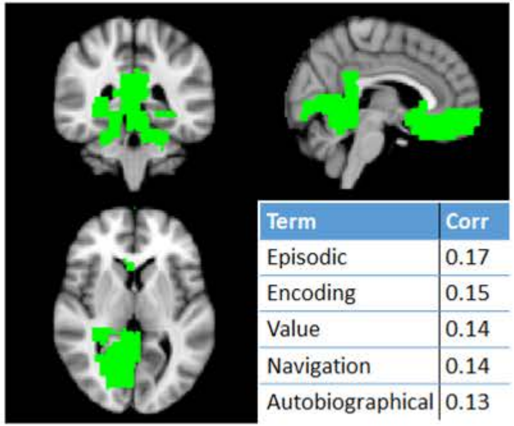
Top Influential Communities for ASD Classification for NYU Dataset

Social



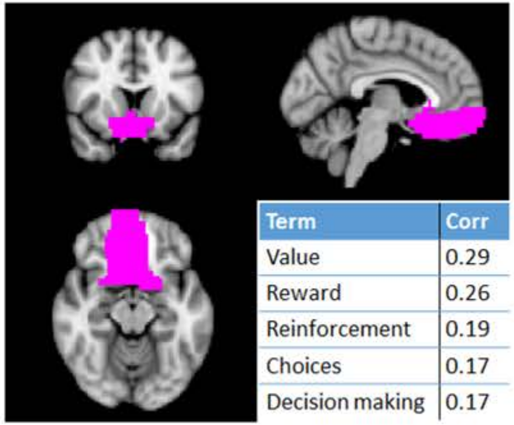
Term	Corr
Semantic	0.22
Social	0.22
Comprehension	0.22
Word form	0.2
Sentence	0.19

Memory



Term	Corr
Episodic	0.17
Encoding	0.15
Value	0.14
Navigation	0.14
Autobiographical	0.13

Reward/Decision Making



Term	Corr
Value	0.29
Reward	0.26
Reinforcement	0.19
Choices	0.17
Decision making	0.17

- Communities are associated with neurocognitive processes affected in ASD

Conclusions

- What we did:
  - Novel RNN-based network for jointly learning discriminative task and generative model for fMRI ROI time-series data
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  - Demonstrated higher ASD classification performance and more robust functional community estimation
- What this means:
  - Can train more generalizable models on smaller fMRI datasets
  - Modeling reliable functional communities facilitates interpretation of discriminative model
- What's next:
  - Handle data from across imaging sites

Thank you!

- NIH Grants T32 MH18268 and R01 NS035193

- Contact: nicha.dvornek@yale.edu