Estimating Reproducible Functional Networks Associated with Task Dynamics using Unsupervised LSTMs

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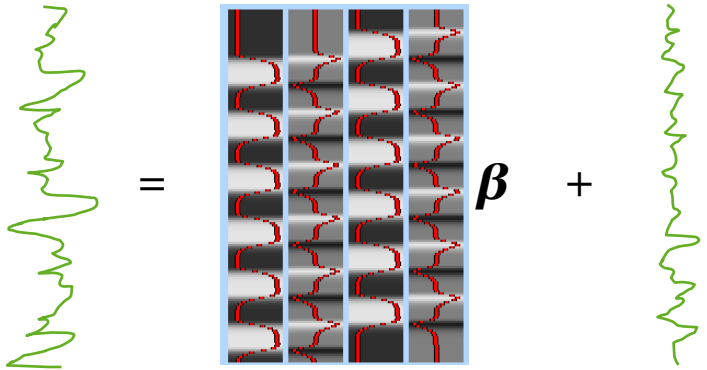
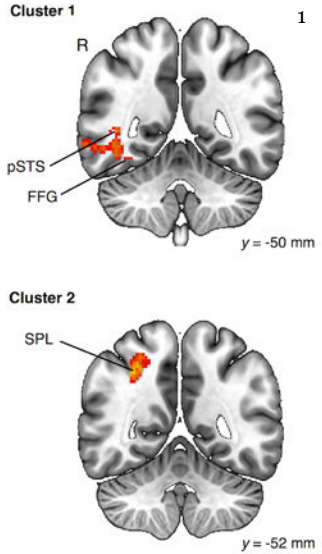
Yale SCHOOL OF MEDICINE

Canonical task-based FMRI Analysis

- Mass univariate analysis using general linear model

Each voxel in whole-brain or ROI:



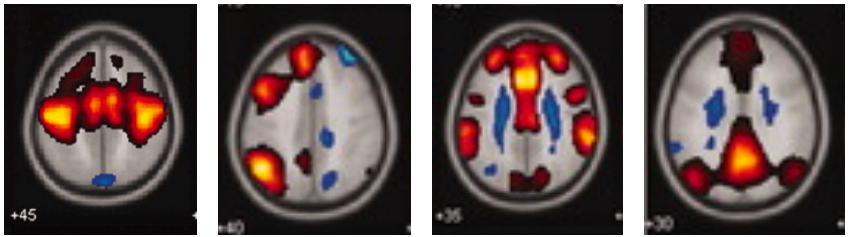


[1]

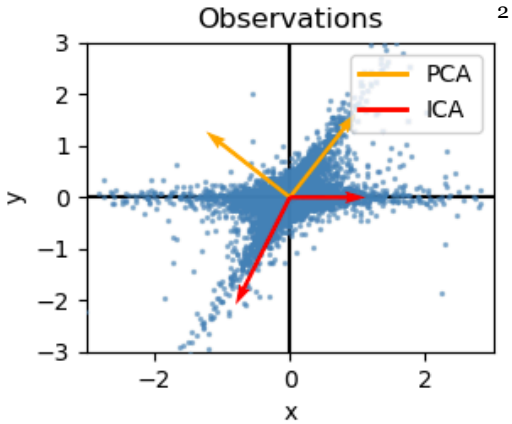
[1]Yang et al., Transl. Psychiatry 2017

Functional brain networks allows higher systems-level view of neurocognitive functions

- Analytical approaches to functional network decomposition:
  - Principal Component Analysis (PCA)
  - Independent Component Analysis (ICA)



[1]



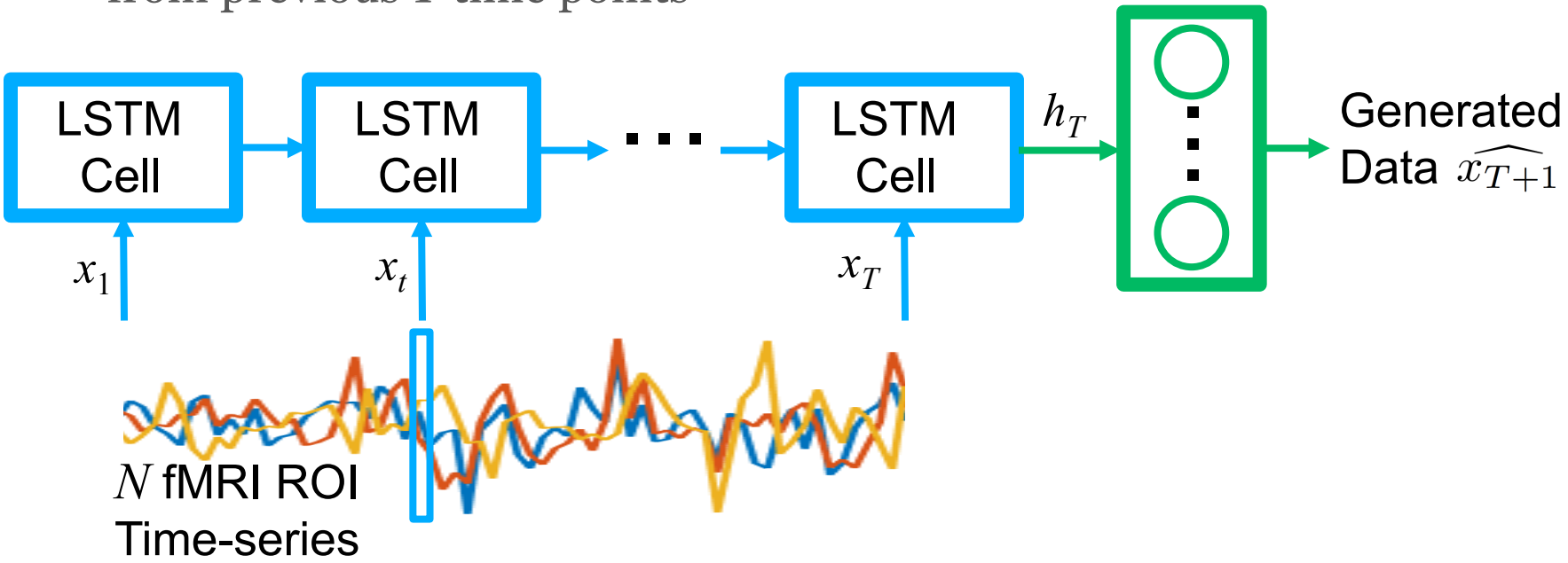
[2]

  - Estimated by fitting to *entire* dataset → poor reproducibility?
- Predictive approach would aim to *generalize* well to new data → improve reproducibility?

[1]Zhang and Li, Human Brain Mapping, 2011; [2]https://scikit-learn.org

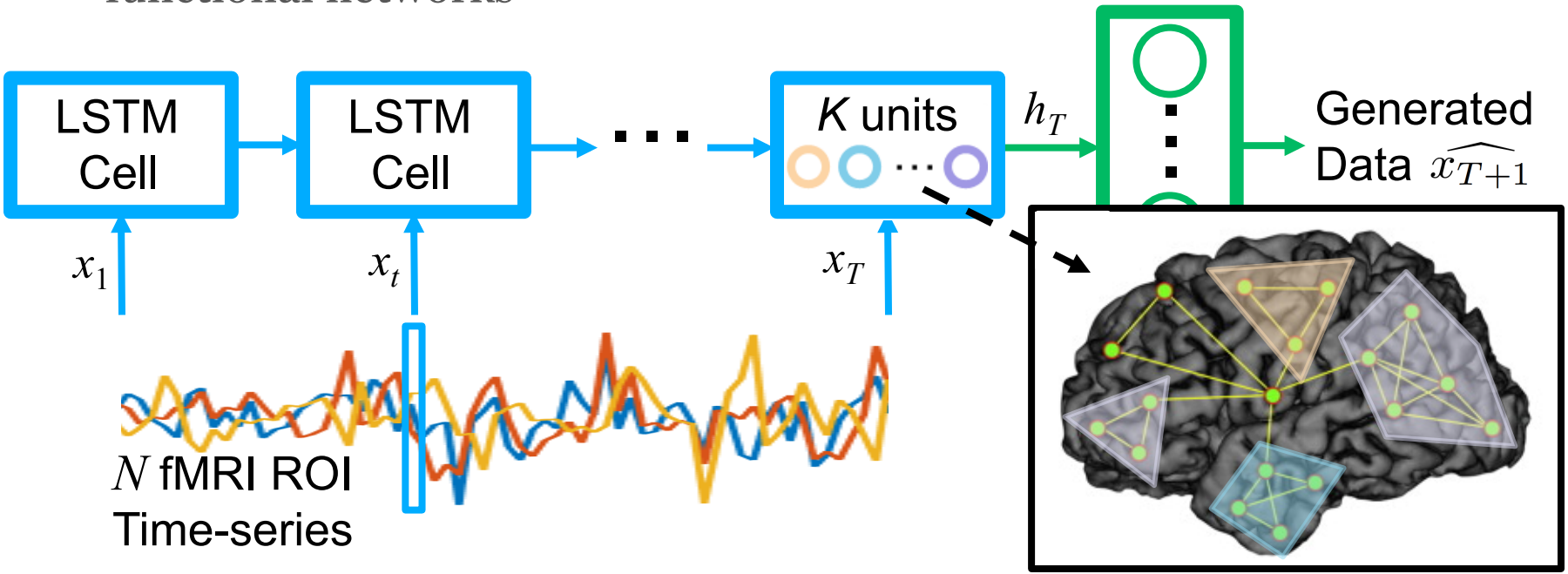
Proposed Approach: LSTM Model for Functional Networks

- LSTM architecture to predict fMRI time-series data at time *T+1* from previous *T* time points

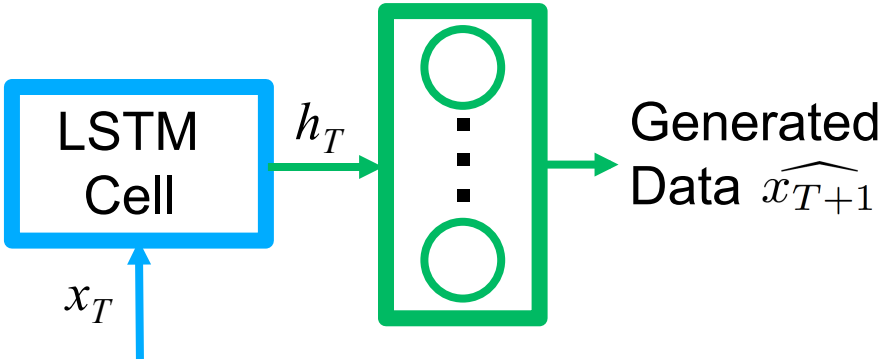


Proposed Approach: LSTM Model for Functional Networks

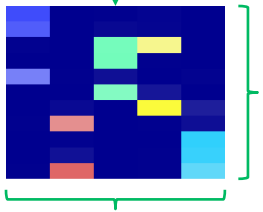
- Network models the interactions between individual ROIs and functional networks



Encourage Sparse Membership and Cooperative Activity within Functional Network



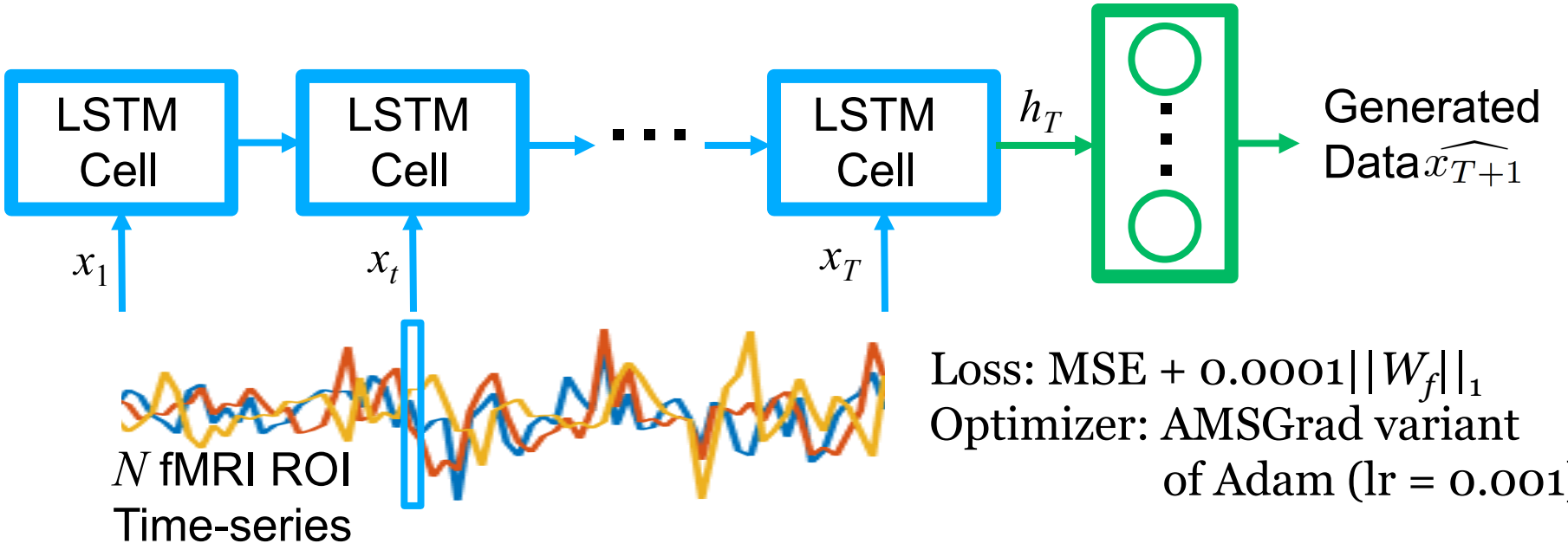
$$\widehat{x_{T+1}} = W_f h_T + b_f$$



- Impose on W_f:
  - L1 Regularization → Sparse ROI membership
  - Non-negative constraint → ROIs work cooperatively in a network

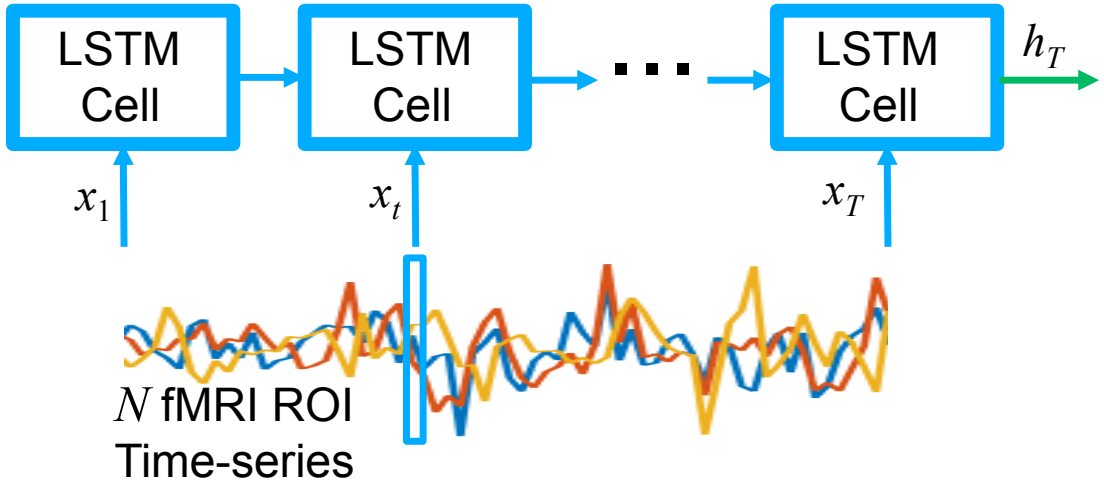
Unsupervised Training of the LSTM Network

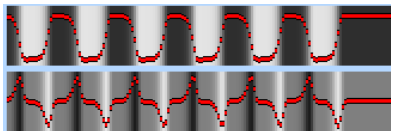
- "Unsupervised" – no additional labels required
- Trained in supervised manner using fMRI time-series alone



Associate LSTM Functional Networks with Task using Group Analysis

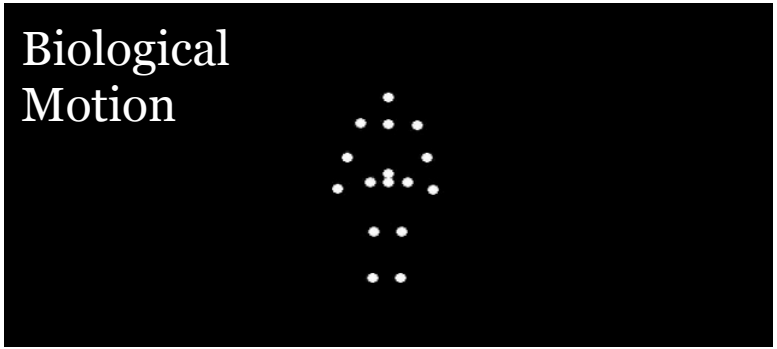
- Activity of functional network k at time t represented by LSTM output $h_t(k)$
- Predict LSTM output for every time point $t >= T$
- Average across subjects
- Correlate mean functional network activity with "design signals"
  - Mean expected fMRI task signal
  - Mean temporal derivative of expected fMRI signal





Datasets

- Dataset 1
  - 82 children with autism, 48 typical controls matched for age and IQ
- Dataset 2
  - 21 children with autism, 19 typical controls matched for age and IQ
- BOLD fMRI scan under biological motion perception paradigm



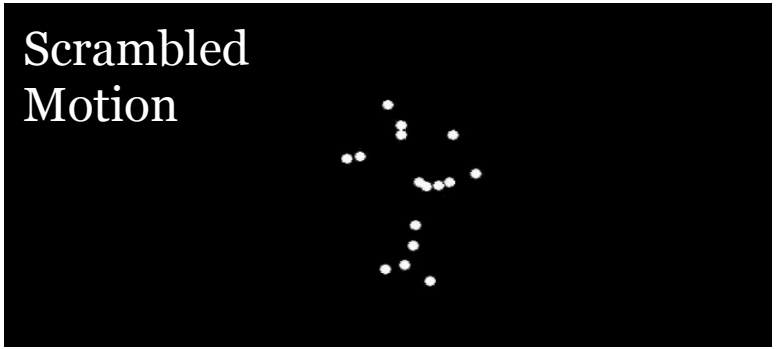
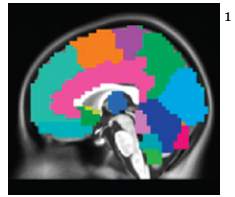
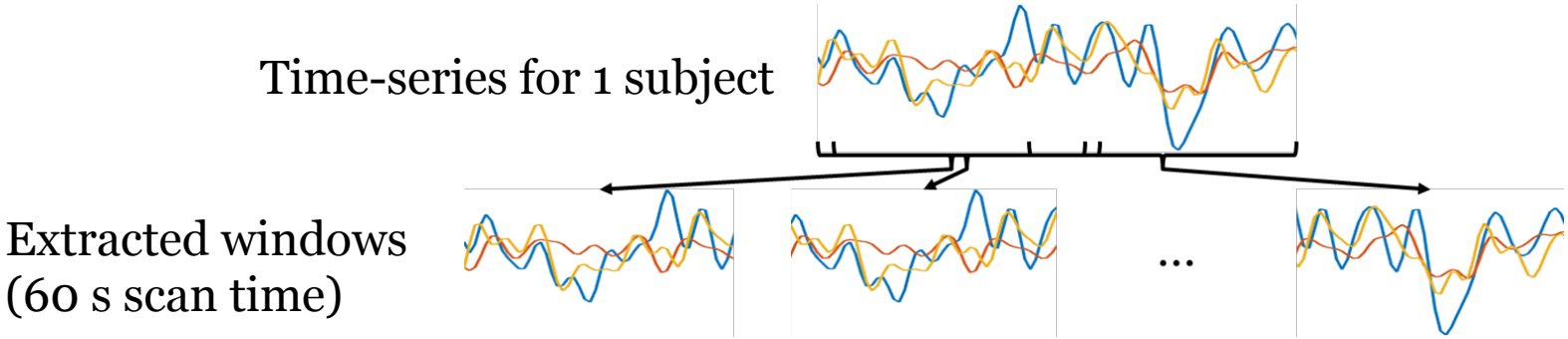


Image Preprocessing

- fMRI preprocessing in FSL
- Brain parcellated into 90 cerebral ROIs using AAL atlas
- Standardized ROI mean time-series
- Data augmentation: extract all possible windows of length $T = 30$
  - Dataset 1: 130 subjects → 15080 samples
  - Dataset 2: 40 subjects → 5040 samples





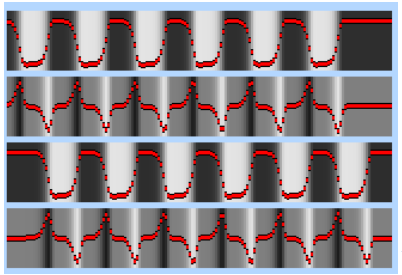
[1]Craddock et al., Nature Methods 2013

Experimental Methods: Comparison of Methods

1. Proposed LSTM
   - Networks: LSTM unit
   - Activity: Output of LSTM
2. Original ROIs
   - Networks: individual ROIs
   - Activity: mean fMRI time-series
3. PCA (concatenate subjects across time)
   - Networks: PCs
   - Activity: Score projecting the fMRI time-series onto the PCs
4. ICA (concatenate subjects across time)
   - Networks: ICs
   - Activity: Mixing matrix

Experimental Methods: Evaluation

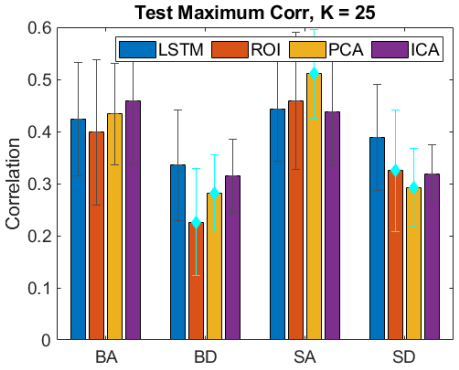
- 10-fold cross-validation
  - LSTM – 10% training data withheld for validation
- Compute correlation between networks and design signals
  - BA: biological motion activity
  - BD: biological motion dynamics
  - SA: scrambled motion activity
  - SD: scrambled motion dynamics
- Evaluate network:
  - Ability to capture task-relevant activity
  - Reliability and reproducibility

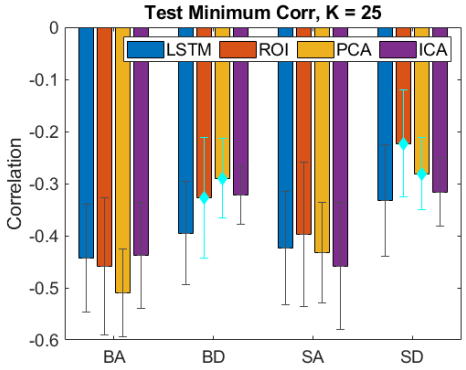


Associated with Task

Associated with Dynamic Changes in Task

Results: Dataset 1, K = 25 Functional Networks





- Significantly different compared to LSTM, two-tailed paired t-test, $p < 0.05$

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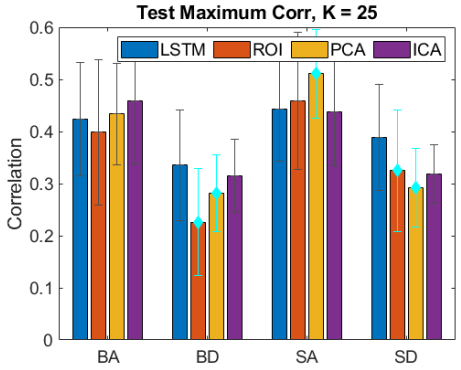

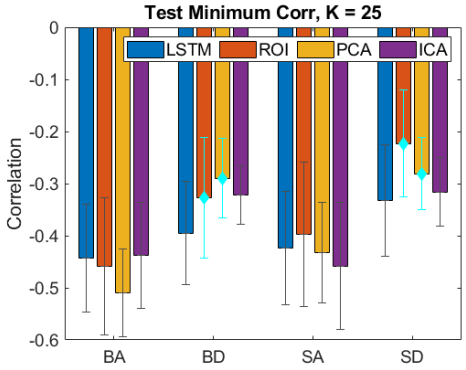

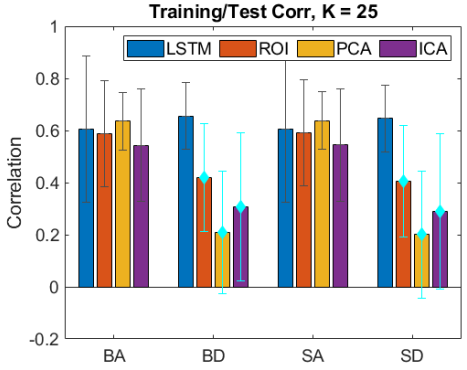

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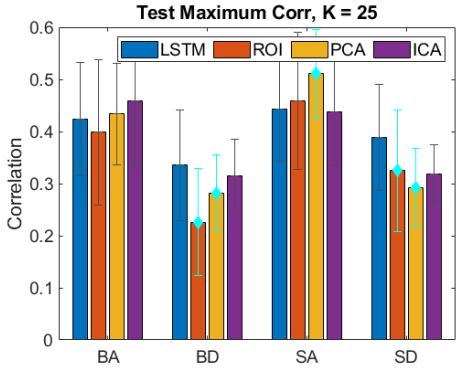

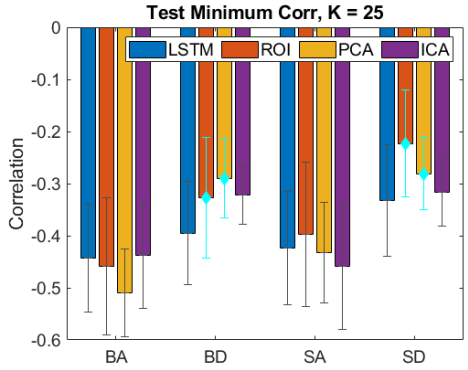

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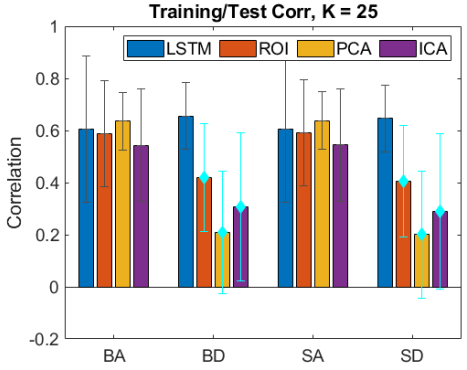
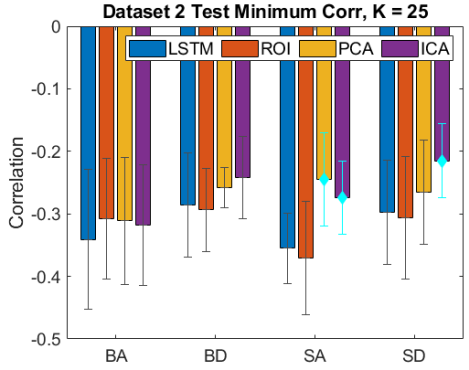
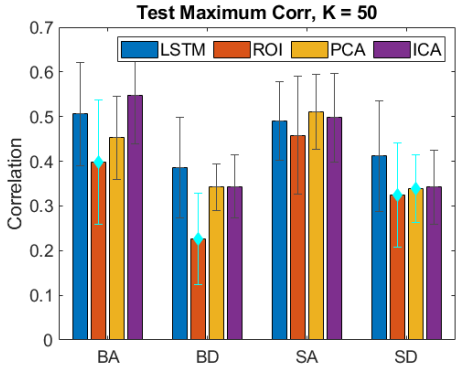
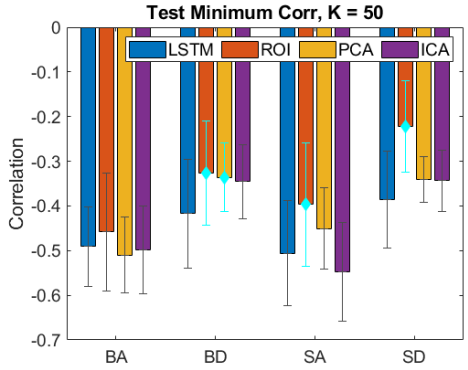




Results: Dataset 1, K = 50 Functional Networks





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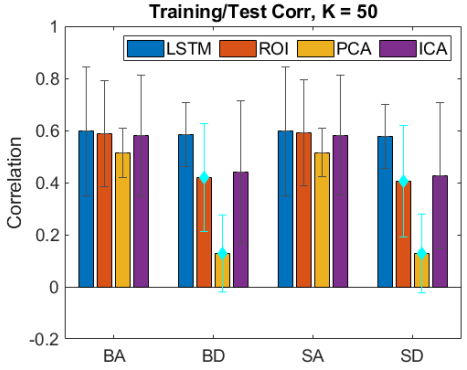
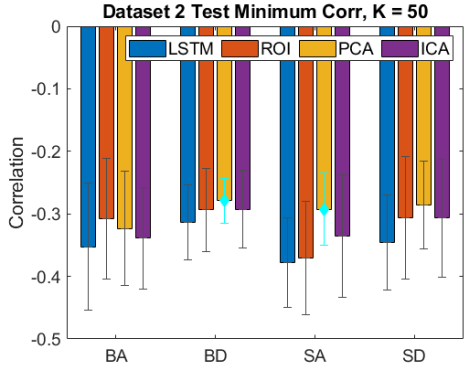
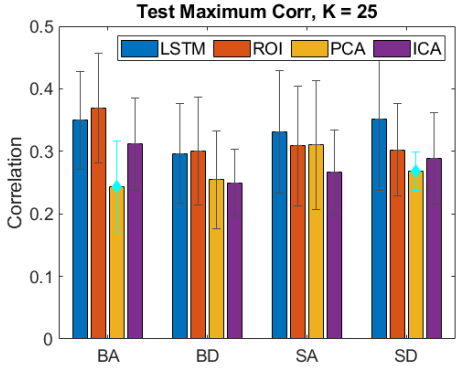




Results: Dataset 2, K = 25 Functional Networks



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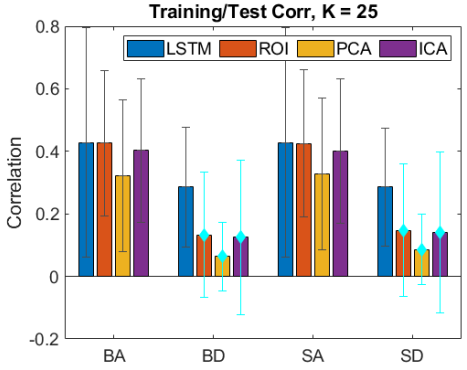

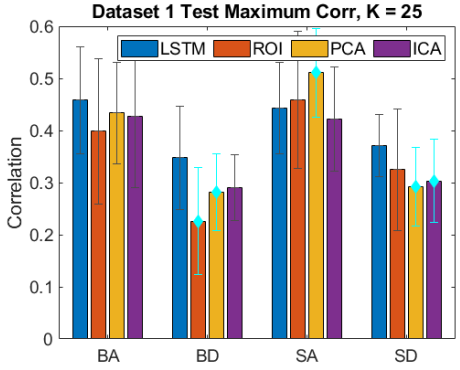

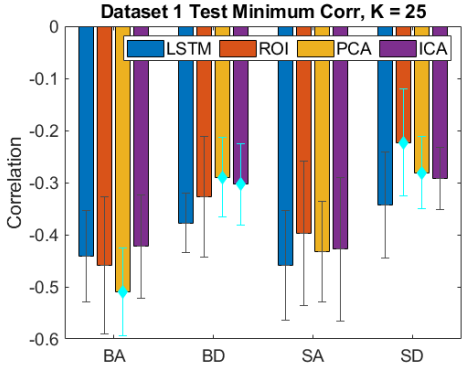

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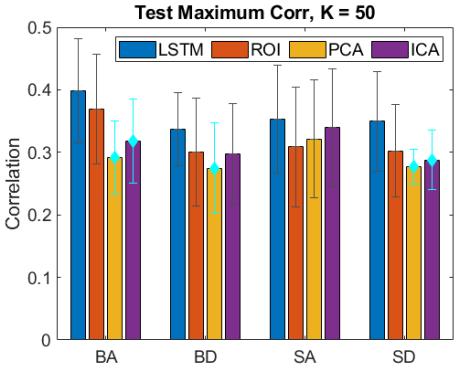

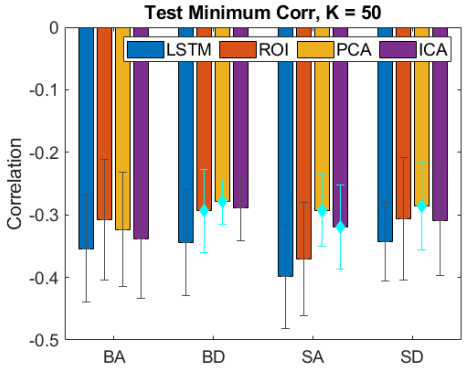

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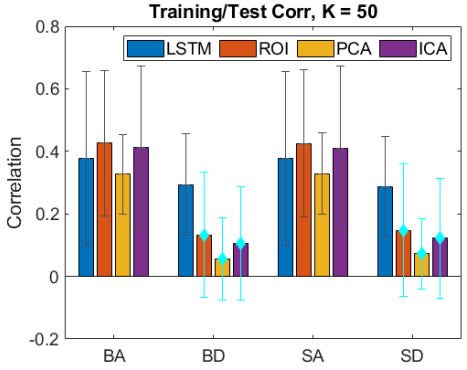

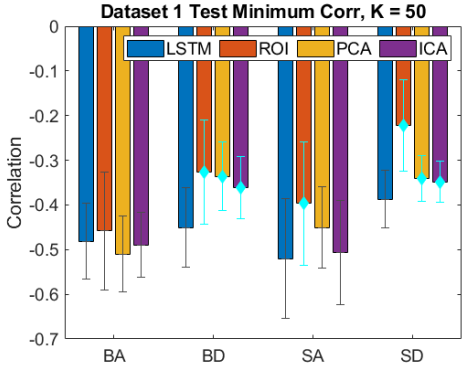

Conclusions

- What we did:
  - Unsupervised LSTM for learning robust functional networks via fMRI time-series signal prediction
  - Demonstrated stronger correlation between LSTM-derived functional networks and task activity and dynamics in biological motion paradigm
  - Produced results that translated better across subjects within the same dataset and across datasets
- What this means:
  - LSTM functional networks are more reproducible and more reliably characterize network activity in the brain

  → Essential for characterizing the neural correlates of a target task

Thank you!

- NIH Grants R01 MH100028 and R01 NS035193

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