Swimming in a sea of under-explored dynamics:
A survey of approaches for capturing time-varying connectivity

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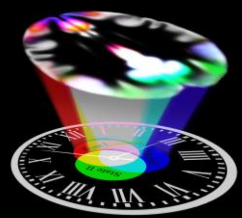
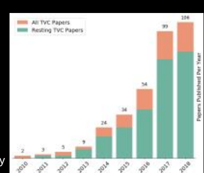


Outline

- Dynamic Connectivity: Brief Intro
- Temporal Dynamics
- Spatial Dynamics
- Classification, Simulation, Validation
- Temporal features (primitives, statelets)
- Additional Clinical Applications
- Conclusion

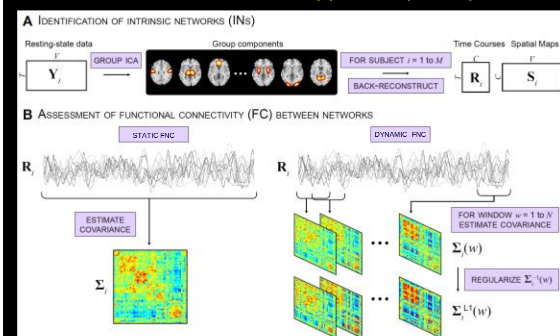
Brief (incomplete) history

- 2010
  - C. Chang et al., Neuroimage 2010
    - Sliding-window, wavelet transform, DMN ROIs, std
  - U. Sakoglu et al, MAGMA 2010
    - Sliding-window, whole brain ICA FNC dynamics, time-locked responses, application to SZ
- 2011
  - Kiviniemi et al.
    - Sliding window, spatial DMN changes
- 2012
  - Allen et al., Cerebral Cortex 2012.
    - ICA FNC 'states', dwell time, etc.
  - Jones et al., PlosOne 2012
    - ICA, dynamic graph metrics, AD
  - Damaraju et al. NI Clinical, 2014
    - ICA FNC static & dynamic states in large SZ study
- Reviews
  - Hutchison 2013, Neuroimage
  - Calhoun et al. Neuron 2014 ["chronnectome"]
  - Calhoun IEEE SPS Letters, 2016
  - Preti et al., Neuroimage 2017
  - Lurie, Network Neuroscience 2019 [extensive coverage of many issues]
  - Iraji, Trends Cog. Sci 2020 [spatial dynamics]



Lurie et al, Network Neuroscience 2019.

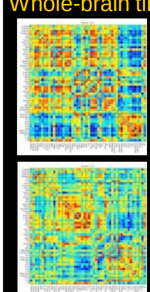
The windowed FNC approach (dFNC)

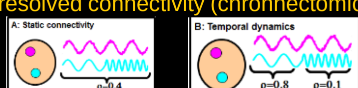


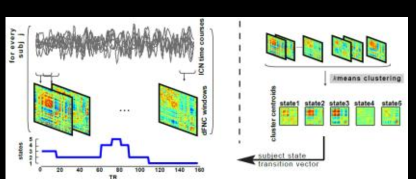
E. Allen, E. Damaraju, S. M. Plis, E. Erhardt, T. Eichele, and V. D. Calhoun, "Tracking whole-brain connectivity dynamics in the resting state," *Cereb Cortex*, 2014.

U. Sakoglu, G. D. Pearlson, K. A. Kiehl, Y. M. Wang, A. M. Michael, and V. D. Calhoun, "A method for evaluating dynamic functional network connectivity and task-modulation: application to schizophrenia," MAGMA, vol. 23, pp. 351-366, 2010.

Whole-brain time-resolved connectivity (chronnectomics)







U. Sakoglu, G. D. Pearlson, K. A. Kiehl, Y. M. Wang, A. M. Michael, and V. D. Calhoun, "A method for evaluating dynamic functional network connectivity and task-modulation: application to schizophrenia," MAGMA, vol. 23, pp. 351-366, Dec 2010, 2891285.

E. Allen, E. Damaraju, S. M. Plis, E. Erhardt, T. Eichele, and V. D. Calhoun, "Tracking whole-brain connectivity dynamics in the resting state," *Cereb Cortex*, 2014.

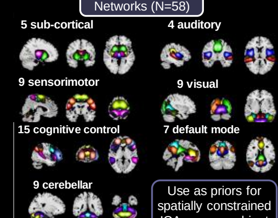
V. D. Calhoun, R. Miller, G. D. Pearlson, and T. Adalı, "The chronnectome: Time-varying connectivity networks as the next frontier in fMRI data discovery," Neuron, vol. 84, pp. 262-274, 2014

Classification from rest fMRI: hybrid models

HCP Data (N=823) 100 Components

GSS Data (N=1005) 100 Components

Common Rest Networks (N=58)

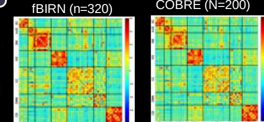


Use as priors for spatially constrained ICA on new subject

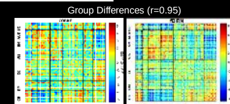
[adapts to individual subjects, preserves network labels, fuzzy parcellations]

Dataset 1: fBIRN (n=320)

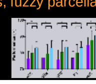
Dataset 2: COBRE (N=200)



Group Differences (r=0.95)



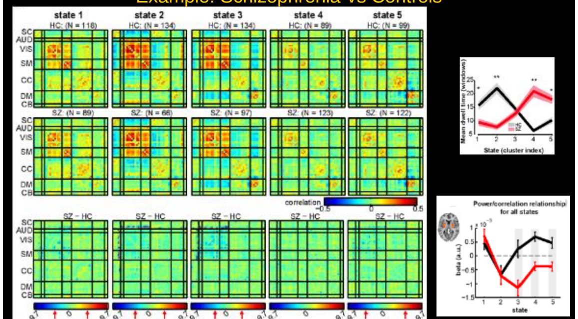
Networks outperforms fixed ROIs



Y. Du, et al. "NeuroMark: An automated and adaptive ICA based pipeline to identify reproducible fMRI markers of brain disorders," Nimg Clin, 28,, 2020.

Y. Du, et al, "Artifact removal in the context of group ICA: A comparison of single-subject and group approaches," *Hum Brain Mapp,* vol. 37, pp. 1005-1025, 2016, PMC5784424.

Example: Schizophrenia vs Controls

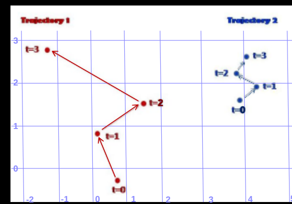


Putamen - Sensorimotor hypo-connectivity

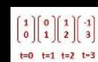
E. Damaraju, E. A. Allen, A. Belger, J. M. Ford, S. McEwen, D. H. Mathalon, B. A. Mueller, G. D. Pearlson, S. G. Potkin, A. Preda, J. A. Turner, J. G. Vaidya, T. G. van Erp, and V. D. Calhoun, "Dynamic functional connectivity analysis reveals transient states of dysconnectivity in schizophrenia," Neuroimage Clin, vol. 5, pp. 298-308, 2014, 4141977.

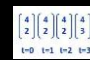
Meta-state approach: add flexibility by allowing occupancy of multiple states at the same time

Imagine the two trajectories from the previous slide moving In an integer lattice. They now have a 2D a parameterization involving the lattice point they are closest two at each moment in time.



The higher dimensional symbol space is clearly giving a better qualitative summary of what we are actually observing.



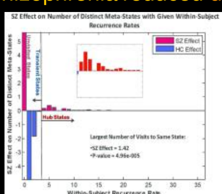


Trajectory in 2D integer-lattice *not* constant: changes at every timepoint, moves L1 distance 6

Trajectory in 2D integer-lattice almost constant moves L1 distance 1

R. L. Miller, M. Yaesoubi, J. A. Turner, D. Mathalon, A. Preda, G. Pearlson, T. Adali, and V. D. Calhoun, "Higher Dimensional Meta-State Analysis Reveals Reduced Resting fMRI Connectivity Dynamism in Schizophrenia Patients," PLoS One, vol. 11, p. e0149849, 2016, PMC4794213.

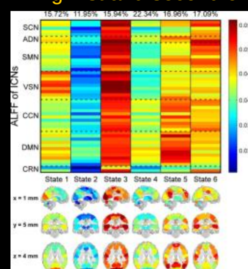
Schizophrenia reduced dynamic fluidity & dynamic range

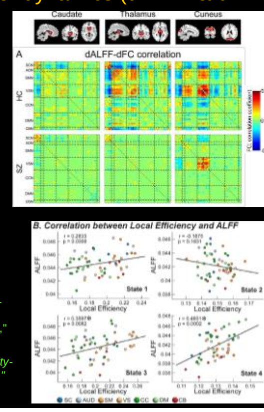


Dynamism Measure	Decomposition method			
	tICA	sICA	PCA	K-means
# Distinct Meta-States	-5.65 (p=4e-6)	-2.63 (p=0.007)	-5.78 (p=6e-8)	-6.52 (p=1.5e-7)
# Meta-State Changes	-2.2 (p=6.6e-8)	-1.29 (p=2.7e-6)	-2.2 (p-2.1e-10)	-5.6 (p=8.2e-7)
L2 Space of Meta-States	-5.37 (p=1.4e-6)	-2.59 (p=0.003)	-4.80 (p=5.9e-7)	-2.7 (p=1.5e-9)
Total Distance Traveled	-9.2 (p.1.9e-6)	-4.3 (p=0.0008)	-6.8 (p=1.8e-6)	-10.0 (p=5.3e-7)

R. L. Miller, M. Yaesoubi, J. A. Turner, D. Mathalon, A. Preda, G. Pearlson, T. Adali, and V. D. Calhoun, "Higher Dimensional Meta-State Analysis Reveals Reduced Resting fMRI Connectivity Dynamism in Schizophrenia Patients," PLoS One, vol. 11, p. e0149849, 2016, PMC4794213.

Linking first and second order dynamics (dALFF & dFNC)





Z. Fu, et al., "Characterizing dynamic amplitude of low-frequency fluctuation and its relationship with dynamic functional connectivity: An application to schizophrenia," *Neuroimage, vol. 180, pp. 619-631, Oct 15 2018.*

Z. Fu, et al., "Dynamic state with covarying brain activity-connectivity: On the pathophysiology of schizophrenia," Neuroimage, vol. 224, Jan 1 2021.

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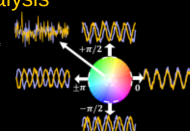
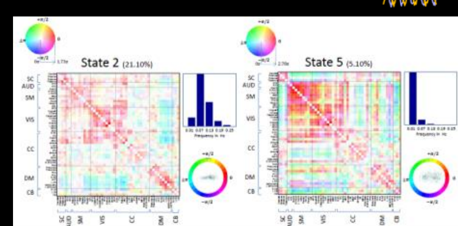
Time-frequency analysis

Sliding-window approaches are based on a locality assumption

There is overwhelming evidence that brain connectivity is a function of frequency (cf. Chang et al., 2010, Cordes et al., 2001)

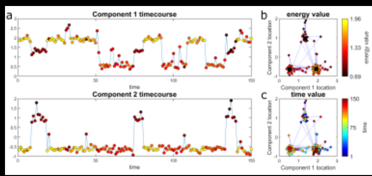
We can use Welch's method to estimate the cross-power spectral density. The Complex Morlet wavelet allows us to capture variation in both temporal and frequency domains by leveraging both temporal and frequency information





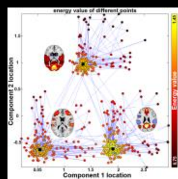
M. Yaesoubi, E. A. Allen, R. L. Miller, and V. D. Calhoun, "Dynamic coherence analysis of resting fMRI data to jointly capture state-based phase, frequency, and time-domain information," NeuroImage, 120, 133-142, 2015.

Brain trajectory dynamics



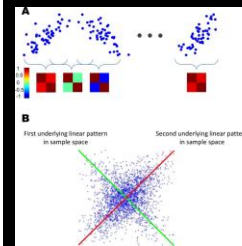
Energy

$$e_{j,t} = \frac{1}{\sum_{\substack{1 \le t_0 \le T \\ t_0 \ne t}} \sqrt{\left\| x_{j,t} - x_{j,t_0} \right\|_2}}$$

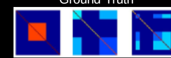


A. Faghiri, et al., "Brain Density Clustering Analysis: A New Approach to Brain Functional Dynamics," Front Neurosci, vol. 15, p. 621716, 2021, PMC8076753.

A windowless approach…



Ground Truth

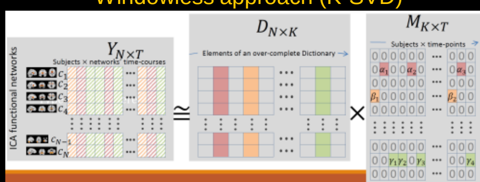


Results

Results on randomly shuffled signal

M. Yaesoubi, T. Adali, and V. D. Calhoun, "A window-less approach for capturing time-varying connectivity in fMRI data reveals the presence of states with variable rates of change," Hum Brain Mapp, 2018.

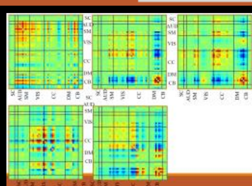
Windowless approach (K-SVD)



$$\min \|A\|_o \; subject\ to\ Y = DM$$

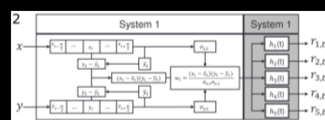
Key assumption avoided:
-locality (windows, HMM)

Assumes:
-Samples are i.i.d.
-Multivariate normal dynamic distribution

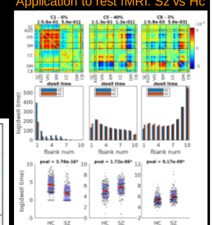


M. Yaesoubi, T. Adali, and V. D. Calhoun, "A window-less approach for capturing time-varying connectivity in fMRI data reveals the presence of states with variable rates of change," Hum Brain Mapp, 2018.

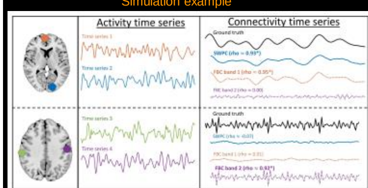
Filterbank connectivity (a unified approach)



Application to rest fMRI: Sz vs Hc

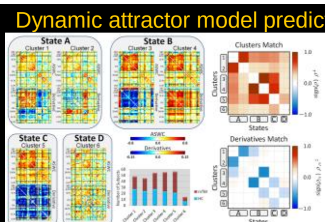


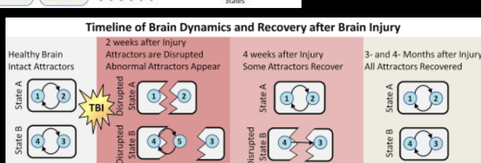
Simulation example



A Faghiri, A Iraji, E Damaraju, J Turner, and V Calhoun, "A unified approach for characterizing static/dynamic connectivity frequency profiles using filter banks," Network Neuroscience, pp. 1-51, 2020

Dynamic attractor model predicts mTBI recovery





H. J. van der Horn, V. M. Vergara, F. A. Espinoza, V. D. Calhoun, A. R. Mayer, and J. van der Naalt, "Functional outcome is tied to dynamic brain states after mild to moderate traumatic brain injury," Hum Brain Mapp, 2019.

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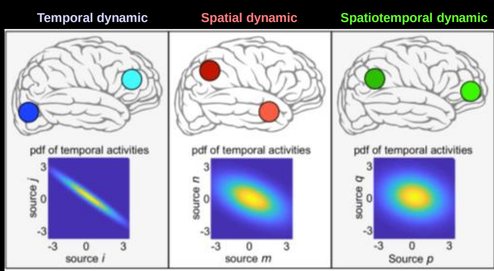
Functional organization evolves over time

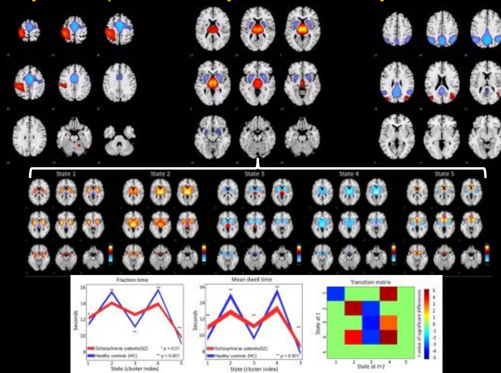


A toy example of three different dynamic behaviors for systems with two latent sources

A. Iraji et al, "The spatial chronnectome reveals a dynamic interplay between functional segregation and integration," Hum Brain Mapp, vol. 40, pp. 3058-3077, Jul 2019, PMC6548674.

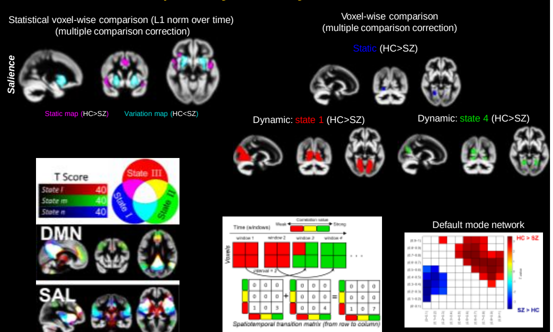
A. Iraji, R. Miller, T. Adali, and V. D. Calhoun, "Space: A Missing Piece of the Dynamic Puzzle," Trends Cogn Sci, vol. 24, pp. 135-149, Feb 2020

A dynamic spatial hierarchy: Less thalamic dynamics in SZ



A. Iraji, et al,, "Spatial dynamics within and between brain functional domains: A hierarchical approach to study time-varying brain function," Human Brain Mapping, vol. 40, pp. 1969-1986, 2019

Spatially fluid dynamics



A. Iraji, T. P. Deramus, N. Lewis, M. Yaesoubi, J. M. Stephen, E. Erhardt, A. Belger, J. M. Ford, S. McEwen, D. H. Mathalon, B. A. Mueller, G. D. Pearlson, S. G. Potkin, A. Preda, J. A. Turner, J. G. Vaidya, T. G. M. van Erp, and V. D. Calhoun, "The spatial chronnectome reveals a dynamic interplay between functional segregation and integration," Hum Brain Mapp, vol. 40, pp. 3058-3077, Jul 2019, PMC6548674.

Lack of systematic categorization of existing approaches

Table 1. A (Noncomprehensive) Categorization of Examples of Existing Analytical Approaches Based on the Type of Estimated Sources

Analytical approach	Node = Source[a]	Multiple spatial patterns	Spatiotemporal dynamic		Refs (example)
			Spatially dynamic	Temporally dynamic	
Seed-based analysis (SBA)	No	No	No	No	[31]
Independent component analysis (ICA)	Yes	Yes	No	No	[32,33]
Co-activation pattern (CAP) analysis[b]	No	Yes	No	No	[30]
Dynamic functional connectivity (dFC) with fixed nodes/seeds	No	No	No	Yes	[34–36]
Dynamic functional network connectivity (dFNC) analysis	Yes	Yes	No	Yes	[37,38]
Dynamic coupling map (dCM) analysis[c]	Yes	Yes	Yes	No	[39]
Windowed ICA/ independent vector analysis (SW-ICA/IVA)[c]	Yes	Yes	Yes	No	[40,41]
Constrained SW-IVA	Yes	Yes	Yes	Yes	[42]
Dynamic hierarchy analysis (dHA)	Yes	Yes	Yes	Yes	[43]

A. Iraji, R. Miller, T. Adali, and V. D. Calhoun, "Space: A Missing Piece of the Dynamic Puzzle," Trends Cogn Sci, vol. 24, pp. 135-149, Feb 2020.

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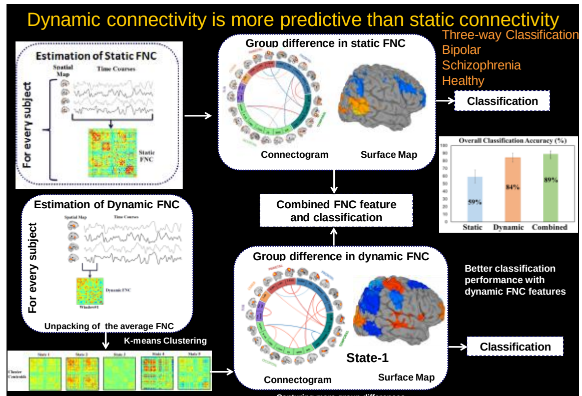
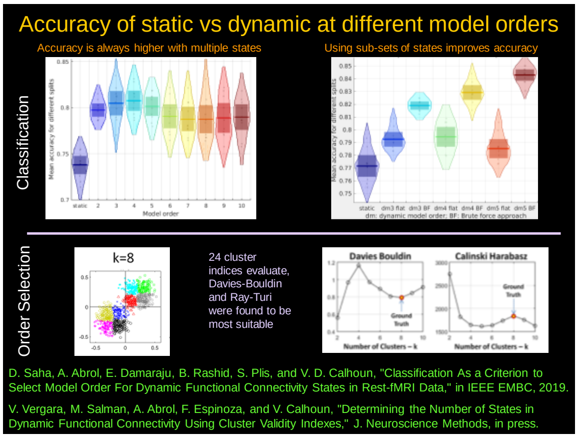
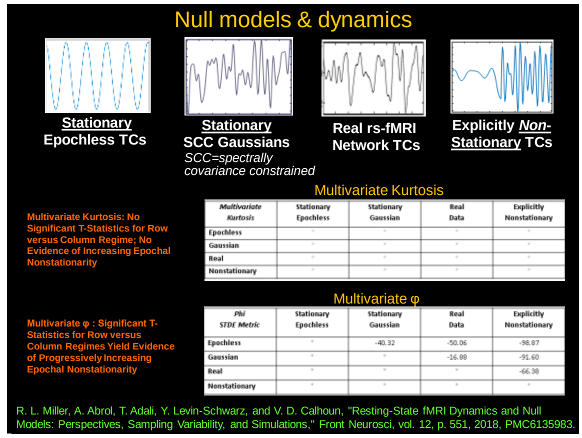
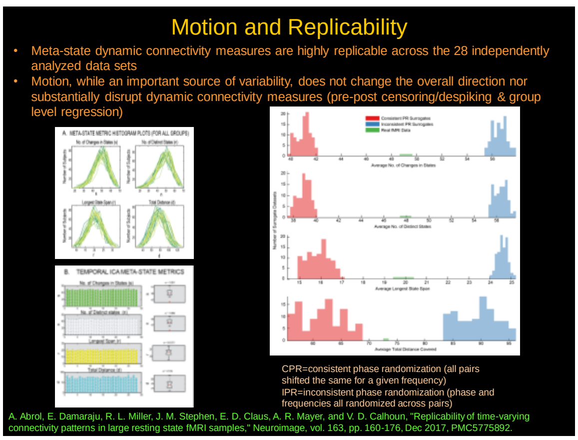
Dynamic connectivity is more predictive than static connectivity

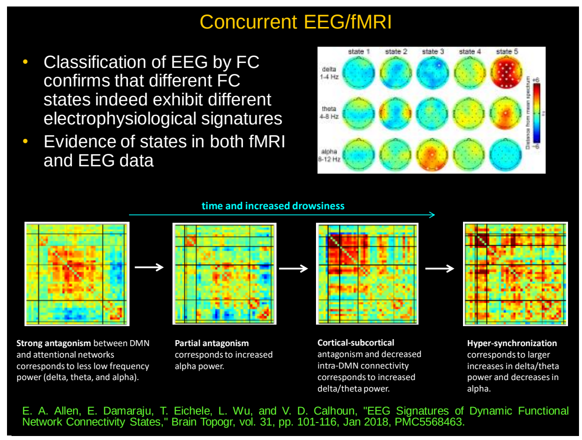


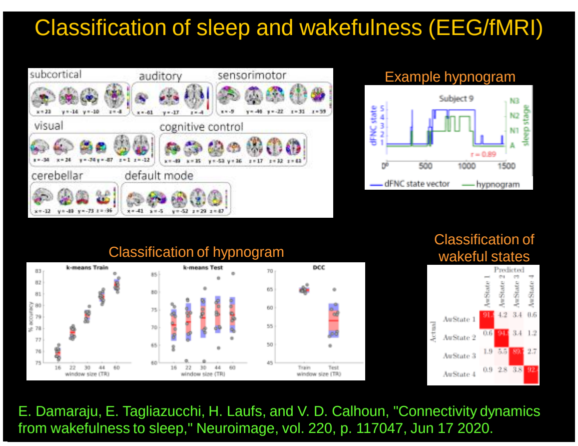
B. Rashid, M. R. Arbabshirani, E. Damaraju, M. S. Cetin, R. Miller, G. D. Pearlson, and V. D. Calhoun, "Classification of schizophrenia and bipolar patients using static and dynamic resting-state fMRI brain connectivity," Neuroimage, 134, 645-657, Apr 23 2016

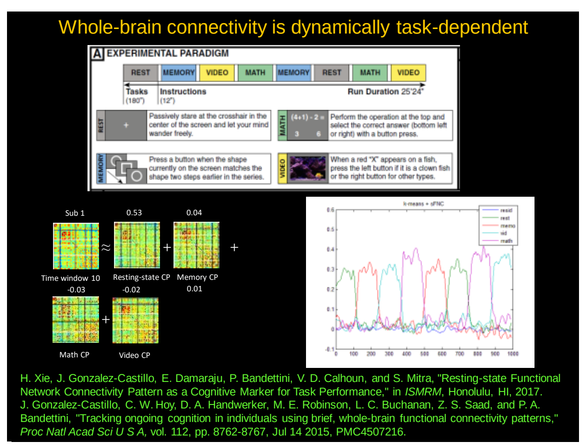

Accuracy of static vs dynamic at different model orders
Accuracy is always higher with multiple states
Using sub-sets of states improves accuracy
Classification
Order Selection
k=8
24 cluster indices evaluate, Davies-Bouldin and Ray-Turi were found to be most suitable
Davies Bouldin
Calinski Harabasz
D. Saha, A. Abrol, E. Damaraju, B. Rashid, S. Plis, and V. D. Calhoun, "Classification As a Criterion to Select Model Order For Dynamic Functional Connectivity States in Rest-fMRI Data," in IEEE EMBC, 2019.
V. Vergara, M. Salman, A. Abrol, F. Espinoza, and V. Calhoun, "Determining the Number of States in Dynamic Functional Connectivity Using Cluster Validity Indexes," J. Neuroscience Methods, in press.


Null models & dynamics
Stationary Epochless TCs
Stationary SCC Gaussians
SCC=spectrally covariance constrained
Real rs-fMRI Network TCs
Explicitly Non-Stationary TCs
Multivariate Kurtosis
Multivariate Kurtosis: No Significant T-Statistics for Row versus Column Regime; No Evidence of Increasing Epochal Nonstationarity
Multivariate Kurtosis | Stationary Epochless | Stationary Gaussian | Real Data | Explicitly Nonstationary
Epochless | * | * | * | *
Gaussian | * | * | * | *
Real | * | * | * | *
Nonstationary | * | * | * | *
Multivariate φ
Multivariate φ : Significant T-Statistics for Row versus Column Regimes Yield Evidence of Progressively Increasing Epochal Nonstationarity
Phi STDE Metric | Stationary Epochless | Stationary Gaussian | Real Data | Explicitly Nonstationary
Epochless | * | -40.32 | -50.06 | -98.87
Gaussian | * | * | -16.88 | -91.60
Real | * | * | * | -66.38
Nonstationary | * | * | * | *
R. L. Miller, A. Abrol, T. Adali, Y. Levin-Schwarz, and V. D. Calhoun, "Resting-State fMRI Dynamics and Null Models: Perspectives, Sampling Variability, and Simulations," Front Neurosci, vol. 12, p. 551, 2018, PMC6135983.


Motion and Replicability
• Meta-state dynamic connectivity measures are highly replicable across the 28 independently analyzed data sets
• Motion, while an important source of variability, does not change the overall direction nor substantially disrupt dynamic connectivity measures (pre-post censoring/despiking & group level regression)
CPR=consistent phase randomization (all pairs shifted the same for a given frequency)
IPR=inconsistent phase randomization (phase and frequencies all randomized across pairs)
A. Abrol, E. Damaraju, R. L. Miller, J. M. Stephen, E. D. Claus, A. R. Mayer, and V. D. Calhoun, "Replicability of time-varying connectivity patterns in large resting state fMRI samples," Neuroimage, vol. 163, pp. 160-176, Dec 2017, PMC5775892.


Concurrent EEG/fMRI
• Classification of EEG by FC confirms that different FC states indeed exhibit different electrophysiological signatures
• Evidence of states in both fMRI and EEG data
state 1
state 2
state 3
state 4
state 5
delta 1-4 Hz
theta 4-8 Hz
alpha 8-12 Hz
time and increased drowsiness
Strong antagonism between DMN and attentional networks corresponds to less low frequency power (delta, theta, and alpha).
Partial antagonism corresponds to increased alpha power.
Cortical-subcortical antagonism and decreased intra-DMN connectivity corresponds to increased delta/theta power.
Hyper-synchronization corresponds to larger increases in delta/theta power and decreases in alpha.
E. A. Allen, E. Damaraju, T. Eichele, L. Wu, and V. D. Calhoun, "EEG Signatures of Dynamic Functional Network Connectivity States," Brain Topogr, vol. 31, pp. 101-116, Jan 2018, PMC5568463.


Classification of sleep and wakefulness (EEG/fMRI)
subcortical
auditory
sensorimotor
visual
cognitive control
cerebellar
default mode
Example hypnogram
Subject 9
dFNC state
sleep stage
dFNC state vector
hypnogram
Classification of hypnogram
k-means Train
k-means Test
DCC
Classification of wakeful states
E. Damaraju, E. Tagliazucchi, H. Laufs, and V. D. Calhoun, "Connectivity dynamics from wakefulness to sleep," Neuroimage, vol. 220, p. 117047, Jun 17 2020.


Whole-brain connectivity is dynamically task-dependent
EXPERIMENTAL PARADIGM
REST
MEMORY
VIDEO
MATH
Run Duration 25'24"
Sub 1
Time window 10
Resting-state CP
Memory CP
Math CP
Video CP
H. Xie, J. Gonzalez-Castillo, E. Damaraju, P. Bandettini, V. D. Calhoun, and S. Mitra, "Resting-state Functional Network Connectivity Pattern as a Cognitive Marker for Task Performance," in ISMRM, Honolulu, HI, 2017.
J. Gonzalez-Castillo, C. W. Hoy, D. A. Handwerker, M. E. Robinson, L. C. Buchanan, Z. S. Saad, and P. A. Bandettini, "Tracking ongoing cognition in individuals using brief, whole-brain functional connectivity patterns," Proc Natl Acad Sci U S A, vol. 112, pp. 8762-8767, Jul 14 2015, PMC4507216.

Outline

- Dynamic Connectivity: Brief Intro
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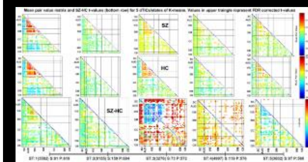
Searching the dynamic space

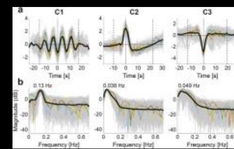
Triclustering to compare apples/apples: Exhaustive search for similarity among: 1) FNC values, 2) windows (time), 3) subjects



MA Rahaman, et al., "N-BiC: A Method for Multi-Component and Symptom Biclustering of Structural MRI Data: Application to Schizophrenia," IEEE Trans Biomed Eng, vol. 67, pp. 110-121, Jan 2020.

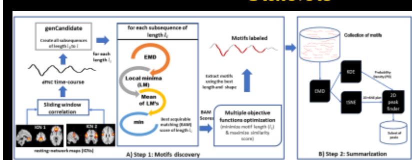
M. A. Rahaman, et al., "A novel method for tri-clustering dynamic functional network connectivity (dFNC) identifies significant schizophrenia effects across multiple states in distinct subgroups of individuals," bioRxiv, p. 2020.2008.2006.239152, 2020.

Deep learning (deep temporal convolutional neural network) to capture repeating temporal primatives with brain networks

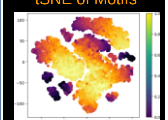


H. Morioka, V. Calhoun, and A. Hyvarinen, "Nonlinear ICA of fMRI reveals primitive temporal structures linked to rest, task, and behavioral traits," Neuroimage, vol. 218, Sep 2020.

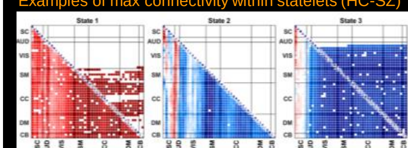
Statelets



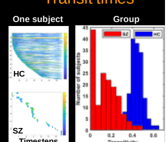
tSNE of Motifs



Examples of max connectivity within statelets (HC-SZ)

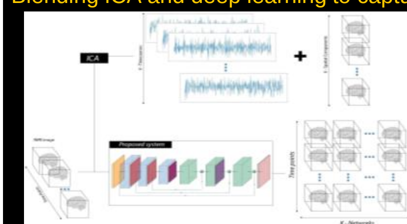


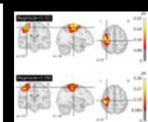
Transit times



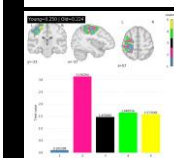
M. Rahaman, E. Damaraju, D. Saha, S. Plis, and V. D. Calhoun, "Statelets: High dimensional predominant shapes in dynamic functional network connectivity," bioRxiv, p. 2020.2008.2016.252999, 2020.

Blending ICA and deep learning to capture 5D dynamics

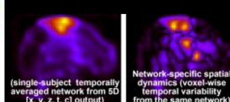




B. Kazemivash and V. D. Calhoun, "A novel 5D brain parcellation approach based on spatio-temporal encoding of resting fMRI data from deep residual learning," *bioRxiv, p. 2021.2004.2022.440936, 2021.*



Age effects on spatial clusters within network

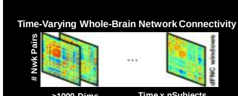


Spatial variation within network

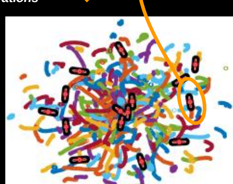
Dynamic FNC among within network avg timecourses

Multiframe evolving dFNC (EVOdFNC) vs 'snapshot' dFNC (SNAPdFNC)

Time-Varying Whole-Brain Network Connectivity



Nonlinear planar embedding (via UMAP) of the high-dimensional dFNC observations

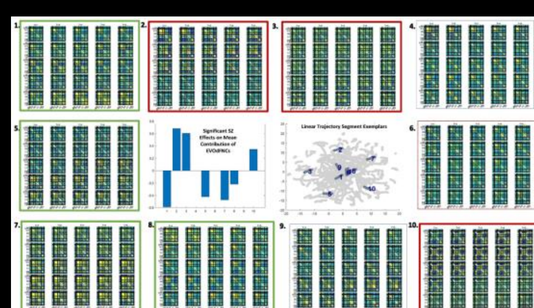


Movie-style dFNC representation

Construct linearized 2D dFNC trajectory *exemplar* γ_k of slope m^k centered at (x^k, y^k); based on the distribution of segment lengths

Continuity-Preserving 2D Embedding

Pervasive SZ vs HC differences



Group differences as well as significant and differential relationship w/ positive symptoms

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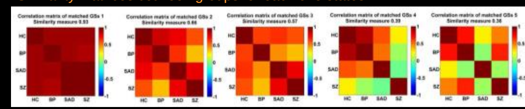
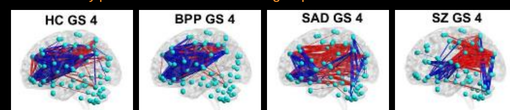
States differentiate along mood/psychosis dimension

States differentiate four groups: 1) Schizophrenia (SZ), 2) Schizoaffective disorder (no manic episodes; SAD), 3) bipolar disorder (BPP), 4) healthy controls (HC)

Similarity matrices between groups for each of 5 states

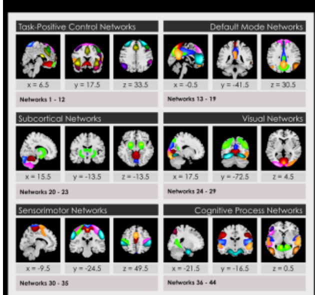


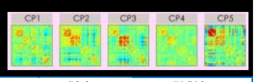
Connectivity patterns in state 4 for each group



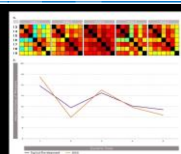
Y. Du, G. D. Pearlson, D. Lin, J. Sui, J. Chen, M. Salman, C. A. Tamminga, E. I. Ivleva, J. A. Sweeney, M. S. Keshavan, B. A. Clementz, J. Bustillo, and V. D. Calhoun, "Identifying dynamic functional connectivity biomarkers using GIG-ICA: Application to schizophrenia, schizoaffective disorder, and psychotic bipolar disorder," Hum Brain Mapp, vol. 38, pp. 2683-2708, May 2017, PMC5399898.

dFNC in ADHD: evidence of multi-scale effects



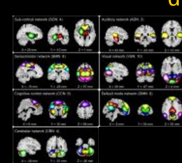


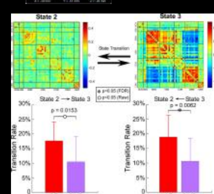
	Native Space			Meta-State Space			
IN Group	Dwell Time	Fraction of Time	State-switching	Number of states	State-switching	L1 Span	Total L1 Distance
Global	0.122-0.936	0.323-0.911	0.349	0.046	0.059	0.010*	0.475
Task-positive Control	0.117-0.896	0.414-0.626	0.157	0.135	0.144	0.501	0.285
DMN	0.012*-0.756	0.255-0.682	0.470	0.040	0.060	0.090	0.036*
Subcortical	0.207-0.786	0.783-0.827	0.542	0.323	0.443	0.702	0.774
Visual	0.134-0.926	0.195-0.830	0.780	0.465	0.487	0.053	0.942
Sensorimotor	0.208-0.515	0.557-0.866	0.347	0.504	0.634	0.470	0.720
Cognitive Processing	0.500-0.970	0.999	0.332	0.890	0.632	0.579	0.853



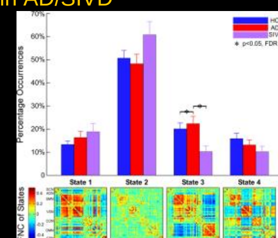
N. de Lacy and V. D. Calhoun, "Dynamic connectivity and the effects of maturation in youth with attention deficit hyperactivity disorder," Netw Neurosci, vol. 3, pp. 195-216, 2019, PMC6372020.

dFNC in AD/SIVD





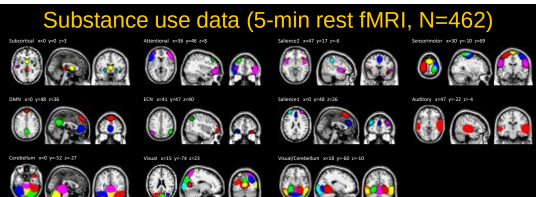
AD patients have more transitions between state 2 and 3 in both directions compared with SIVD patients.



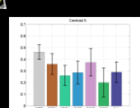
Compared with HC, AD patients have more occurrences while SIVD patients have fewer occurrences in state 3 with highly positive within-DMN FNC and negative DMN-to-sensory FNC.

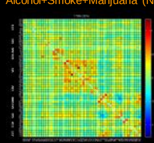
Z. Fu, A. Iraji, A. Caprihan, J. C. Adair, J. Sui, G. A. Rosenberg, and V. D. Calhoun, "In search of multimodal brain alterations in Alzheimer's and Binswanger's disease," *Neuroimage Clin,* 2019

Substance use data (5-min rest fMRI, N=462)



Control (N=121), Alcohol (N=62), Smoke (N=65), Alcohol+Smoke (N=50), Marijuana + Alcohol (N=35), Smoke+Marijuana (N=31), Alcohol+Smoke+Marijuana (N=62)





Mean Time Spent

	CTR	DRN	SMK	SAD	MAD	SAM	ALL
State 1	5.76%	13.53%	16%	12%	9%	8%	11%
State 2	11.24%	11.01%	19%	9%	125	18%	15%
State 3	14.74%	11.10%	14%	15%	24%	21%	19%
State 4	21.94%	28.36%	25%	35%	17%	33%	26%
State 5	46.32%	36.00%	26%	29%	37%	20%	29%

V. M. Vergara, B. J. Weiland, K. E. Hutchison, and V. D. Calhoun, "The Impact of Combinations of Alcohol, Nicotine, and Cannabis on Dynamic Brain Connectivity," Neuropsychopharmacology, vol. 43, pp. 877-890, 2018.

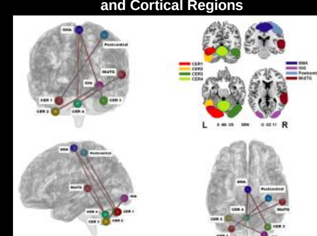
Prediction of mild TBI

Connections between Cerebellum and Cortical Regions

Fractional Anisotropy
AUC 66%

Rest fMRI:
AUC 78%

Dynamic Rest fMRI:
AUC 92%

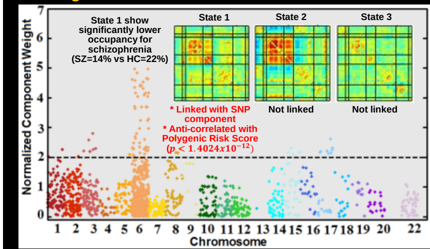


Impact of pipelines (filter/motion/window size/etc)

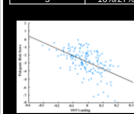
V. M. Vergara, A. R. Mayer, E. Damaraju, and V. D. Calhoun, "The effect of preprocessing in dynamic functional network connectivity used to classify mild traumatic brain injury," Brain Behav, vol. 7, p. e00809, Oct 2017, PMC5651393.

V. M. Vergara, A. R. Mayer, K. A. Kiehl, and V. D. Calhoun, "Dynamic functional network connectivity discriminates mild traumatic brain injury through machine learning," Neuroimage Clin, vol. 19, pp. 30-37, 2018, PMC6051314.

Image/Genomic Fusion: SNPs & time-resolved connectivity



Significant dFNC cells/state	
State#	Occupancy (HC/SZ)
1	22%/14%
2	32%/11%
3	20%/18%
4	9%/32%
5	16%/27%



Correlation= -0.5401 (p-value=1.4024e-12)

Parallel ICA was used to link dFNC matrices to 4000 SNPs identified via the PGC study

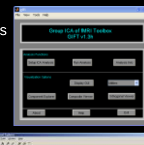
One state was linked with SNPs (primarily from ch 6) and associated with SZ risk

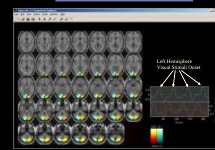
Biological Functions	Gene Name
Neurological Disease, Psychological Disorders	CHRNA3
Hereditary Disorder, Neurological Disease	ATXN7
Molecular Transport, RNA Trafficking	SMG6,THOC7
Visual System Development and Function	ATXN7
Cell Morphology, Embryonic Development	CCHCR1
Nervous System Dev., Tissue Morphology	ATXN7
Developmental Disorder, Neurological Disease	SMG6
Immunological Disease	RERE
Immunological Dis., Inflammatory Dis./Response	HLA-C

B. Rashid, J. Chen, I. Rashid, E. Damaraju, J. Liu, R. Miller, O. Agcaoglu, T. van Erp, K. Lim, J. Turner, D. Mathalon, J. Ford, J. Voyvodic, B. Mueller, A. Belger, S. McEwen, S. Potkin, A. Preda, J. Bustillo, G. Pearlson, and V. D. Calhoun, "A framework for linking resting-state chronnectome/genome features in schizophrenia: A pilot study," Neuroimage, vol. 184, pp. 843-854, 2019.

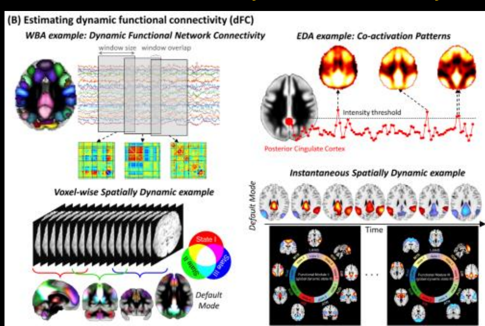
Software

- http://trendscenter.org/software
- freeware, written in MATLAB (also offering compiled versions), python, etc: over 20,000 unique downloads
- GIFT (Group ICA of fMRI Toolbox)
  - Single subject/Group ICA
  - MANCOVA testing framework
  - Source based morphometry
  - ICASSO (clustering/stability)
  - Dynamic FNC/Coherence
- FIT (Fusion ICA Toolbox)
  - Parallel ICA, jICA
  - mCCA+jICA & much more!
- Simulation Toolbox (SimTB)
  - Flexible generation of fMRI-like data
- COINS (data management/capture/sharing)
  - http://coins.trendscenter.org
- COINSTAC (decentralized analysis, privacy)
  - https://github.com/MRN-Code/coinstac
- CORTEX (deep learning)
  - https://github.com/rdevon/cortex





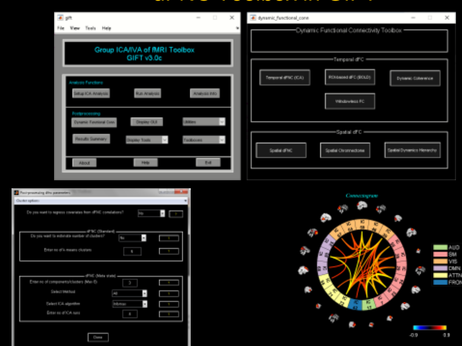
For more details on dynamic connectivity



A. Iraji, A. Faghiri, N. Lewis, Z. Fu, S. Rachakonda, and V. D. Calhoun, "Tools of the trade: Estimating time-varying connectivity patterns from fMRI data," Soc Cogn Affect Neurosci, Aug 12 2020.

https://trendscenter.org/software/gift/videos/

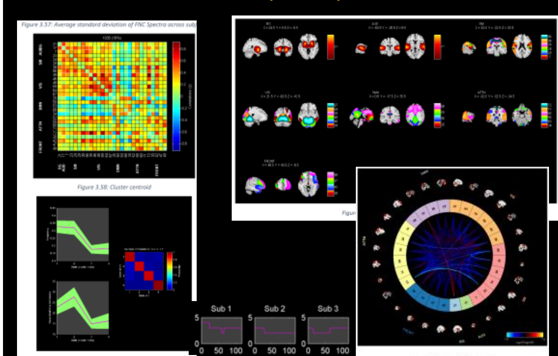
dFNC Toolbox in GIFT



A. Iraji, A. Faghiri, N. Lewis, Z. Fu, S. Rachakonda, and V. D. Calhoun, "Tools of the trade: Estimating time-varying connectivity patterns from fMRI data," Soc Cogn Affect Neurosci, Aug 12 2020.

http://trendscenter.org/software/gift

Example output



http://trendsdenter.org/software/gift

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Center for Translational Research in Neuroimaging and Data Science (TReNDS)

http://trendscenter.org

R01EB005846 , R01EB006841, P20GM103472, 1U01NS082074, 5R41MH100070, R01MH094524, 1R01MH104680