Opposing engagement of cerebellar and basal ganglia networks with shifts of cortical network topology

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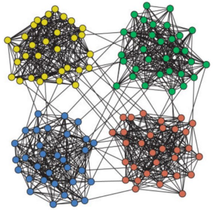
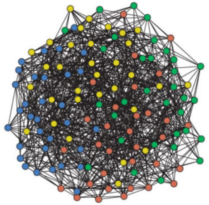
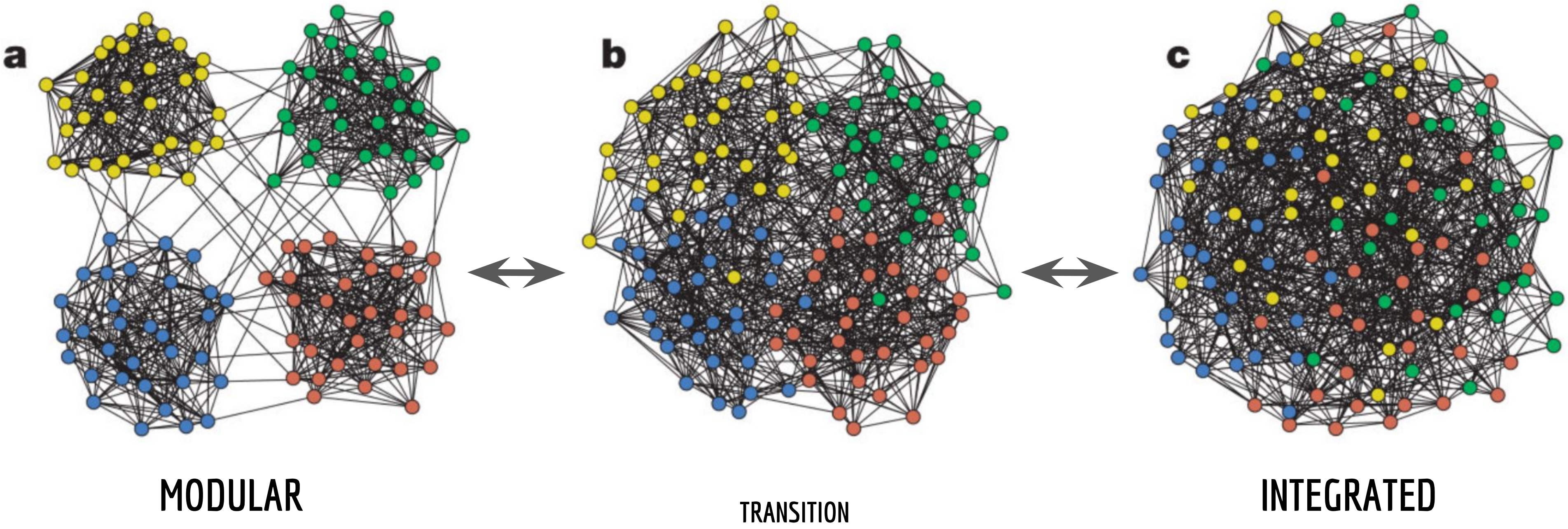
Cognitive flexibility allows you to accomplish a wide range of tasks





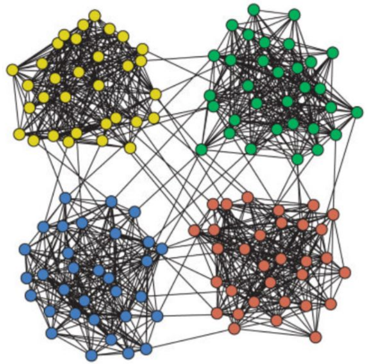
Network connectivity is mutable and can change from modular to integrated



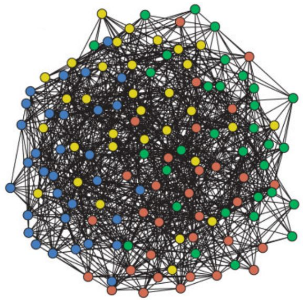
Guimerà & Nunes Amaral, 2005

How does the brain adapt to an ever changing landscape?

Reorganization occurs on a fast and slow timescale
(Zhou et al., 2019)

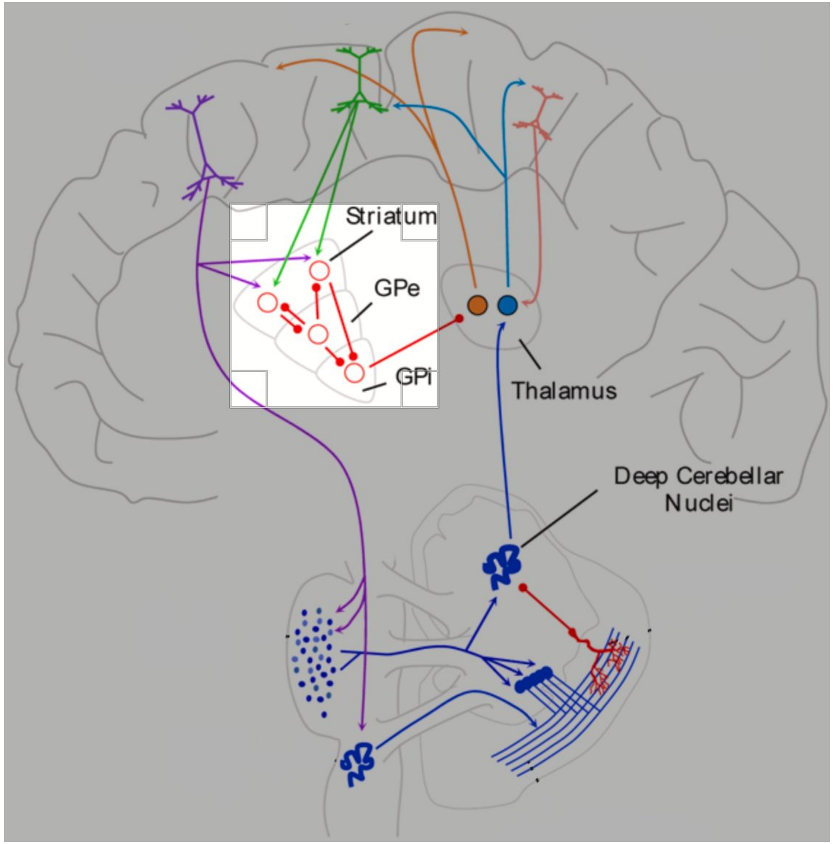


Cortical topology is linked to task cognitive complexity
(Owen et al., 2021)



Cortical topology can indicate richness of memory recall
(Geib et al., 2017)

Subcortical regions are highly connected with cortical regions

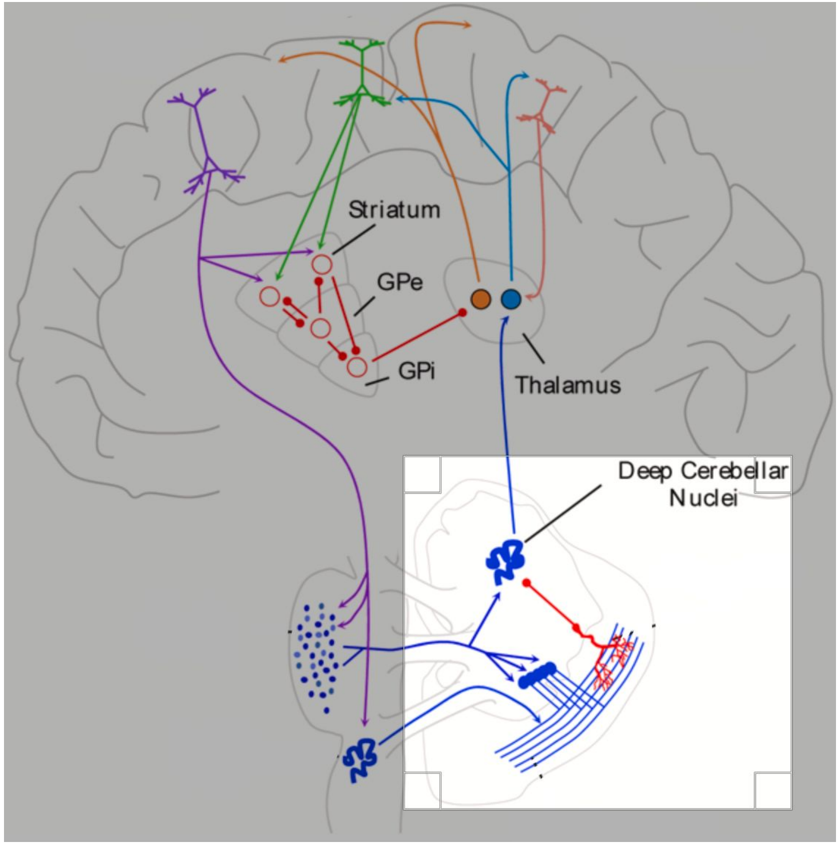


Integration

- Basal ganglia projects to matrix thalamus from globus pallidus interna (GPi).
    - Matrix thalamus projects diffusely to cortical regions

Shine, 2021

Subcortical regions are highly connected with cortical regions

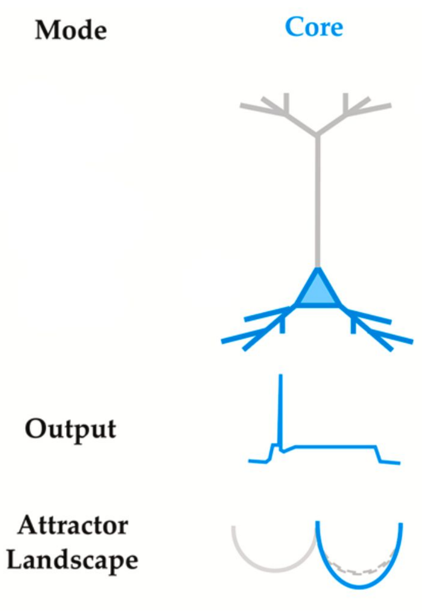


Segregation

- Cerebellum projects to core thalamus from the deep cerebellar nuclei
    - Core thalamus projects focally to cortical hubs

Shine, 2021

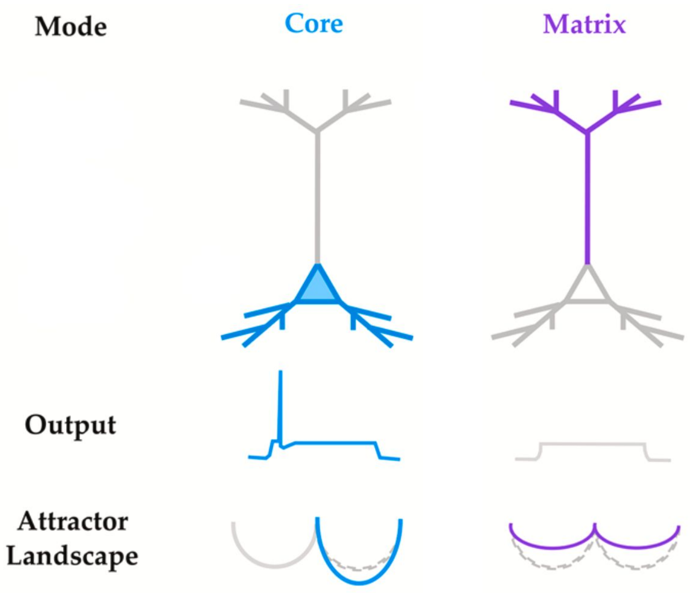
Cellular activation input to the thalamus drive changes in the attractor landscape



- Segregation leads to deepening of the wells
  - Greater stores of energy to select regions
  - Excitatory, glutamatergic input from the deep cerebellar nuclei to core thalamus (Shine, 2021).

Shine, 2021

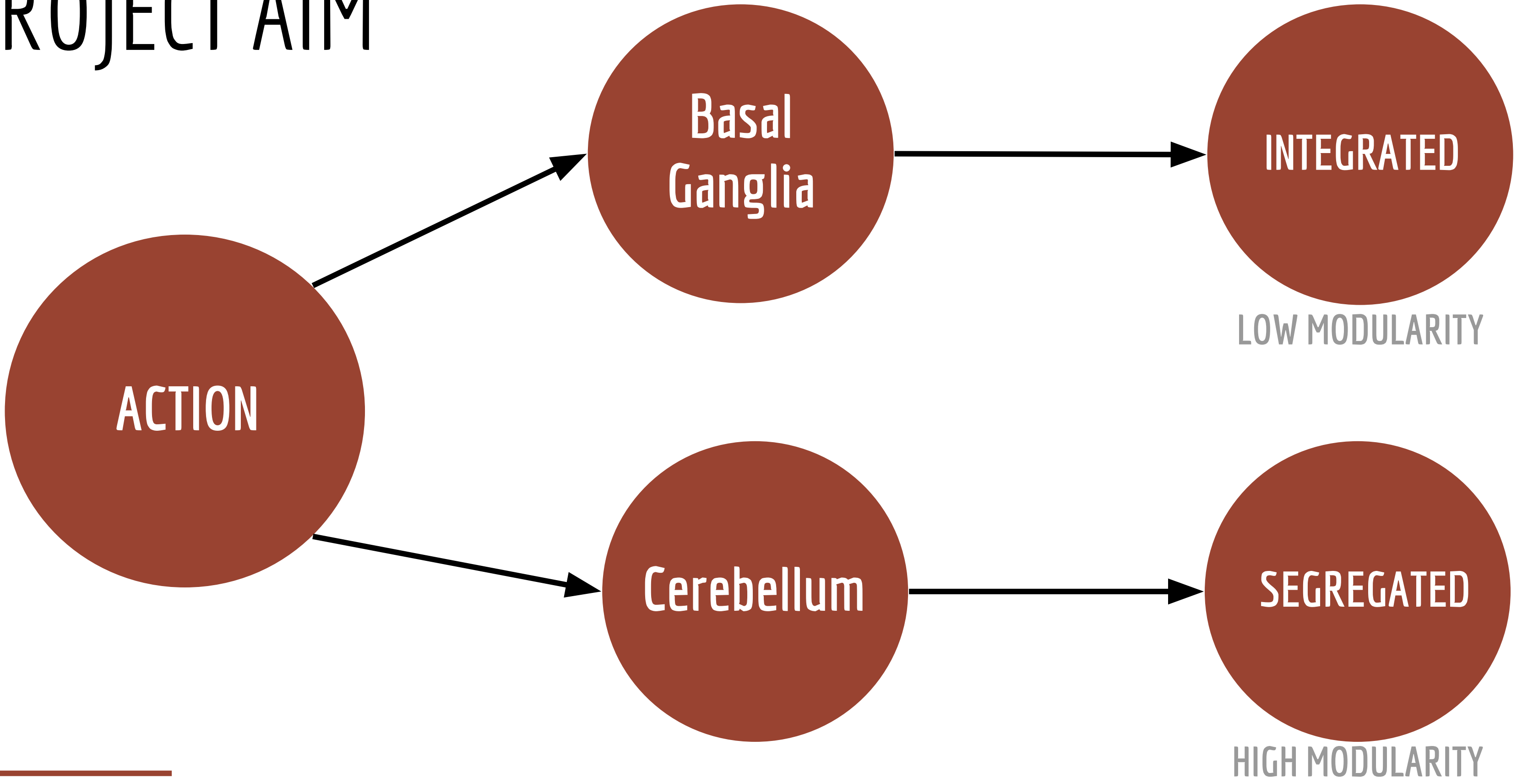
Cellular activation input to the thalamus drive changes in the attractor landscape



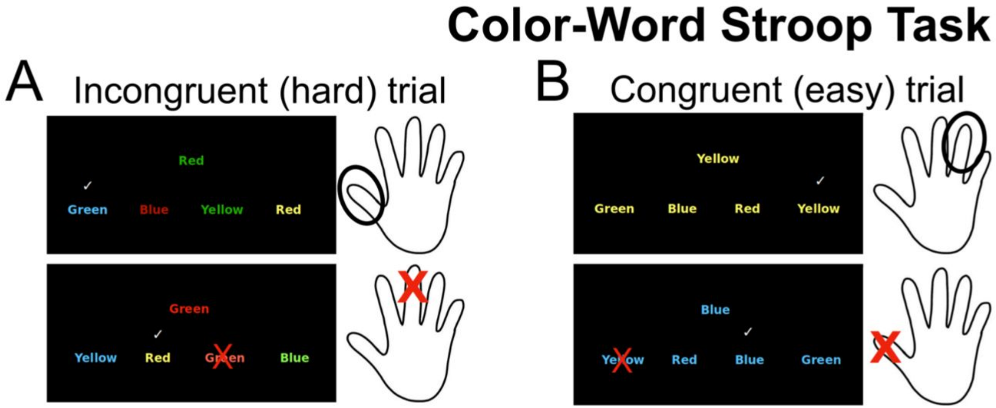
- Segregation leads to deepening of the wells
  - Greater stores of energy to select regions
  - Excitatory, glutamatergic input from the deep cerebellar nuclei to core thalamus (Shine, 2021).
- Shallowing of wells and global integration
  - Less energy stored in regions, but spread across landscape
  - Inhibitory GABAergic cells of the GPi to matrix thalamus cause tonic inhibition causing cortical activation (Shine, 2021).

Shine, 2021

PROJECT AIM


ACTION
Basal Ganglia
Cerebellum
INTEGRATED
LOW MODULARITY
SEGREGATED
HIGH MODULARITY

METHODS



Participants - total n=242

Female=119, Male=123

Mean age=40 ± 6 years, min=30, max=51

Scanner - Siemens 3T Trio

12-channel head coil

fMRI = T2*weighted; 3mm isotropic; RT = 2s; ET = 28ms; Flip = 90^0

Task Acquisition - Stroop Task and Multi-Source Interference Task (MSIT)

Adaptive dependent on participant accuracy only in incongruent blocks

Interleaved, four congruent and four incongruent blocks (60s), rest (10s)

Gianaros et al., 2017
Rasero et al., 2021

METHODS

Data analysis

Shen functional atlas parcellation - determinines clusters of brain areas, where k=268

Edge time series - fMRI analysis method, allows examination of network across entire timescale

Modularity index

Estimate value Q, for modularity across a network

Automatically determines segmented communities

Eigenvector centrality

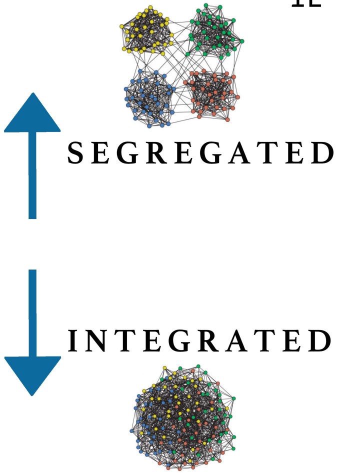
Recursively determines centrality for children of target node

Cross correlation

Determines time lagged relationships between Bg, Cb and cortex

Shen, 2021
Zamani Esfahlani et al., 2021
Shine et al., 2016
Newman, 2010

METHODS: Detailed

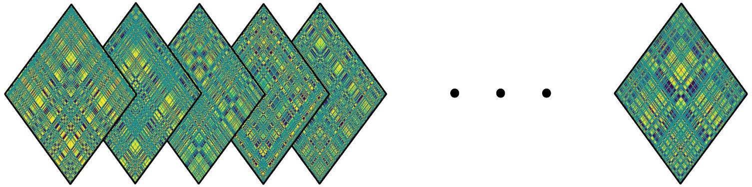


Edge time series

$$z_i = \frac{x_i - \mu_i}{\sigma_i}$$

$$Let\ c_{ij} = [z_i(1) \cdot z_j(1), \ldots, z_i(T) \cdot z_j(T)]$$

$$and\ c_{uv} = [z_u(1) \cdot z_v(1), \ldots, z_u(T) \cdot z_v(T)]$$



Modularity index

$$B = A - P$$

Modularity matrix

Observed

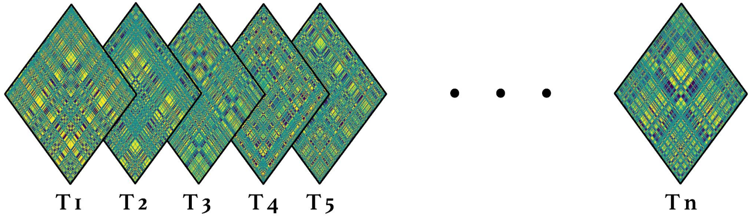
Expected

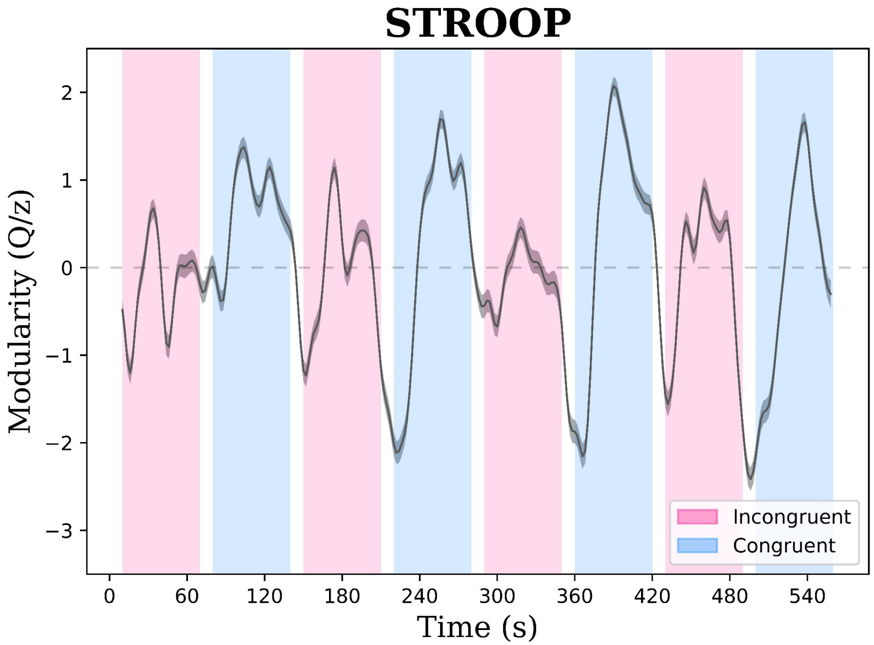
$$Q^{signed} = \sum_{ij} [B_{ij}^{+} - B_{ij}^{-}]\delta\left(\sigma_i, \sigma_j\right)$$

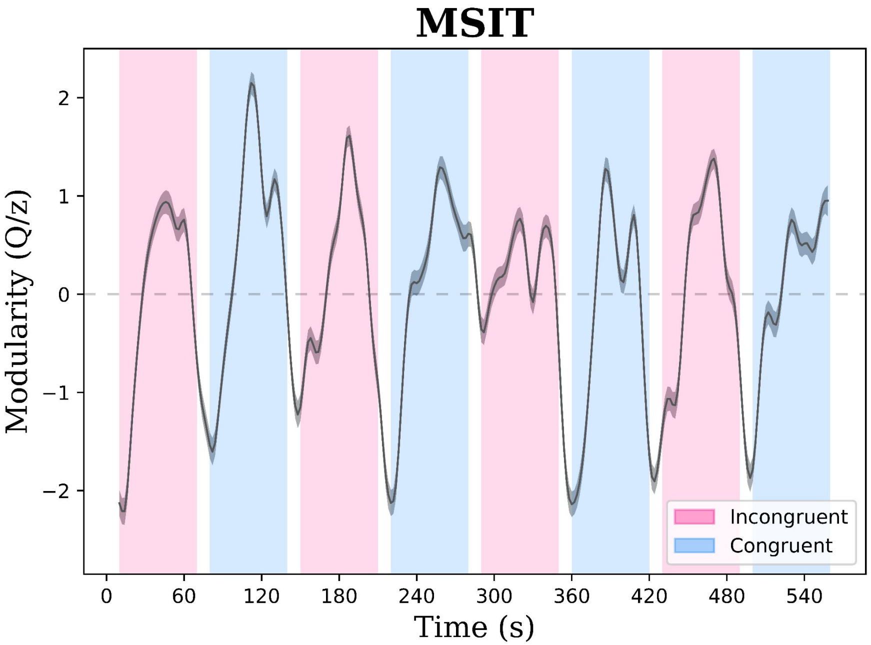
Kronecker function

RESULTS: AIM 1

Modularity Index

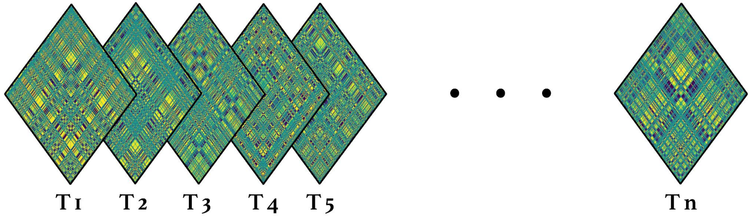


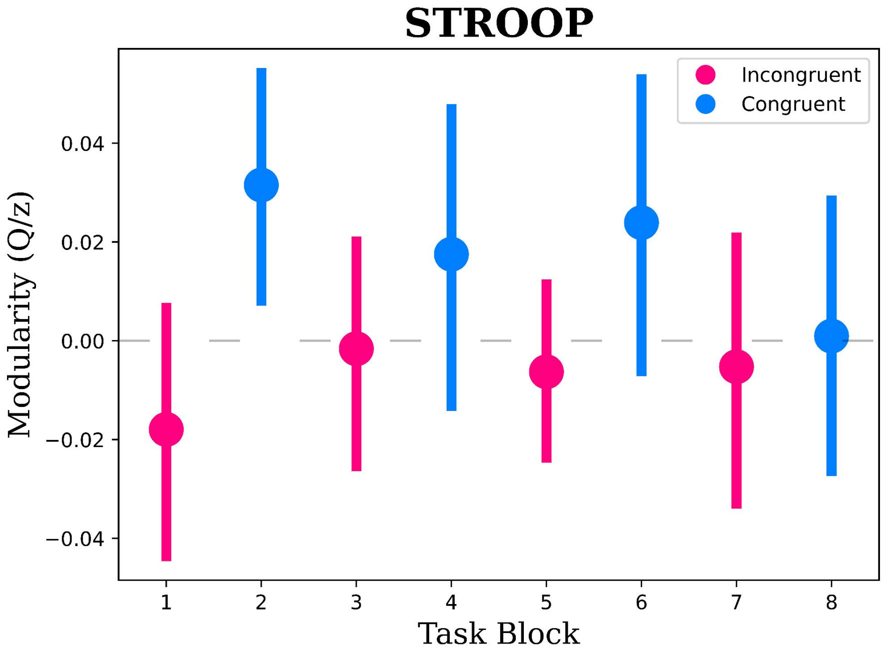


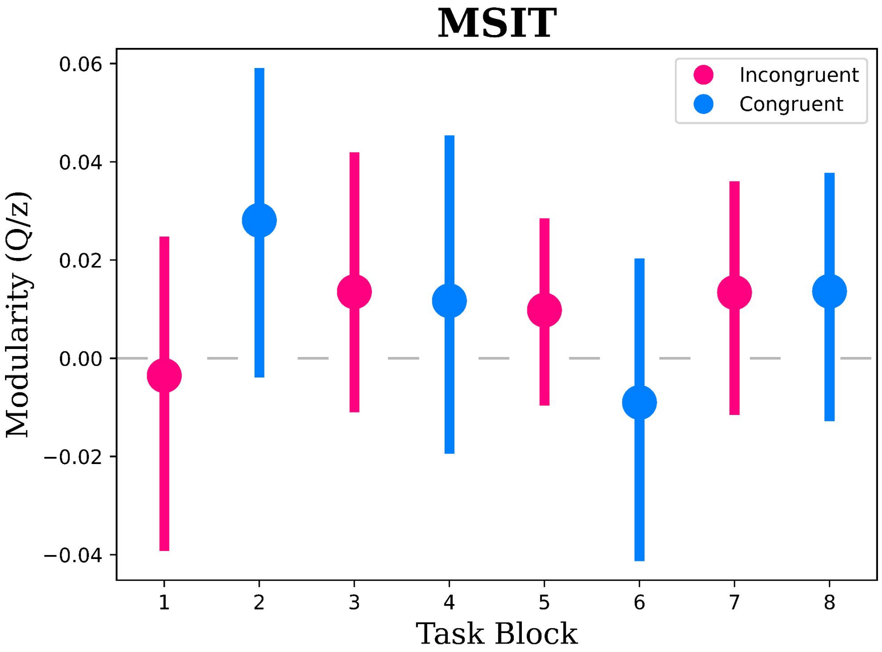


RESULTS: AIM 1

Modularity Index







METHODS: Detailed

MORE ENGAGEMENT

LESS ENGAGEMENT

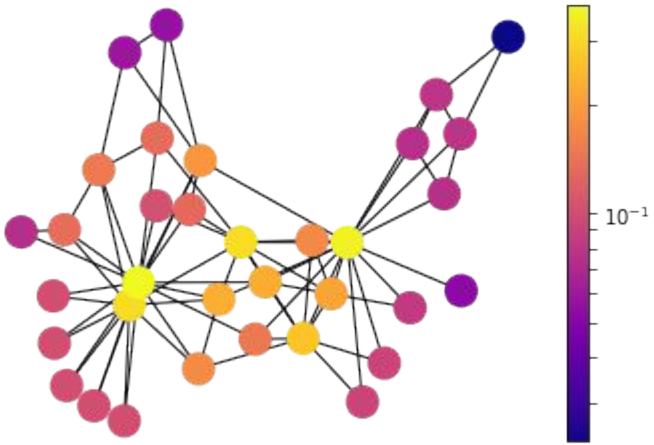
Eigenvector centrality

$$x_i = K_1^{-1} \sum_j A_{ij} x_j$$

Maximum eigenvalue

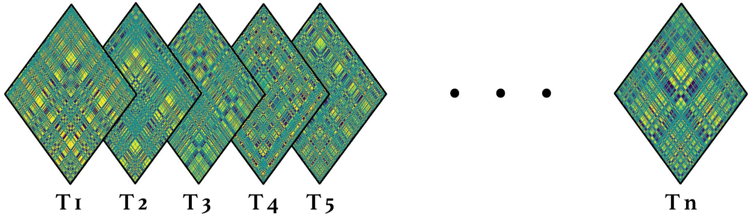
Adjacency matrix

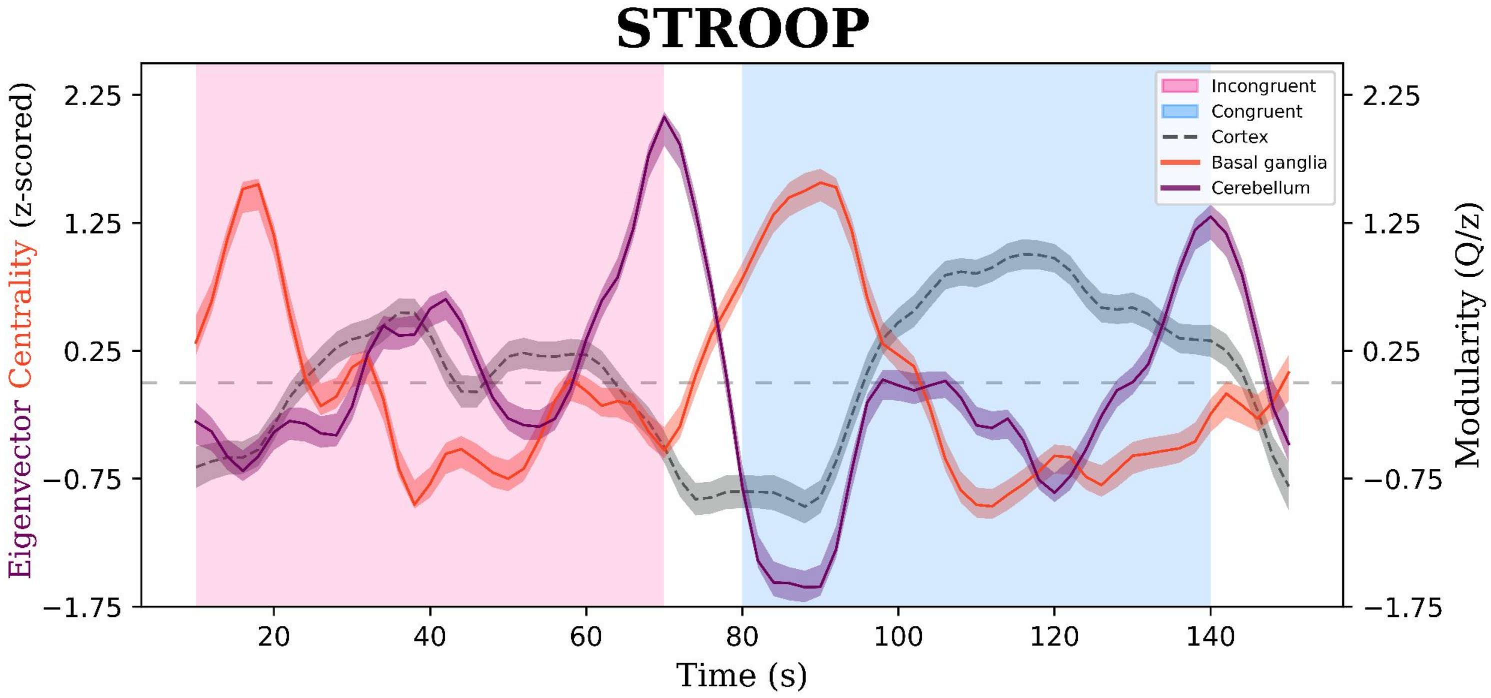
Child node eigenvector



RESULTS: AIM 2

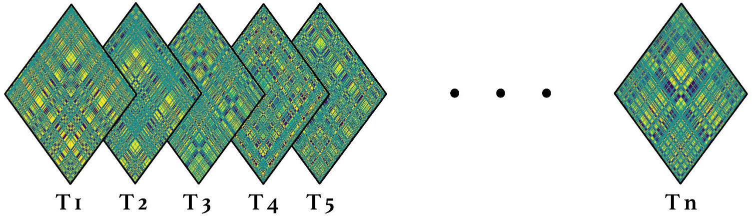
Eigenvector Centrality

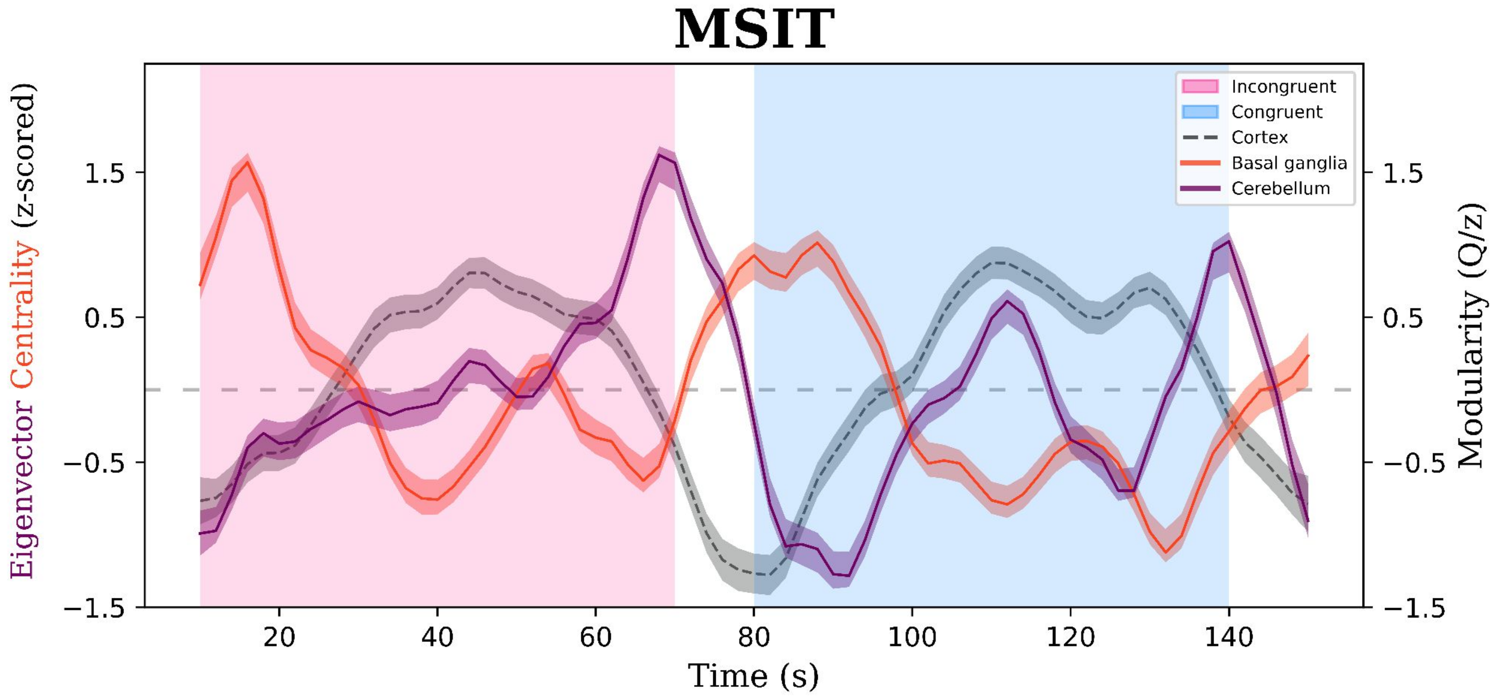




RESULTS: AIM 2

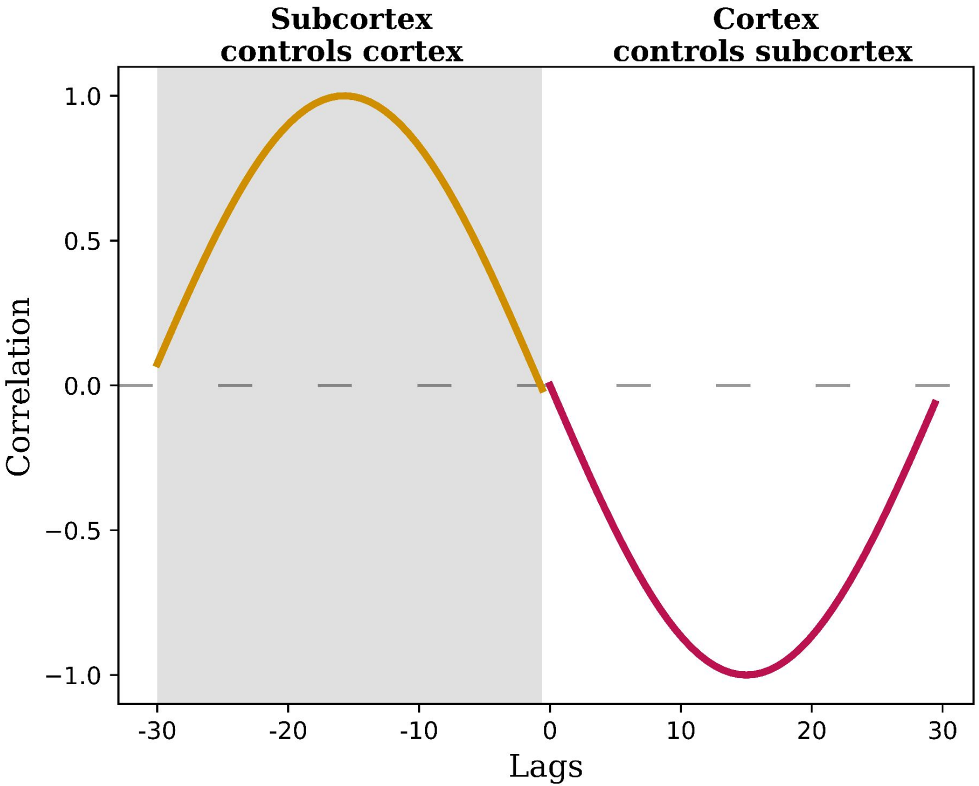
Eigenvector Centrality





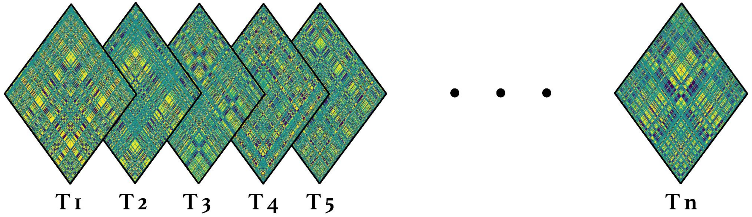
CROSS CORRELATION

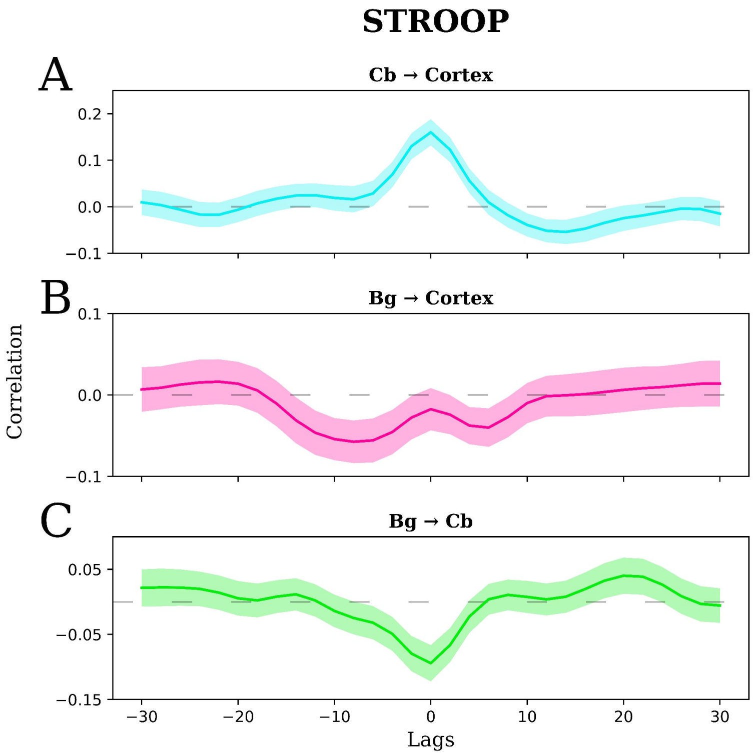
INTERPRETATION

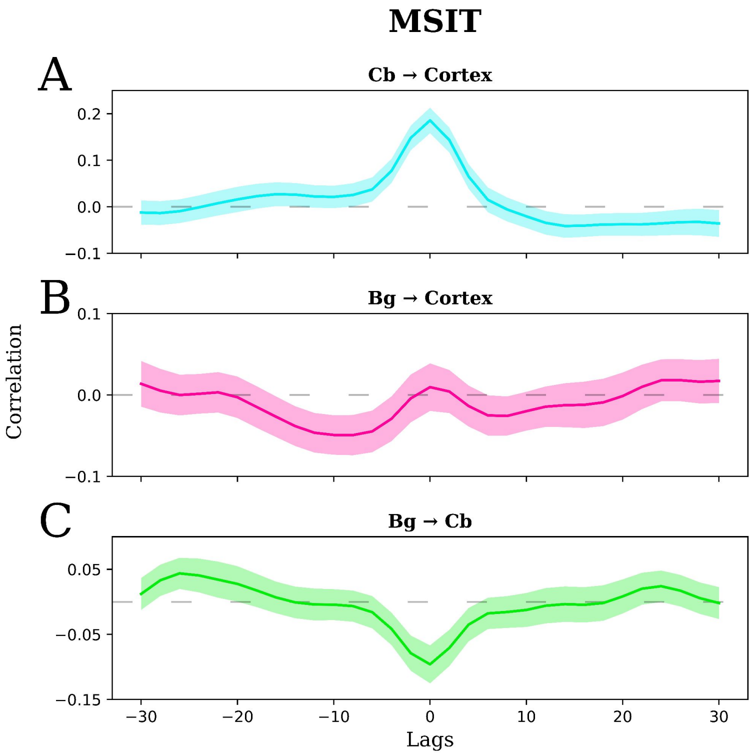


RESULTS: AIM 2

Cross Correlation







CONCLUSION

- Cortical network topologies are highly flexible.
- Basal ganglia engagement peaks at the beginning of task blocks, while cerebellum at the end.
- Evidence for basal ganglia as a control mechanism for cortical network topology, but not cerebellum

References

Newman, M. E. J. (2010). Networks: An introduction. Oxford University Press.

Shen, X., Tokoglu, F., Papademetris, X., & Constable, R. T. (2013). Groupwise whole-brain parcellation from resting-state fMRI data for network node identification. NeuroImage, 82, 403–415.

Shine, J. M. (2021). The thalamus integrates the macrosystems of the brain to facilitate complex, adaptive brain network dynamics. Progress in Neurobiology, 199, 101951. https://doi.org/10.1016/j.pneurobio.2020.101951

Shine, J. M., Koyejo, O., & Poldrack, R. A. (2016). Temporal metastates are associated with differential patterns of time-resolved connectivity, network topology, and attention. Proceedings of the National Academy of Sciences, 113(35), 9888–9891. https://doi.org/10.1073/pnas.1604898113

Gianaros, P. J., Sheu, L. K., Uyar, F., Koushik, J., Jennings, J. R., Wager, T. D., Singh, A., & Verstynen, T. D. (2017). A Brain Phenotype for Stressor-Evoked Blood Pressure Reactivity. Journal of the American Heart Association, 6(9), e006053.

Guimerà, R., & Nunes Amaral, L. A. (2005). Functional cartography of complex metabolic networks. Nature, 433(7028), 895–900. https://doi.org/10.1038/nature03288

Zhou, X., Tien, R. N., Ravikumar, S., & Chase, S. M. (2019). Distinct types of neural reorganization during long-term learning. Journal of Neurophysiology, 121(4), 1329–1341. https://doi.org/10.1152/jn.00466.2018

Rasero, J., Betzel, R., Sentis, A. I., Kraynak, T. E., Gianaros, P. J., Timothy Verstynen, T. (2021). Similarity in evoked responses does not imply similarity in network states across tasks. https://www.biorxiv.org/content/10.1101/2021.11.27.470015v1

Owen, L. L. W., Chang, T. H., & Manning, J. R. (2021). High-level cognition during story listening is reflected in high-order dynamic correlations in neural activity patterns. Nature Communications, 12(1), 5728. https://doi.org/10.1038/s41467-021-25876-x

Geib, B.R., Stanley, M.L., Wing, E.A., Laurienti, P.J., 2015. Hippocampal contributions to the large-scale episodic memory network predict vivid visual memories. Cereb. Cortex 27, 680–693.

Zamani Esfahlani, F., Jo, Y., Puxeddu, M. G., Merritt, H., Tanner, J. C., Greenwell, S., Patel, R., Faskowitz, J., & Betzel, R. F. (2021). Modularity maximization as a flexible and generic framework for brain network exploratory analysis. NeuroImage, 244, 118607.

THANK YOU !!

Committee members

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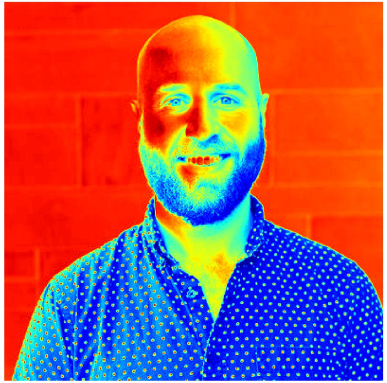

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QUESTIONS ?