Using Topological Data Analysis to reveal the intrinsic dynamical organization of the brain in individuals with fragile X syndrome

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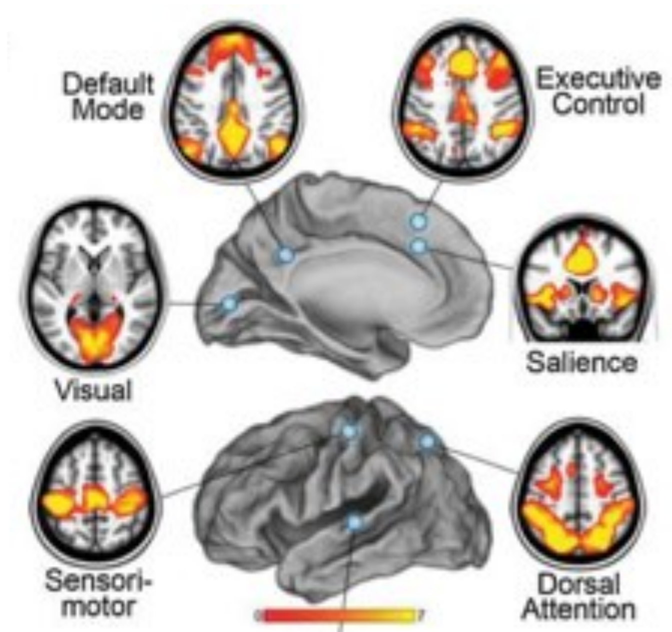
Abstract:

To study the brain at rest, most previous work has analyzed "average" changes in co-fluctuations between a set of brain regions. We argue that by collapsing data in space or time, we stand to lose information about the brain's dynamical organization. Here, using Topological Data Analysis (TDA) and Markov Chains (MC), we reveal the overall organization of intrinsic brain activity in individuals with fragile X syndrome (FXS) at a single participant level. The rsfMRI data (8min) were gathered from n=21 individuals with FXS (10F, age-range=10-24 years, mean IQ=65.67; Hall et al. (2013), *JAMA Psychiatry*). After preprocessing, data from 9 individuals were discarded due to head movement artifacts, leaving n=12 (6F, age-range=10-24 years, mean IQ=63.75). The severity of autism symptoms was assessed using Social Communication Questionnaire. Without collapsing data in space or time, we extracted a representation of overall brain dynamics for each participant using TDA (Saggar et al. (2018), *Nature Communications*). The TDA-derived representation was used to construct discrete-time finite-state MC. The MC were represented as directed graphs with nodes as states and directed edges denoting transition probabilities between states. The states were defined as a set of quasi-stationary whole-brain configuration maps. The average degree of the MC graph was observed to be negatively associated with the severity of autism symptoms (rho=-0.58, p=0.047). Lower degree of a MC graph indicates lower probability of transition between states (or increased repetition of states). Our results suggest that individuals with FXS with higher severity of autism symptoms had increased repetition of quasi-stationary whole-brain configuration maps at rest.

Background:

Large-scale brain networks (on-average)



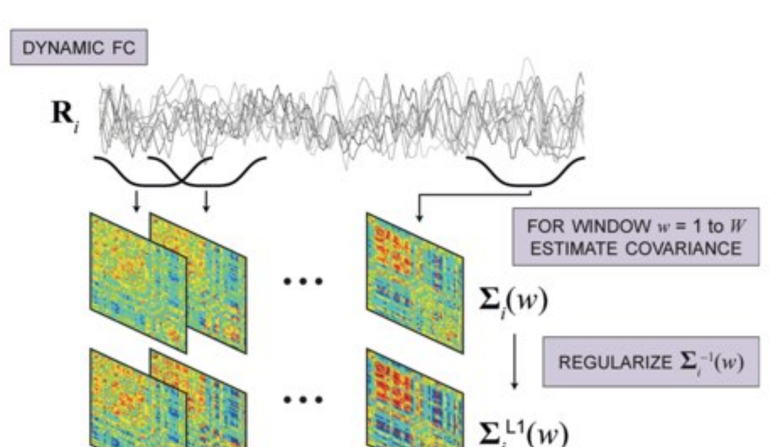
Raichle 2010

Gaps:

- Lack of disorder specificity across clinical populations
- Lack of individualized information (e.g., neurosurgical planning or neurofeedback)
- We know very little about the dynamical brain organization

Hope: to study brain dynamics

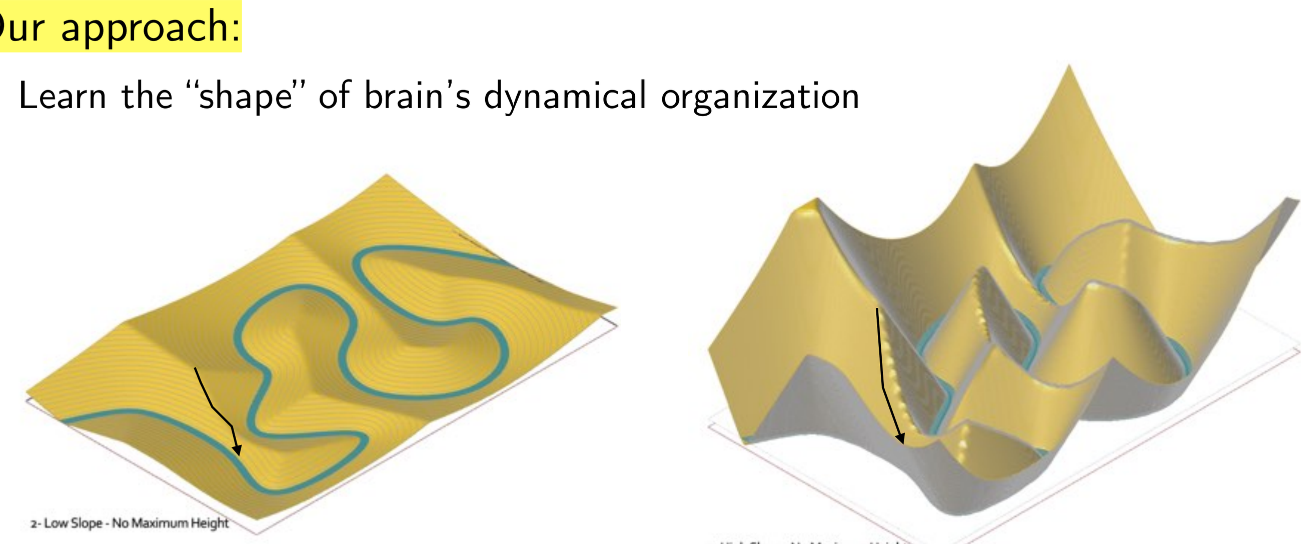
- Dynamics of large-scale brain networks could result in richer set of features — better insights — better biomarkers
- Issues remain
  - Best spatiotemporal resolution?
  - No ground truth about transitions



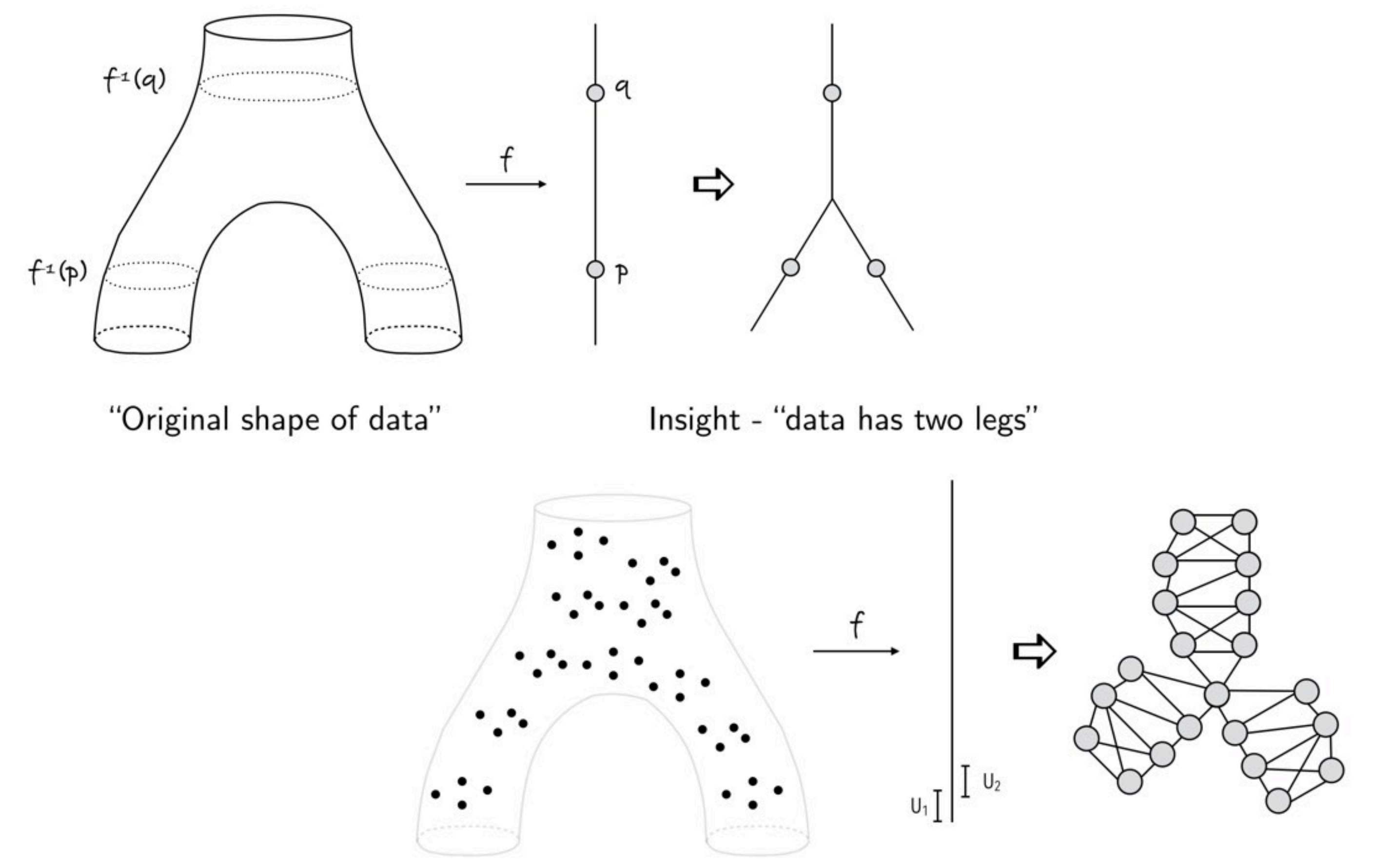
Calhoun et al 2014

Our approach:

Learn the "shape" of brain's dynamical organization

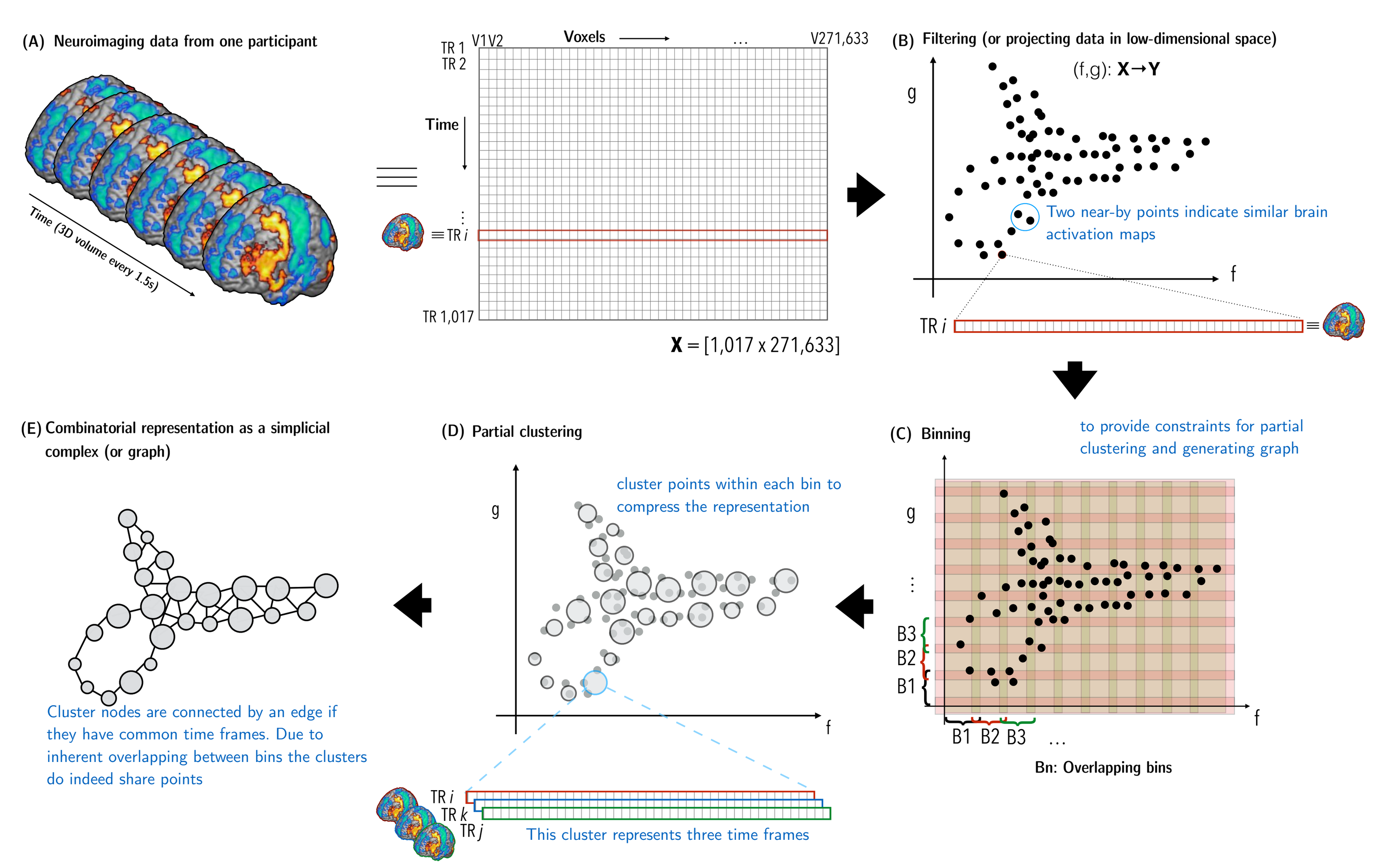


To learn the shape, we employed Topological Data Analysis (TDA)



Carlsson 2009

Application of TDA-based Mapper to fMRI data

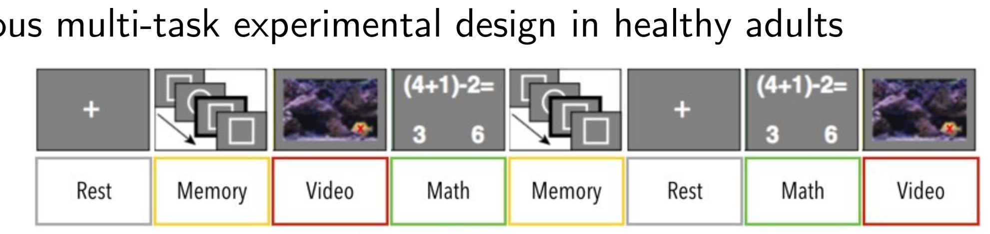


Saggar et al. 2018

Previous work using a continuous multi-task experimental design in healthy adults

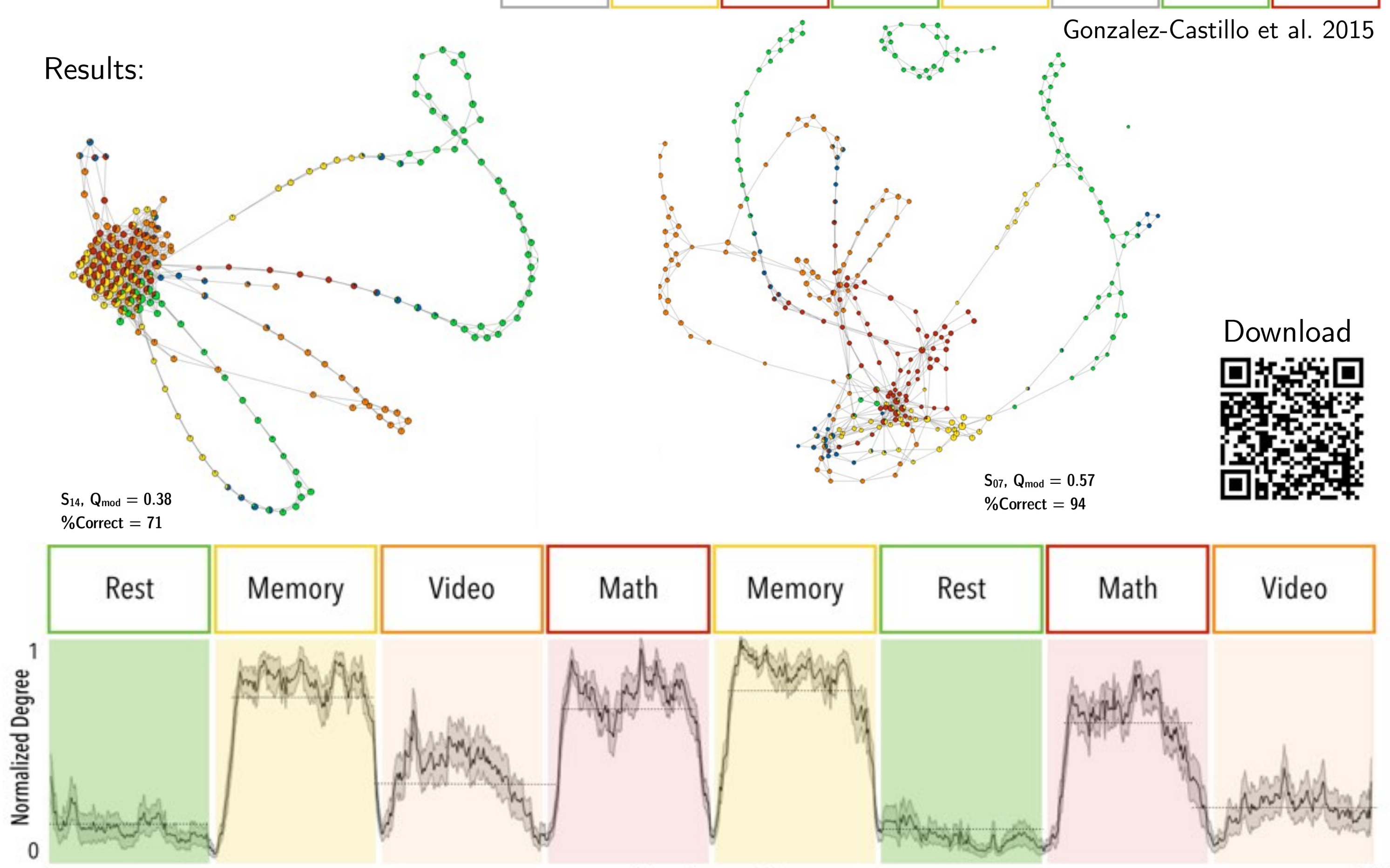
Dataset:

- Known transitions between tasks and behavioral performance



Gonzalez-Castillo et al. 2015

Results:



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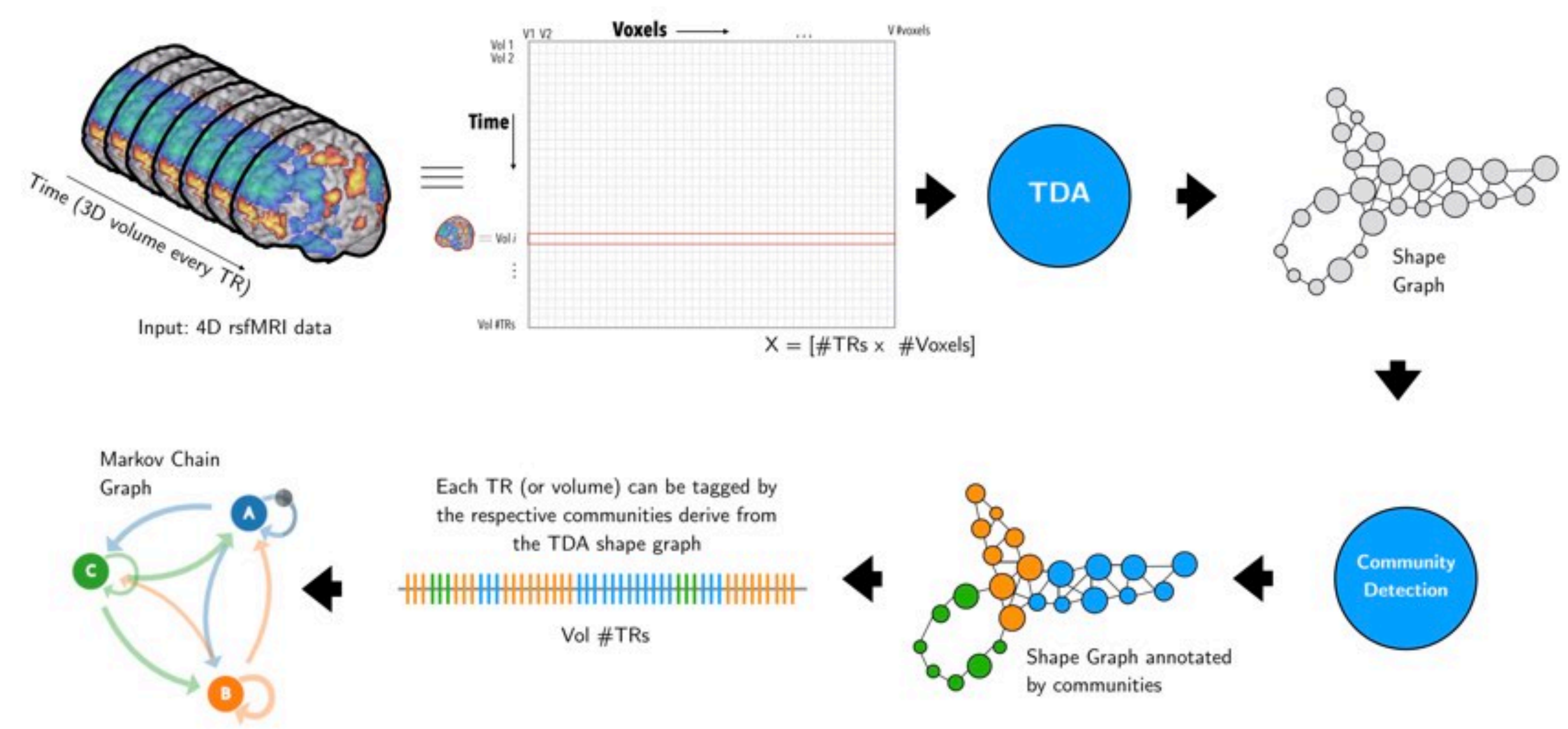
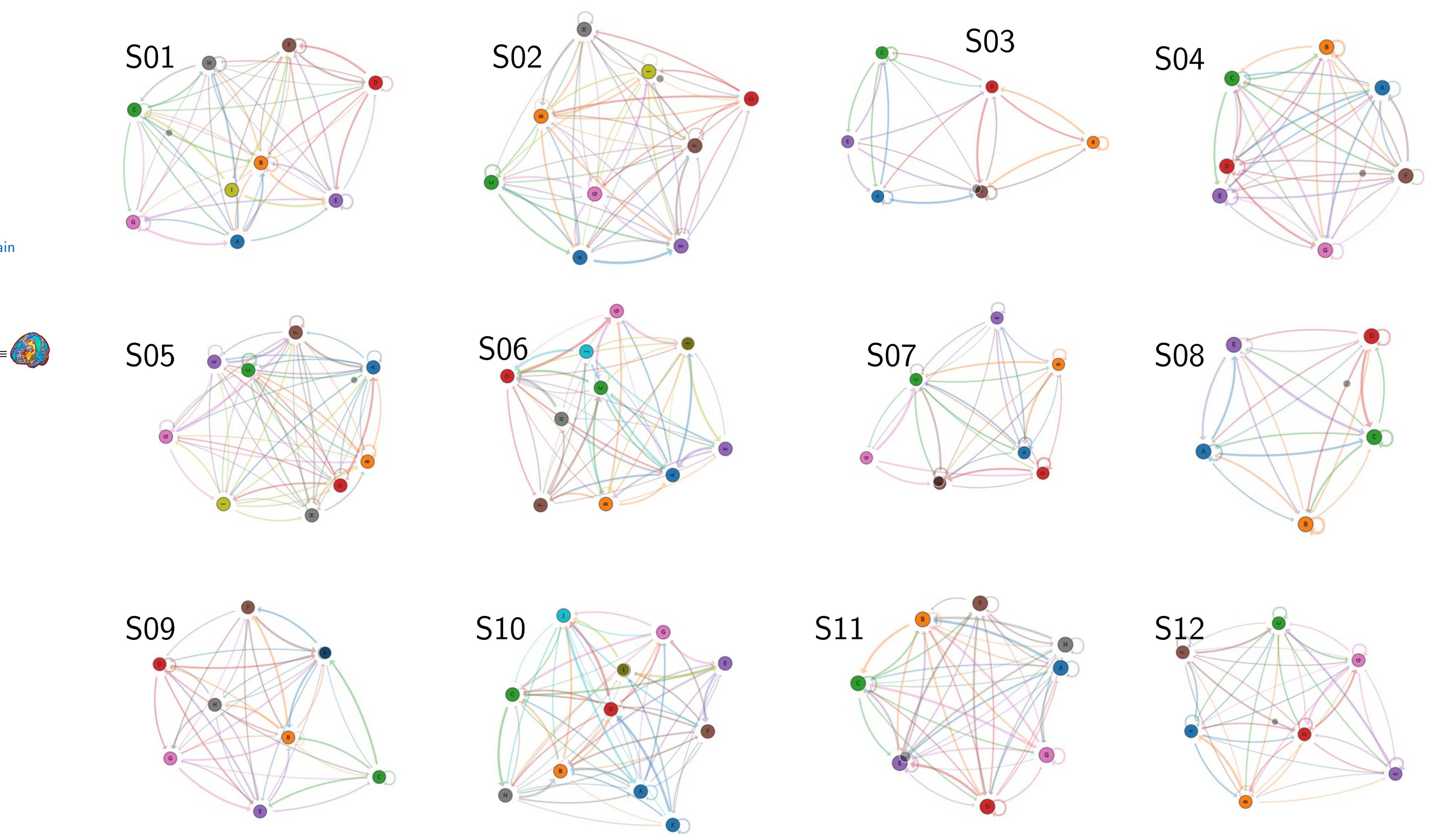
Application of TDA-based Mapper to rsfMRI data from individuals with FXS

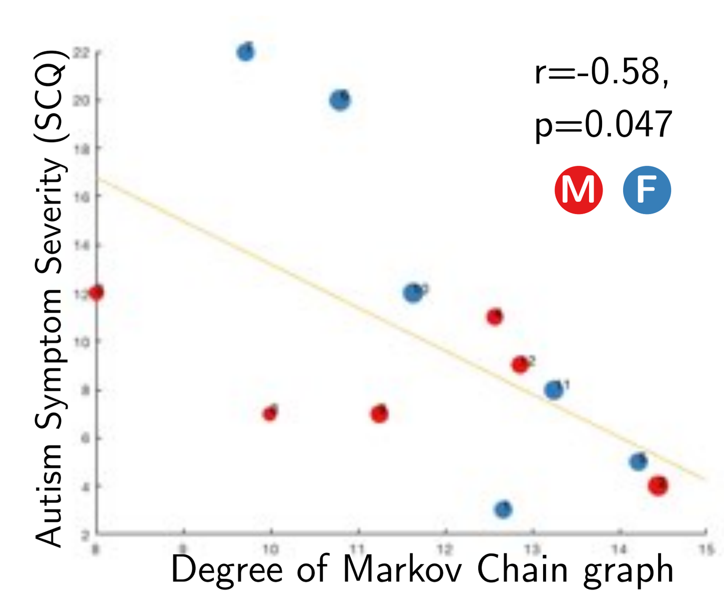
Method



Saggar et al. [in-preparation]

Results





	Degree MC	SCQ	#frames	Sex
S01	12.67	3	173	F
S02	14.44	4	221	M
S03	8.00	12	122	M
S04	12.57	11	155	M
S05	14.22	5	174	F
S06	10.80	20	240	F
S07	9.71	22	169	F
S08	10.00	7	108	M
S09	11.25	7	174	M
S10	11.64	12	217	F
S11	13.25	8	202	F
S12	12.86	9	167	M

Conclusions

- Lower degree of a MC graph suggests high repeatability of states. The observed association of lower degree with higher SCQ scores points toward the repeatability observed in brain dynamics to be the basis for repetitive behaviors observed in autism spectrum disorders.
- In the near future, we plan to use large-scale biophysical network models to better understand the biological basis for observed repeatability in brain dynamics.

References

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2. Saggar, M., Sporns, O., Gonzalez-Castillo, J., Bandettini, P. A., Carlsson, G., Glover, G., & Reiss, A. L. (2018). Towards a new approach to reveal dynamical organization of the brain using topological data analysis. *Nature Communications*, *9*(1), 1399.

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