Multilayer Networks in Neuroscience

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Outline

- Something completely different
- Multilayer networks
- Multilayer networks in neuroscience
  - Frequency-based multilayer brain networks
  - Time-dependent functional brain networks
  - Motor chunking and multilayer networks
- Conclusions and Challenges

Something Completely Different

(plugging an IPAM workshop and a review article)

IPAM Workshop: "Mathematical Approaches for Connectome Analysis"

- February 12–16, 2024, IPAM (on UCLA campus)
- https://www.ipam.ucla.edu/programs/workshops/mathematical-approaches-for-connectome-analysis/
- Applications received by 12/12/23 receive full consideration

Review Article: "Oscillatory Networks: Insights from Piecewise-Linear Modeling"

- Authors: Stephen Coombes, Mustafa Sayli, Rüdiger Thul, Rachel Nicks, Mason A. Porter, and Yi Ming Lai
- Available at arXiv:2308.09655

Multilayer Networks

(Note: ***Not*** the machine-learning use of the term.)

Review Articles and a Book

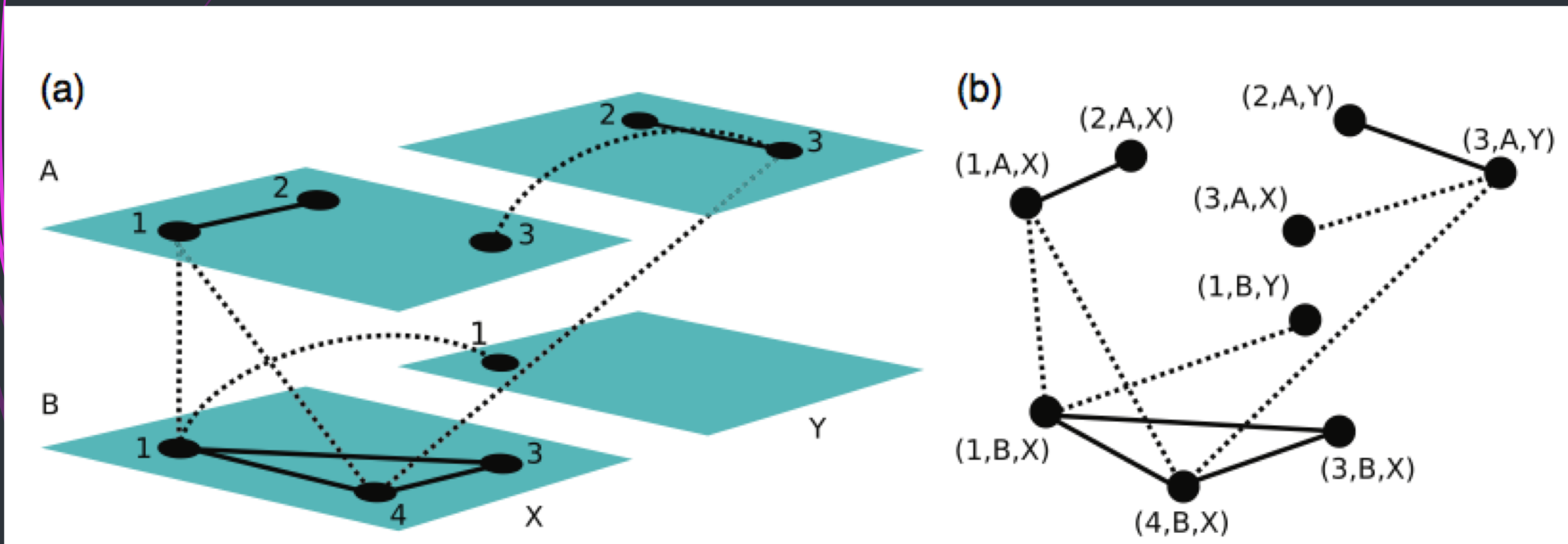
- M. Kivelä, A. Arenas, M. Barthelemy, J. P. Gleeson, Y. Moreno, & MAP [2014], "Multilayer Networks", *Journal of Complex Networks*, **2**(3): 203–271

- MAP [2018], "WHAT IS… A Multilayer Network", *Notices of the American Mathematical Society,* **65**(11): 1419–1423

- Manlio De Domenico [2022], "Multilayer Networks: Analysis and Visualization: Introduction to muxViz with R", Springer International Publishing, Cham, Switzerland

- Michael Vaiana & Sarah Feldt Muldoon [2020], "Multilayer Brain Networks", *Journal of Nonlinear Science,* **30**: 2147–2169

Multilayer Networks



Example: Node-Colored Network

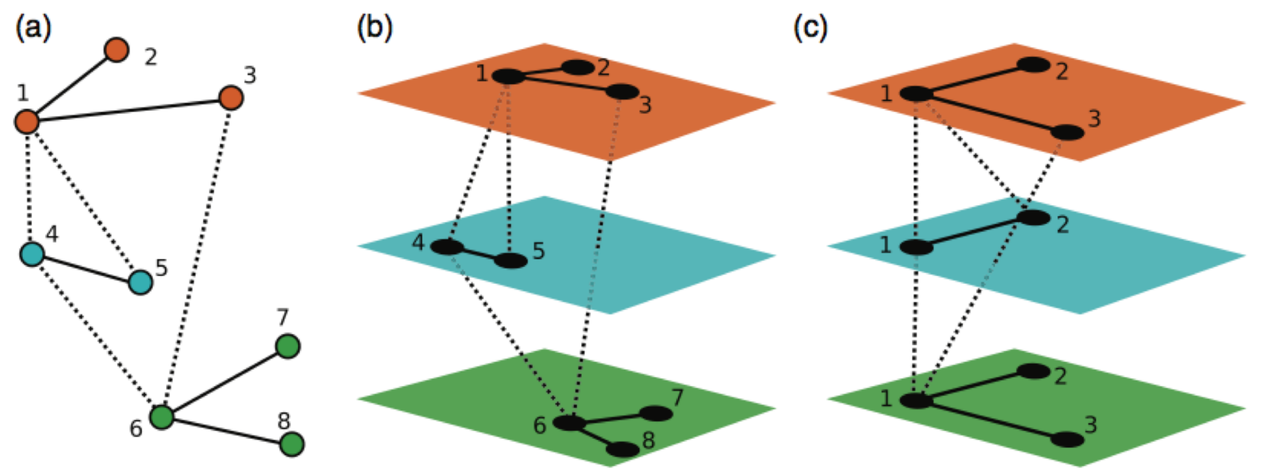
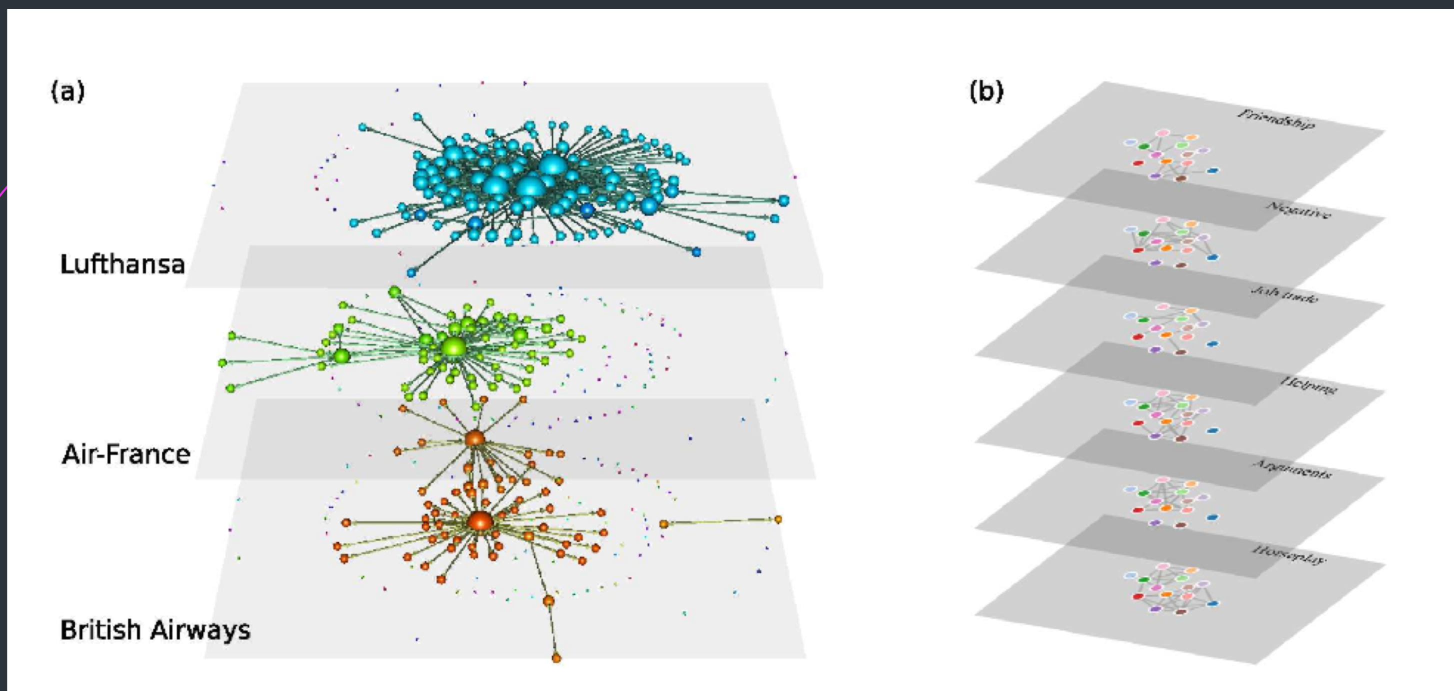


FIG. 5. (a) An example of a node-coloured network (i.e. an interconnected network, a network of networks etc.). (b) Representation of the same node-coloured network using our multilayer network formalism. We keep the node names from the original network. (c) Alternative representation of the same node-coloured network in our multilayer network formalism. This time, we use consecutive integers starting from 1 to name the nodes in each layer, so we also need to include the identity of the layer to uniquely specify each node.

- Node-colored network: also known as interconnected network, network of networks, etc.
- Figure: three alternative representations

Example: Multiplex Network

- Traditional setting: Different types of relationships in different layers
- An old idea from the social-networks literature
- Simplest situation: an edge-colored multigraph



Structural Neuronal Network coupled to Functional Neuronal Network
[Figure 1 of Vaiana & Muldoon]

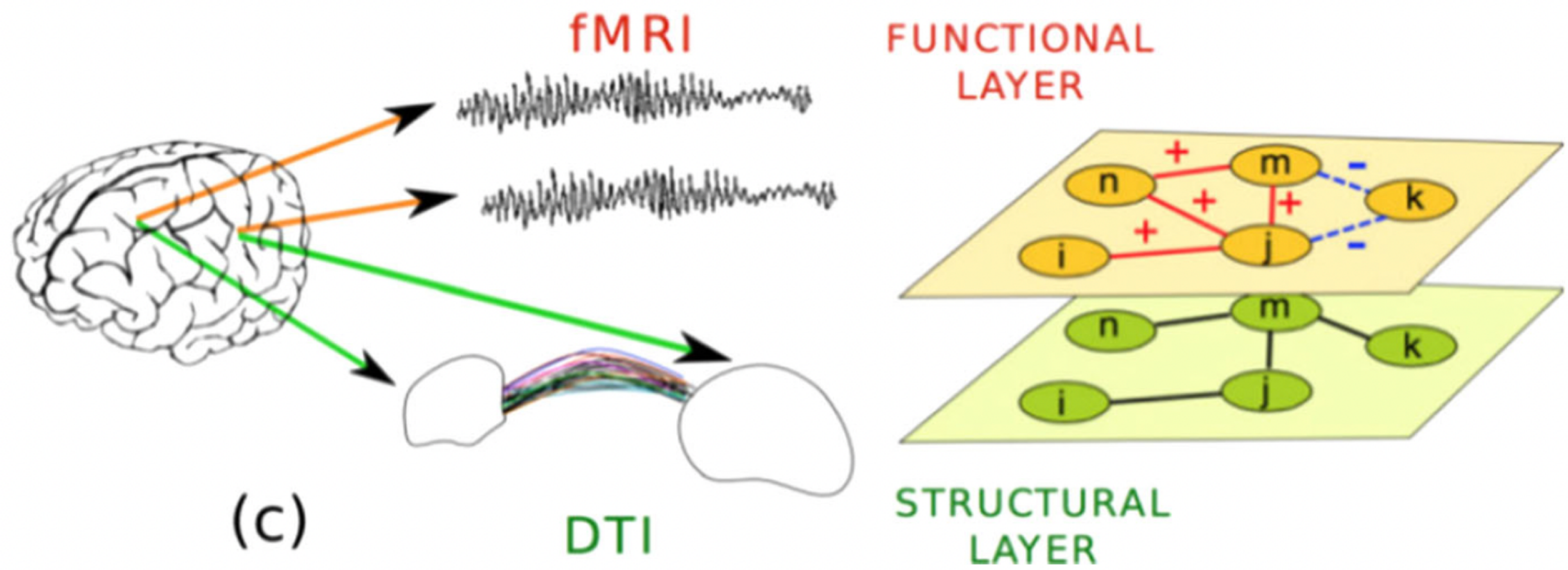
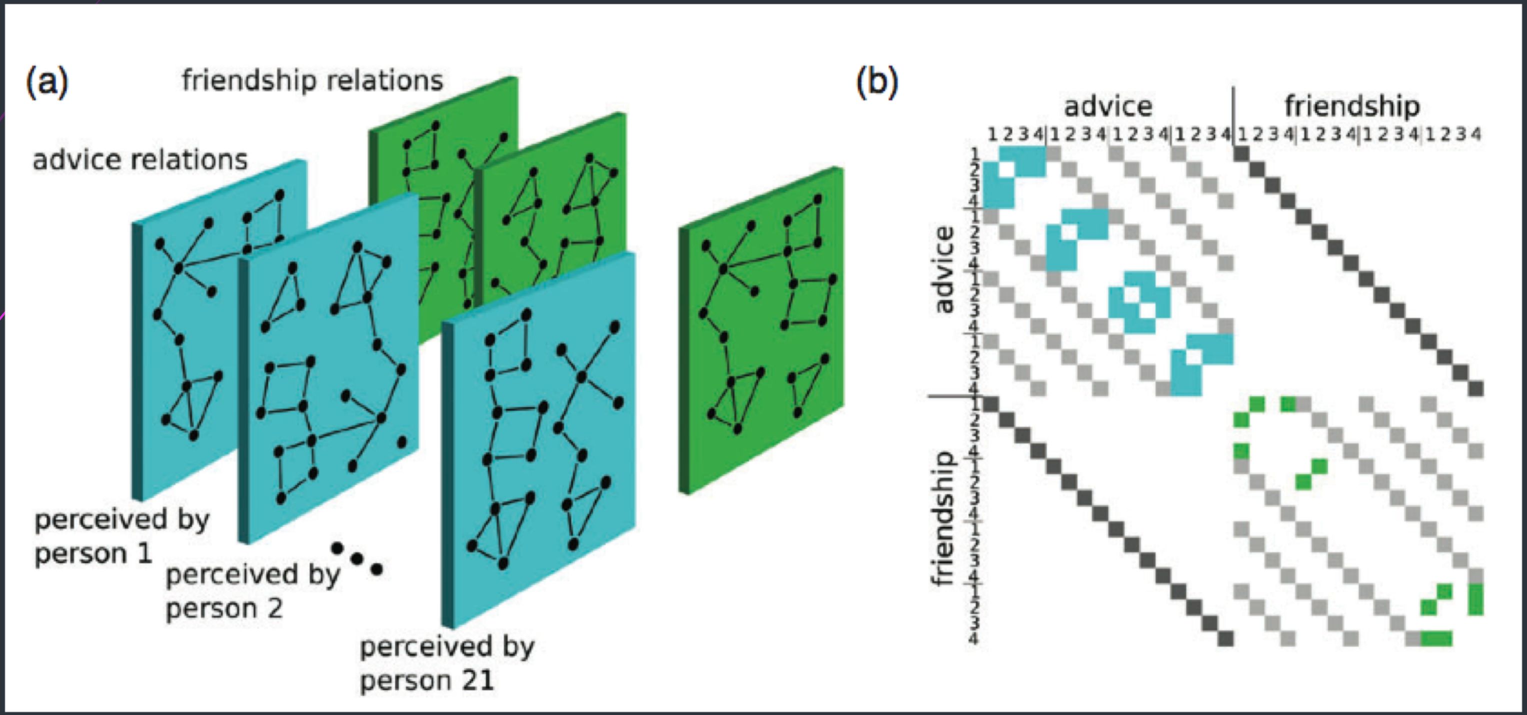


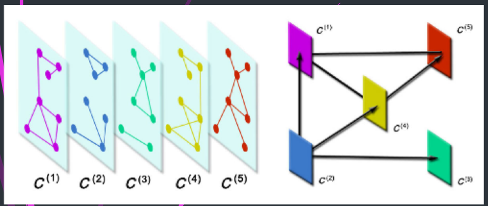
Fig. 1 A multilayer network created from recording both fMRI and DTI data from a single brain. (Reprinted with permission from Battiston et al. 2017)

Example: Cognitive Social Structure



(conceptual idea from David Krackhardt, 1987)

General Form of a Multilayer Network



- Definition of a *multilayer network M*
  - $M = (V_M, E_M, V, L)$
    - V: set of nodes ("entities")
      - As in ordinary graphs
    - L: sequence of sets of possible layers
      - One set for each additional "aspect" $d \geq 0$ beyond an ordinary network (example: $d = 1$ in schematic on this page)
    - V_M: set of tuples that represent *node-layers*
    - E_M: multilayer edge set that connects these tuples

- Note 1: Allow weighted multilayer networks by mapping edges to real numbers with $w: E_M \rightarrow \mathbf{R}$
- Note 2: The case $d = 0$ yields the usual single-layer ("monolayer") networks

A Few Possible Constraints

- 1. Node-aligned (or fully interconnected): All layers include all nodes
- 2. Layer disjoint: Each node exists in at most one layer
- 3. Equal size: Each layer has the same number of nodes (but they need not be the same ones)
- 4. Diagonal coupling: Interlayer edges can exist only between nodes and their counterparts
- 5. Layer coupling: coupling between layers is independent of node identity
  - Note: this is a special case of "diagonal coupling"
- 6. Categorical coupling: diagonal couplings in which interlayer edges can be present between any pair of layers

- Example 1: Most (but not all) *multiplex networks* that have been studied in the literature satisfy (1,3,4,5,6) and include $d = 1$ aspects
  - Note: Many important situations need (1,3) to be relaxed. (E.g. Some people have Facebook accounts but not Twitter accounts.)
  - Property (4) is the key defining feature of a multiplex network as a special type of multilayer network

- Example 2: The *networks of networks* that have been investigated typically satisfy (3) and have additional constraints (which can be relaxed)

Tensorial Representation

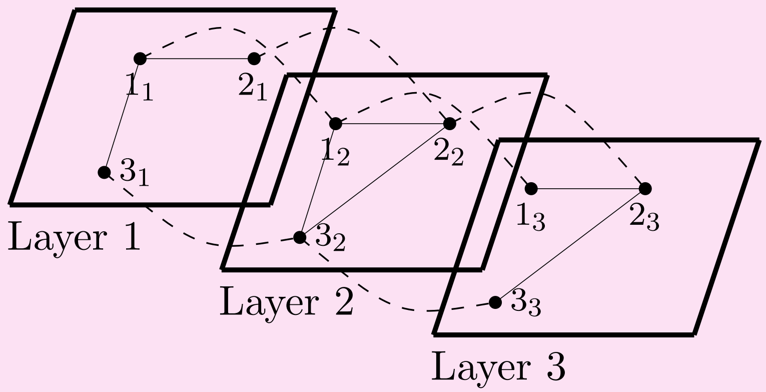
- *Adjacency tensor* for unweighted case:

$$\mathcal{A} \in \{0,1\}^{|V|\times|V|\times|\mathbf{L}_1|\times|\mathbf{L}_1|\times\cdots\times|\mathbf{L}_d|\times|\mathbf{L}_d|}$$

- Elements of adjacency tensor:
  - $A_{uv\boldsymbol{\alpha}\boldsymbol{\beta}} = A_{uv\alpha 1\beta 1 \ldots \alpha d\beta d} = 1$ if and only if $((u,\boldsymbol{\alpha}), (v,\boldsymbol{\beta}))$ is an element of E_M (otherwise, $A_{uv\boldsymbol{\alpha}\boldsymbol{\beta}} = 0$)

- Note: ‘padding’ layers with empty nodes
  - One needs to distinguish between a node not present in a layer and nodes existing but edges not present (use a supplementary tensor with labels for edges that could exist), as this is important for normalization in many quantities.
    - “Missing edges” versus “forbidden edges”

“Flattened” Multilayer Networks (supra-adjacency representation)

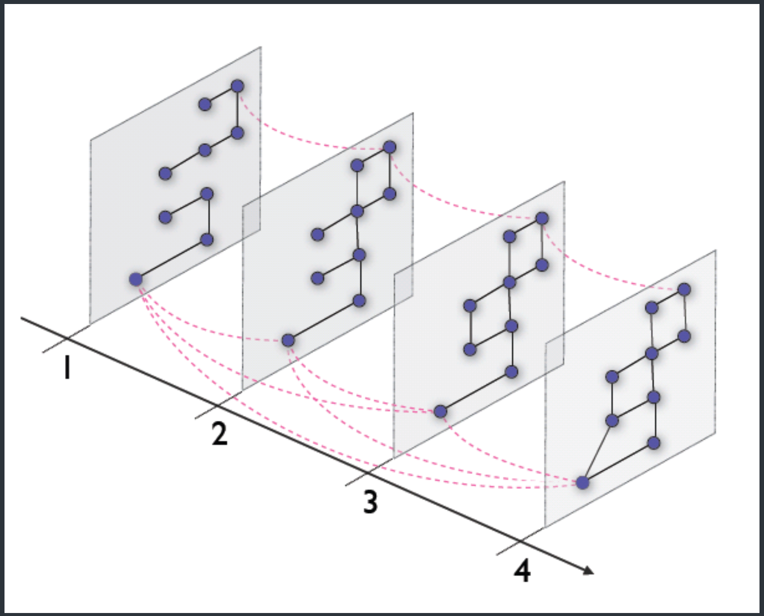


$$\longleftrightarrow \left[\begin{array}{ccc|ccc|ccc}
0 & 1 & 1 & \omega & 0 & 0 & 0 & 0 & 0 \\
1 & 0 & 0 & 0 & \omega & 0 & 0 & 0 & 0 \\
1 & 0 & 0 & 0 & 0 & \omega & 0 & 0 & 0 \\
\hline
\omega & 0 & 0 & 0 & 1 & 1 & \omega & 0 & 0 \\
0 & \omega & 0 & 1 & 0 & 1 & 0 & \omega & 0 \\
0 & 0 & \omega & 1 & 1 & 0 & 0 & 0 & \omega \\
\hline
0 & 0 & 0 & \omega & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & \omega & 0 & 1 & 0 & 1 \\
0 & 0 & 0 & 0 & 0 & \omega & 0 & 1 & 0
\end{array}\right]$$

- Schematic from M. Bazzi, MAP, S. Williams, M. McDonald, D. J. Fenn, & S. D. Howison [2016] *Multiscale Modeling and Simulation: A SIAM Interdisciplinary Journal*, **14**(1): 1–41

"Diagonal" Multilayer Networks: Ordinal and Categorical Coupling

- Ordinal coupling: diagonal interlayer edges among consecutive layers (e.g., multilayer representation of a temporal network)
- Categorical coupling: diagonal interlayer edges between all pairs of edges
- Both can be present in a multilayer network, and both can be generalized



Schematic from P. J. Mucha, T. Richardson, K. Macon, MAP, & J.-P. Onnela [2010], "Community Structure in Time-Dependent, Multiscale, and Multiplex Networks", *Science*, Vol. 328, No. 5980: 876–878

A Few Notes on Data and Practicalities

- Lots of reliable data on intralayer relations (i.e., the usual kind of edges)
- It is often more challenging to collect reliable data for interlayer edges (e.g., how to determine edge weights?)
- Determining interlayer edges as a problem in trying to reconcile node identities across networks.
  - Example: Can you figure out that a Twitter account and Facebook account belong to the same person?
- Layers can have different numbers of entities, but one needs to normalize properly when developing network diagnostics (e.g., transitivity and clustering coefficients; Cozzo et al., *New J. Phys.*, 2015).

- **Questions:** In various neuroscience applications, what are the intralayer edges and what are the interlayer edges? How easy is it to determine or infer edge weights for each type of edge?

Multilayer Networks in Neuroscience

(a few examples)

Constructing a Multilayer Frequency Network
[Figure 4 of Vaiana & Muldoon]

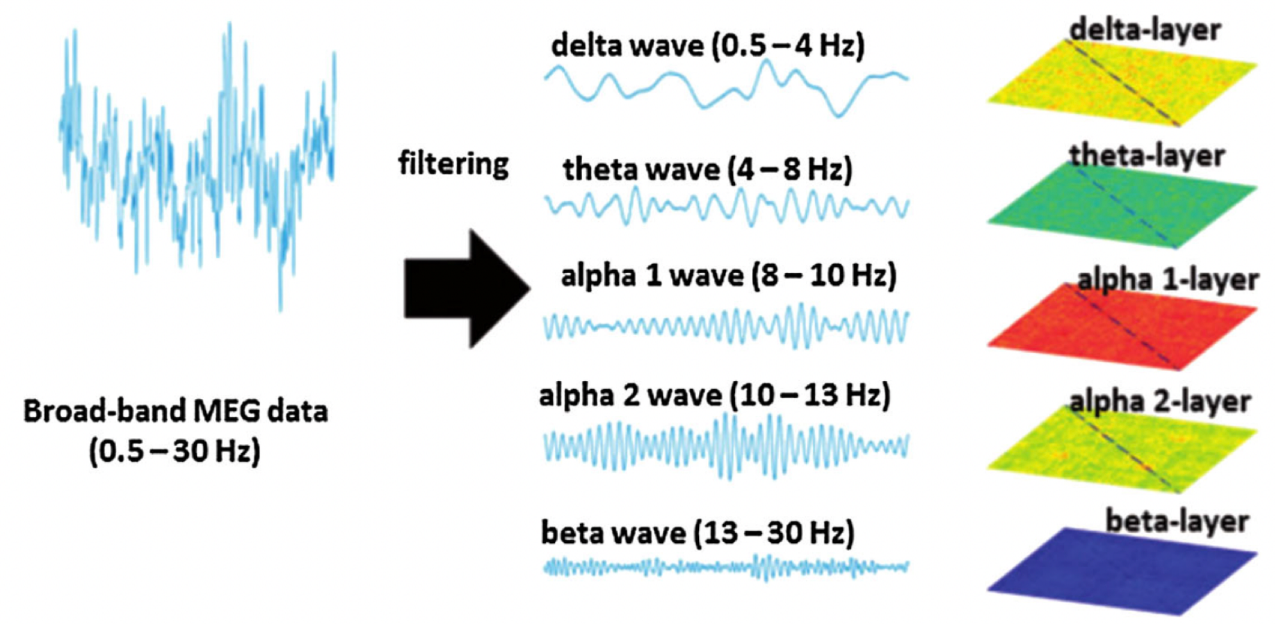


Fig. 4 Constructing a multilayer frequency network from an MEG signal. (Reprinted with permission from Yu et al. 2017)

Multilayer Frequency-Based Brain Networks

- J. M. Buldú & MAP [2018], "Frequency-based brain networks: From a multiplex framework to a full multilayer description", *Network Neuroscience*, **2**(4): 418–441

- How do results differ depending on whether or not one includes cross-frequency coupling between two different brain regions (i.e., "non-diagonal" interlayer edges, in our multilayer-networks language)?
  - I.e., including edges of types {1,2,3} versus including only edges of types {1,2}
    - The latter is what it means for a multilayer network to be of the special case "multiplex"

- Three types of edges
  - 1: intralayer edges: quantify coordination between different brain regions at the same frequency band
  - 2: "diagonal" interlayer edges: couple the activity of the same brain region at different frequency bands
  - 3: "non-diagonal" interlayer edges: quantifies cross-frequency coupling (CFC) between different brain regions

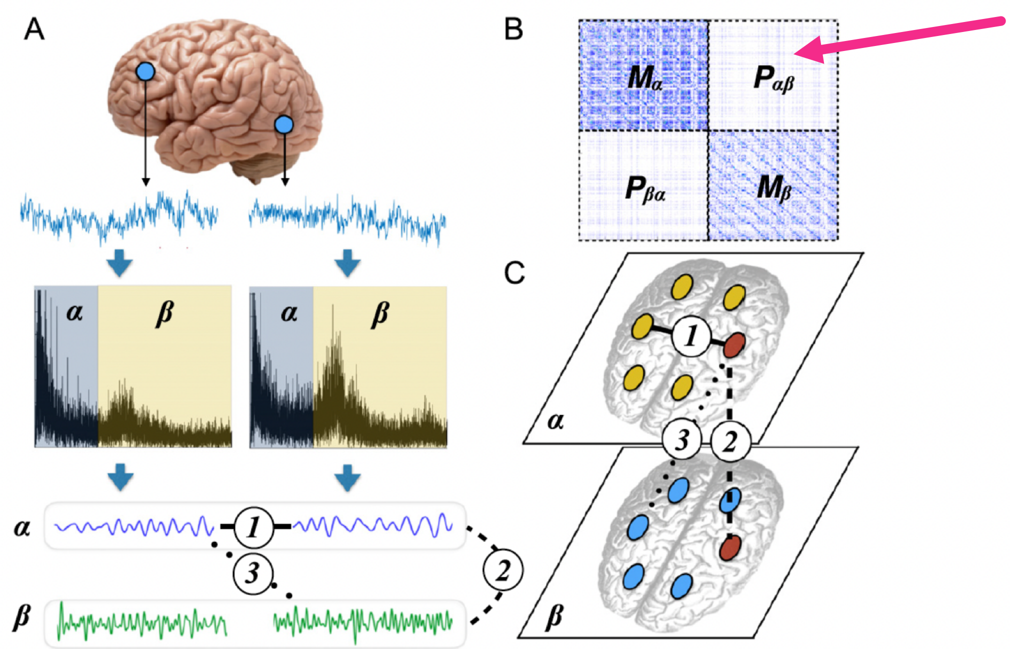
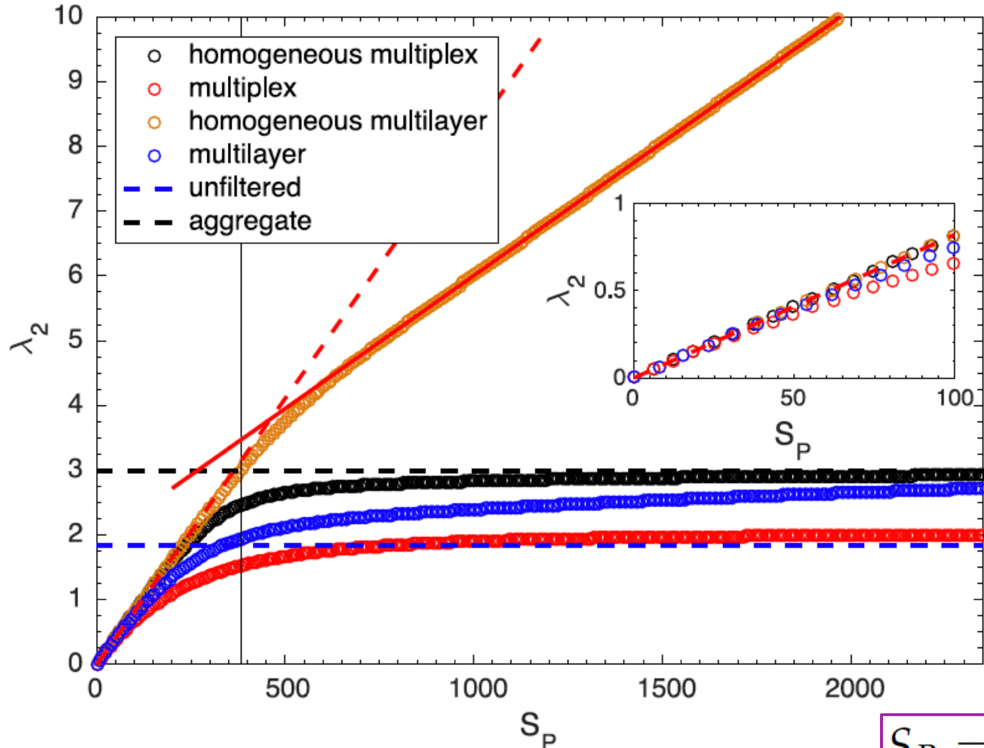


Figure 1. Encoding brain dynamics as a multilayer functional network. We show an illustrative example with two frequency bands (alpha and beta). (A) We band-pass filter the MEG signals at two frequency bands: alpha [8–12] Hz and beta [12–30] Hz. We use mutual information (MI; MacKay, 2003) to quantify coordination between brain regions. This yields three different type of functional edges: Edge type "1" quantifies coordination between different regions at the same frequency band; edge type "2" corresponds to interlayer edges, which couple the activity of the same region at different frequency bands; and edge type "3" quantifies cross-frequency coupling (CFC) between two brain regions. Multiplex networks include only edges of types 1 and 2, whereas more general multilayer networks include all three types of edges. (B) Schematic of the supra-adjacency matrix of a two-layer network constructed from the data in panel A. (C) Schematic of the intralayer and interlayer edges in the multilayer functional network.

$$\mathcal{L}^{\alpha,\beta}_{ij} = \begin{cases} s_i\,, & \text{if } i=j \\ -1\,, & \text{if } i \text{ and } j \text{ are adjacent}\,, \\ 0\,, & \text{otherwise} \end{cases}$$

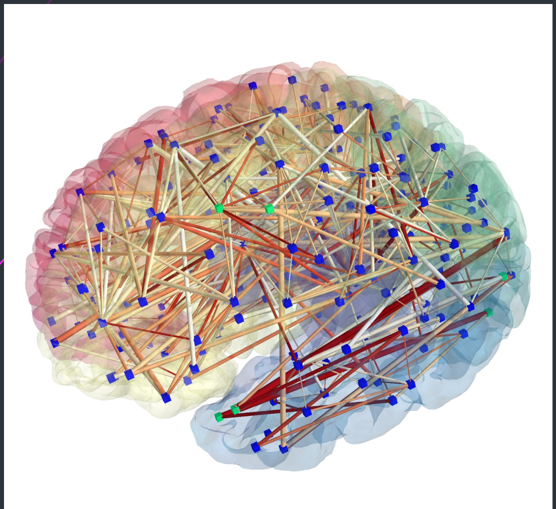
$$\mathcal{L}^{\alpha\beta} = \begin{pmatrix} \mathcal{L}^{\alpha} + \vec{p}\,\mathbb{I} & -\vec{p}\,\mathbb{I} \\ -\vec{p}\,\mathbb{I} & \mathcal{L}^{\beta} + \vec{p}\,\mathbb{I} \end{pmatrix}$$

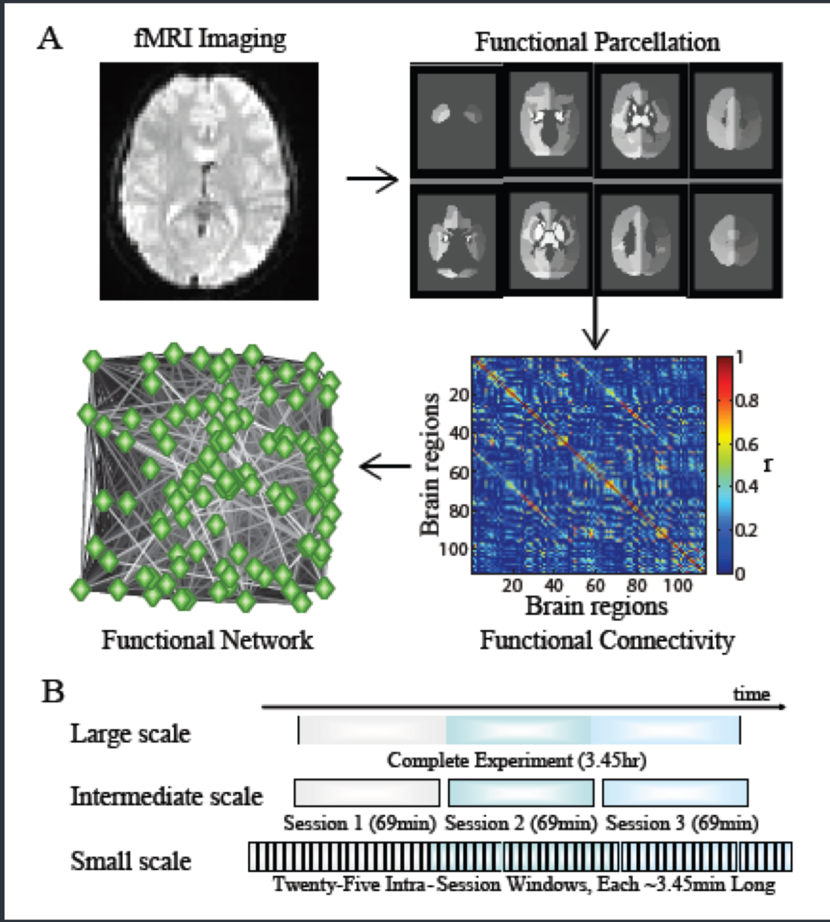


$$S_P = \sum_{ij} p_{ij}.$$

Figure 6. Edge heterogeneity and missing interlayer edges in frequency-based functional brain networks. Algebraic connectivity λ_2 of the combinatorial supra-Laplacian matrix $\mathcal{L}^{\alpha\beta}$ as a function of the mean strength of the interlayer connectivity matrix $\mathbf{P}^{\alpha\beta} = p\mathbf{C}$, where $\mathbf{C}$ encodes the weights of the interlayer edges, for four different types of networks: (i) homogeneous multiplex networks

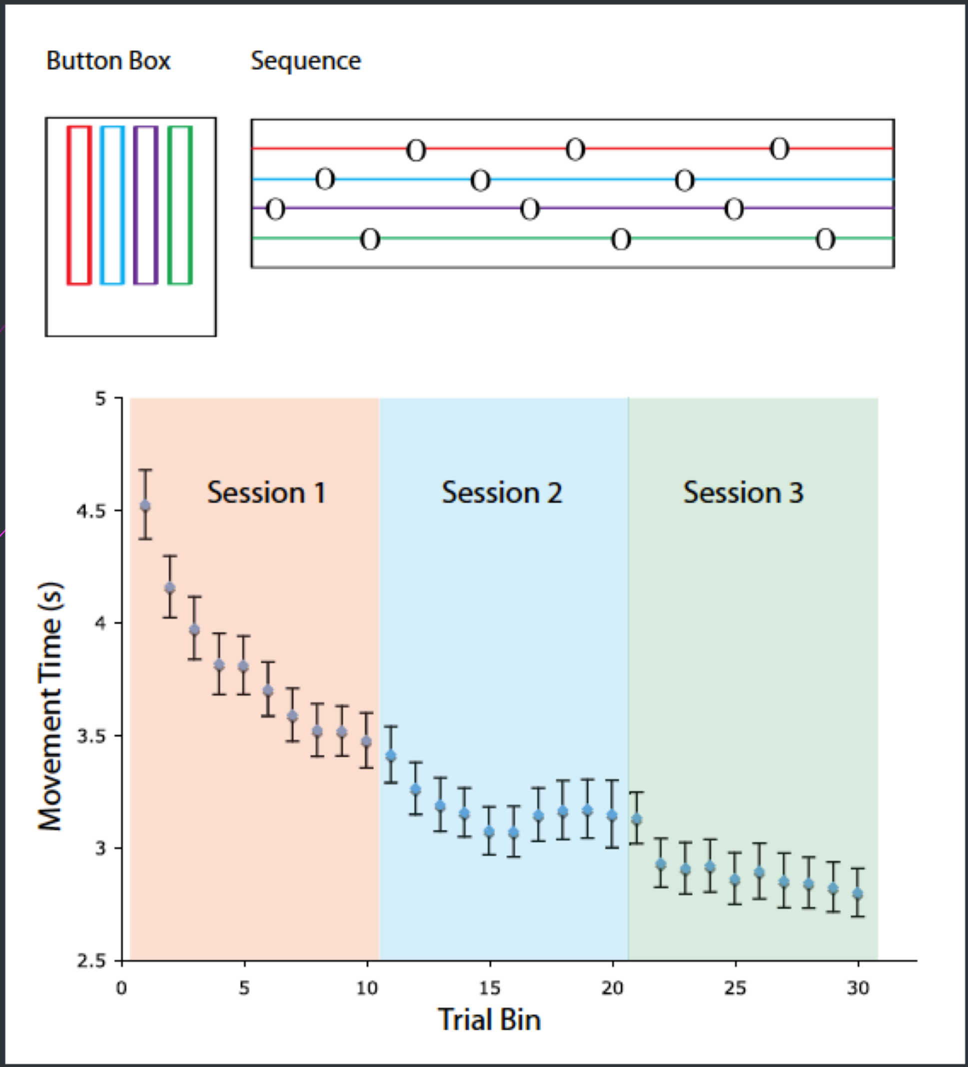
Community Structure in Time-Dependent Functional Brain Networks



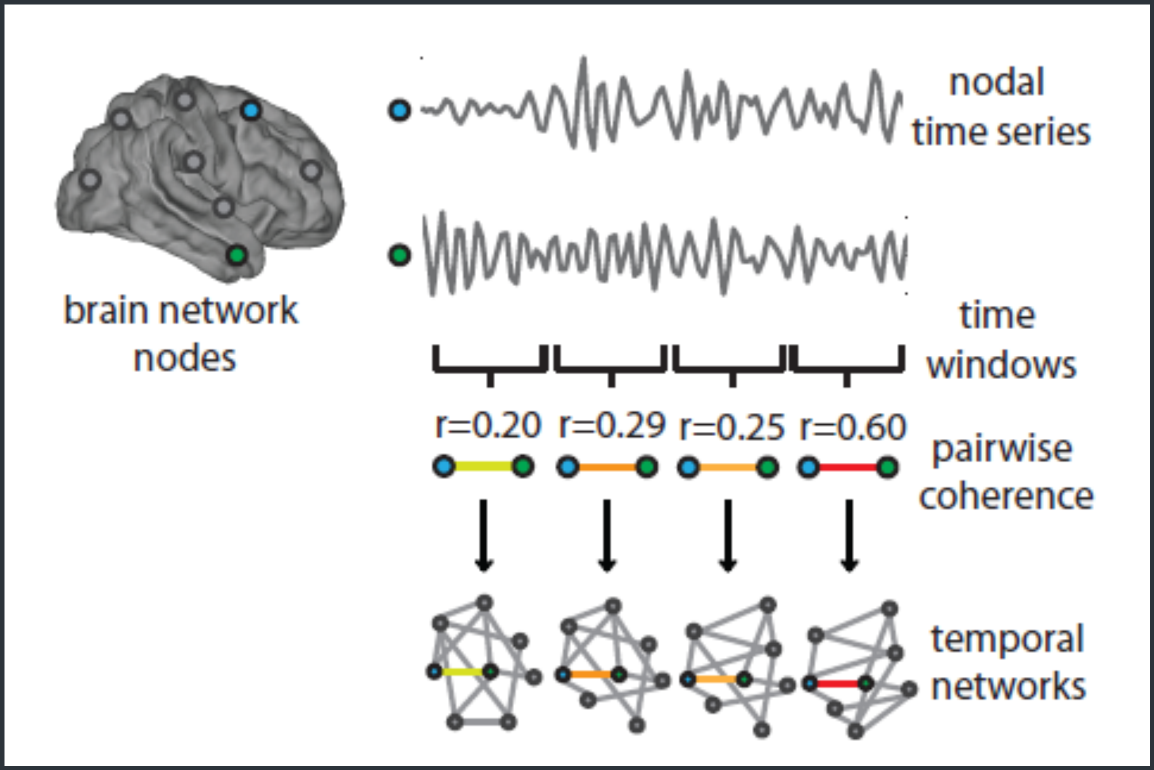


- D. S. Bassett, N. F. Wymbs, MAP, P. J. Mucha, J. M. Carlson, & S. T. Grafton [2011], "Dynamic Reconfiguration of Human Brain Networks During Learning", *Proceedings of the National Academy of Sciences of the United States of America*, Vol. 108, No. 18: 7641–7646

Experiments



Constructing Time-Dependent Functional Brain Networks



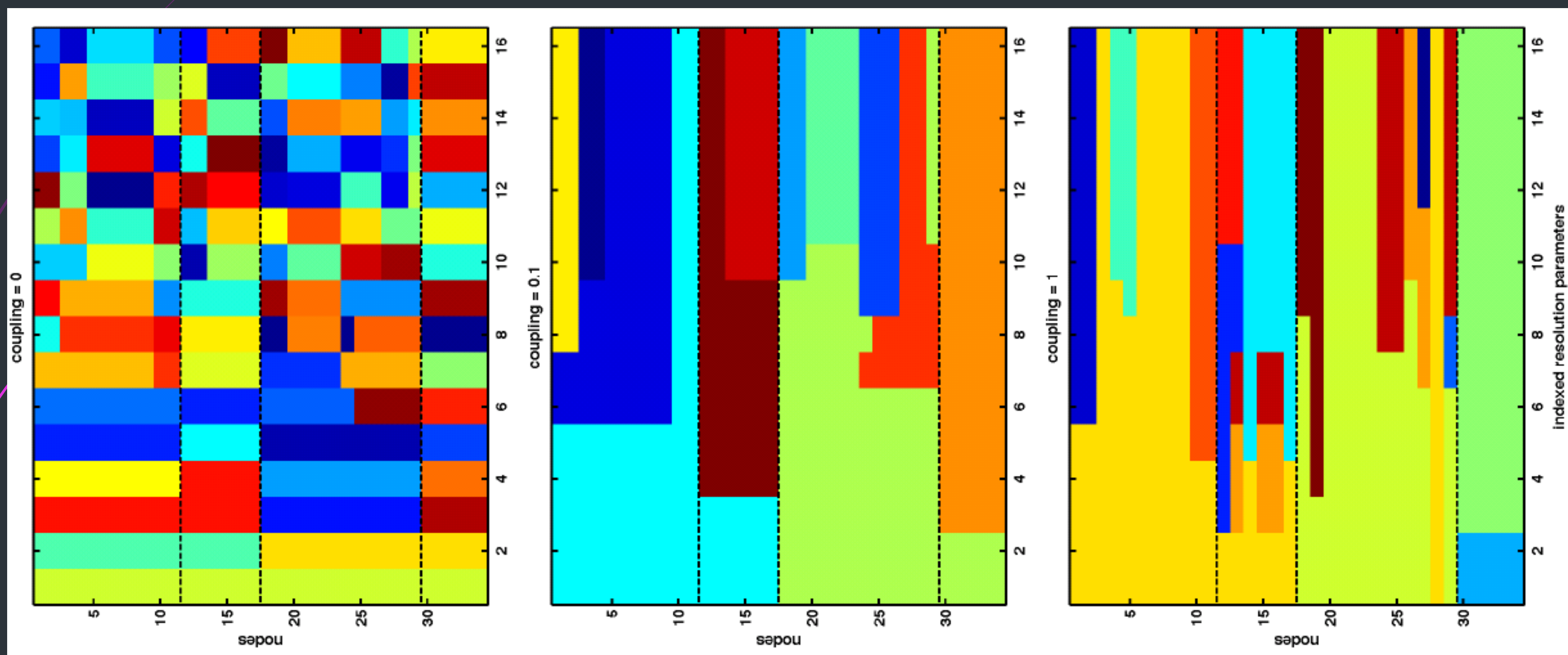
Detect Communities by Optimizing a Multilayer Modularity Objective Function

$$Q_{\text{multislice}} = \frac{1}{2\mu} \sum_{ijsr} \left\{ \left(A_{ijs} - \gamma_s \frac{k_{is} k_{js}}{2m_s} \right) \delta_{sr} + \delta_{ij} C_{jsr} \right\} \delta(g_{is}, g_{jr})$$

- Assign node-layers to communities to maximize Q
- Recall: Node x in layer r is a different node-layer from node x in layer s

- We derived this function in Mucha et al. (2010) by linearizing Laplacian dynamics

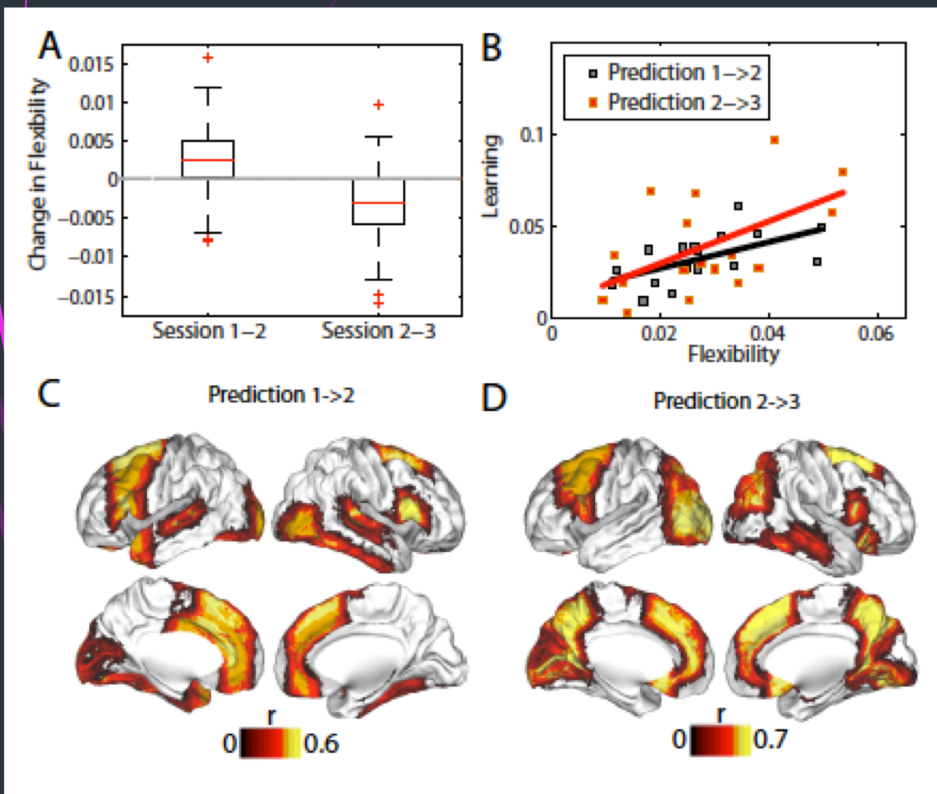
Example: Zachary Karate Club



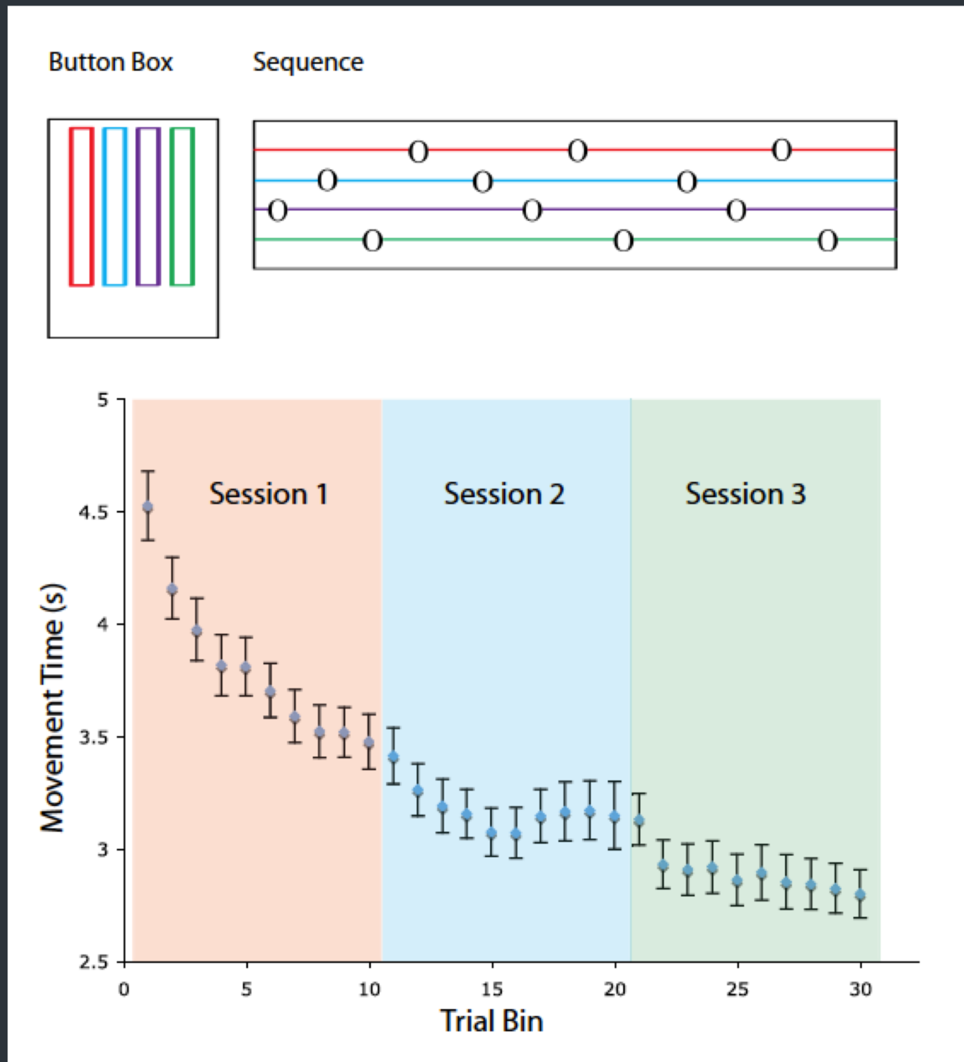
$$C_{jsr} = \{0, \omega\}$$

Figure from Mucha et al. (2010)

Dynamic Reconfiguration of Human Brain Networks During Learning



- fMRI data: network from coherences of the time series in regions of the brain parcellation
- Examine role of modularity in human learning by identifying dynamic changes in modular organization over multiple time scales
- Main result: Flexibility, as measured by allegiance of nodes to communities, in one session predicts amount of learning in subsequent session
- Much subsequent work on this in the last decade



Button Box
Sequence
Session 1
Session 2
Session 3
Movement Time (s)
Trial Bin
5
4.5
4
3.5
3
2.5
0
5
10
15
20
25
30

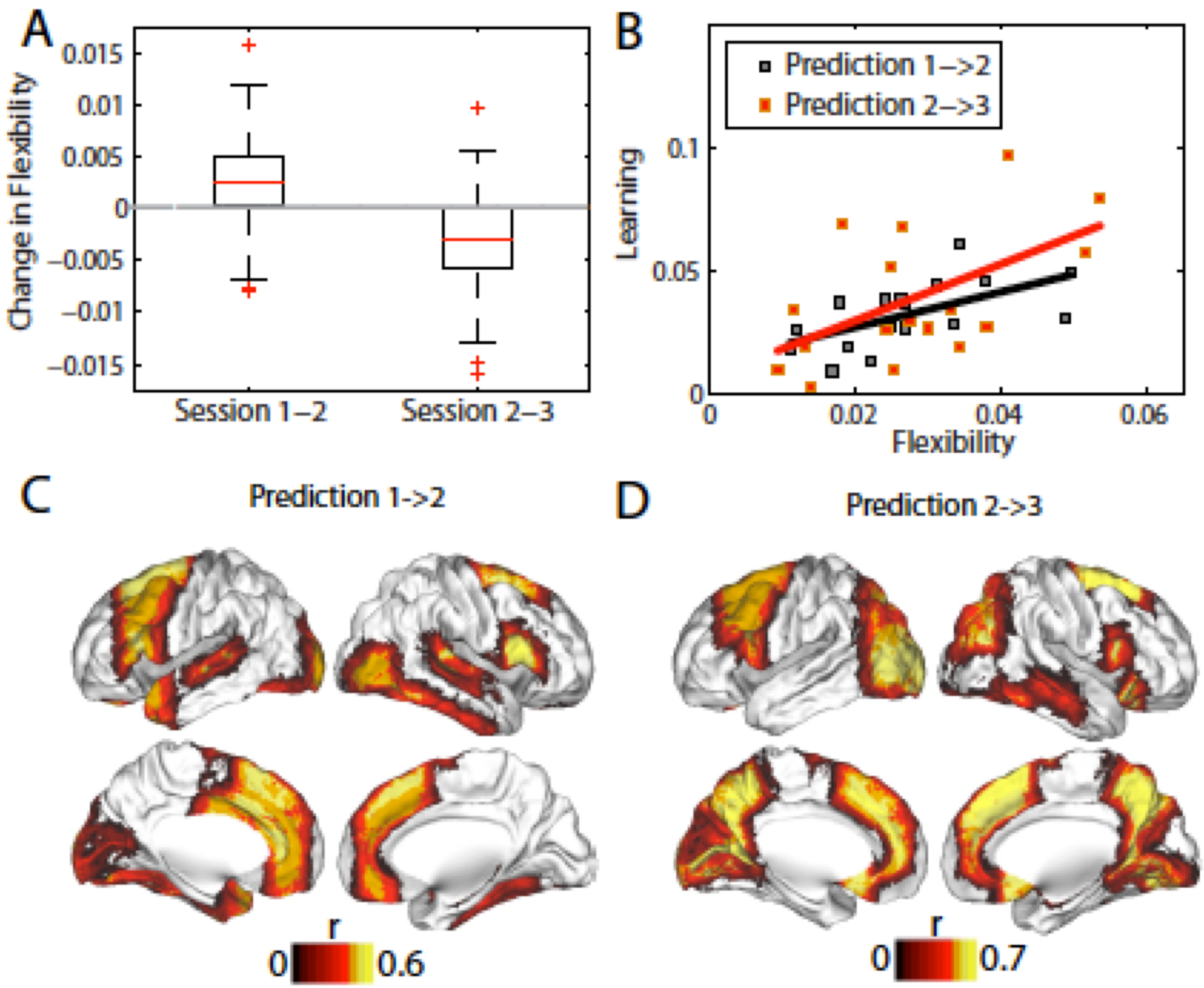
Stationarity and Flexibility

- Community stationarity ζ (autocorrelation over time of community membership):

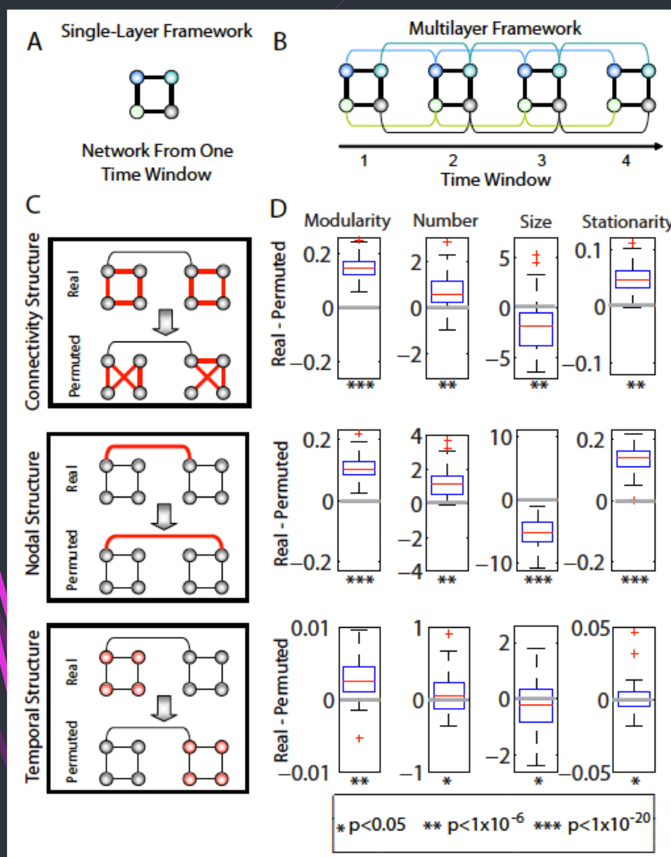
$$U(t, t+m) \equiv \frac{|G(t) \cap G(t+m)|}{|G(t) \cup G(t+m)|}$$

$$\zeta \equiv \frac{\sum_{t=t_0}^{t'-1} U(t, t+1)}{t' - t_0 - 1}$$

- Node flexibility:
  - f_i = number of times node i changed communities divided by total number of possible changes
  - flexibility $f = \langle f_i \rangle$

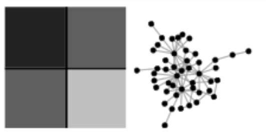

A
0.015
0.01
0.005
0
−0.005
−0.01
−0.015
Change in Flexibility
Session 1−2
Session 2−3
B
Prediction 1−>2
Prediction 2−>3
Learning
0.1
0.05
0
0
0.02
0.04
0.06
Flexibility
C
Prediction 1->2
r
0
0.6
D
Prediction 2->3
r
0
0.7

Dynamic Community Structure
(different types of randomization)



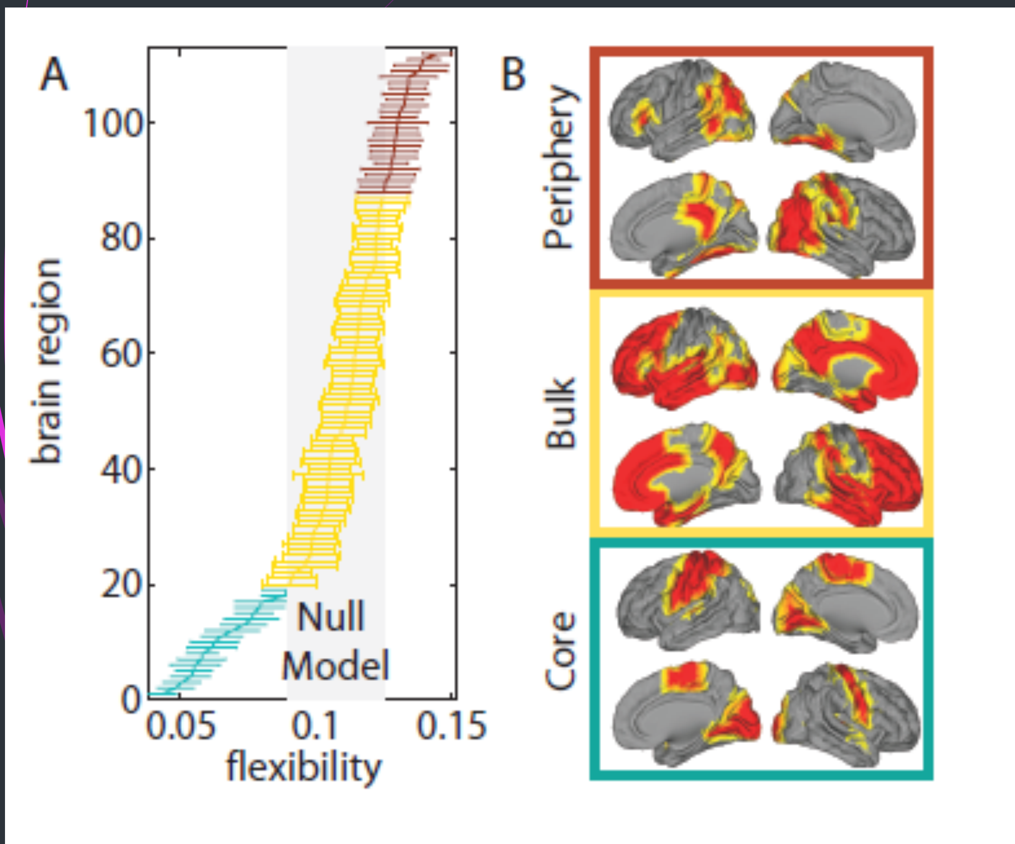
- Investigating community structure in a multilayer framework requires consideration of new null models

- Many more details!
  - E.g., robustness of results to choice of size of time window, size of interlayer coupling, particular definition of flexibility, complicated modularity landscape, choice of how one calculates the ‘similarity’ of the time series, etc.

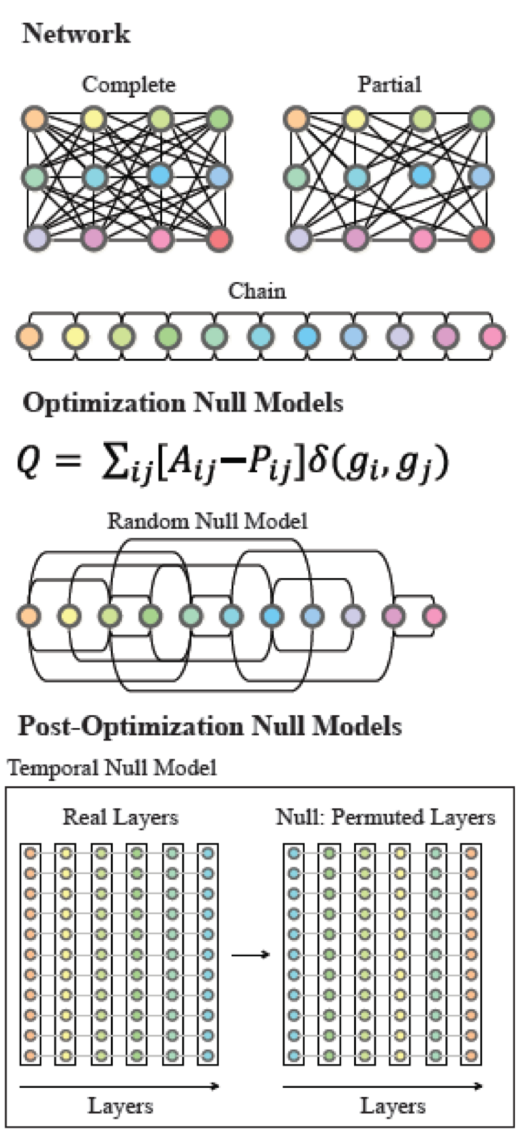


(b) Core-periphery structure

Which Brain Regions are "Flexible"?



- D. S. Bassett, N. F. Wymbs, M. P. Rombach, MAP, P. J. Mucha, & S. T. Grafton [2013], *PLoS Comput. Bio.* **9**(9): 1003171
  - Experimental protocol and notion of "learning" a bit different than in the 2011 paper
- Flexible nodes are consistently in a "periphery" in time-indepenent networks across different time windows
- Nodes that are not flexible (call them "stiff") are consistently in a structural core in these time-independent networks
- Methodology for computing core–periphery structure:
  - M. P. Rombach, MAP, J. H. Fowler, & P. J. Mucha [2014], *SIAM J. App. Math.*, Vol. 74, No. 1: 167–190
    - The 2017 'reboot' of this paper in *SIAM Review* has extra material with subsequent development of methods for core–periphery detection



Development of Null Models for Multilayer Networks

- D. S. Bassett, MAP, N. F. Wymbs, S. T. Grafton, J. M. Carlson, & P. J. Mucha [2013], *Chaos*, **23**(1): 013142

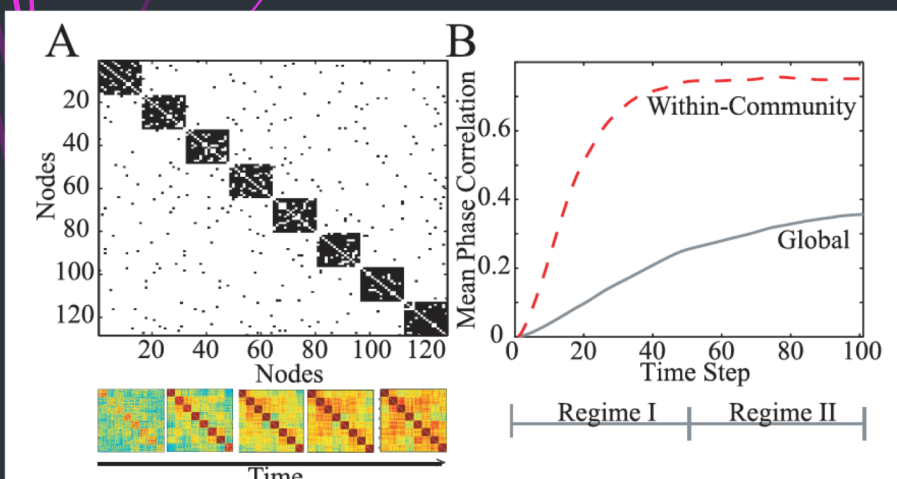
- Additional structure in adjacency tensors gives more freedom (and responsibility) for choosing null models.
- Null models that incorporate information about a system
  - E.g., chain null model fixes network topology but randomizes network "geometry" (edge weights)
- Also: Examine null models from shuffling time series directly (before turning into a network)
- Structural (γ) versus temporal resolution parameter (ω)
  - More generally, how to choose interlayer terms C_{jrs}

Functional Networks from Time-Series Output of Dynamical Systems

(also in D. S. Bassett et al., *Chaos*, 2013)

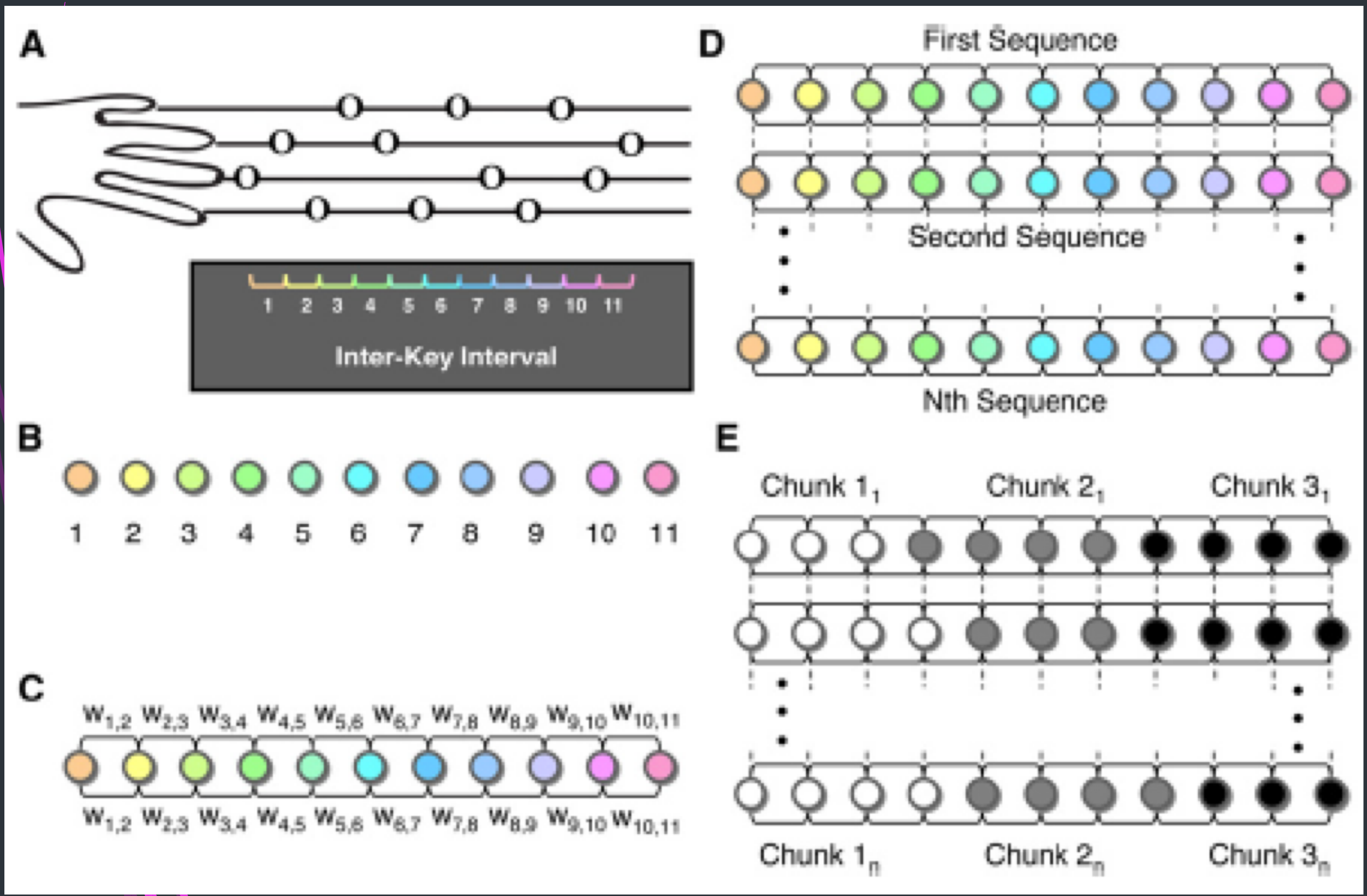
$$\frac{d\theta_i}{dt} = \omega_i + \sum_j \kappa A_{ij} \sin(\theta_j - \theta_i)\,, \quad i \in \{1, \ldots, N\}$$

$$\phi_{ij}(t) = \langle |\cos[\theta_i(t) - \theta_j(t)]| \rangle$$



- Multilayer community detection doesn’t care whether the time series come from experimental measurements or output from dynamical systems.
- Leverage knowledge of well-known dynamical systems to help with methodological development, validation, explore ideas, perhaps obtained insights on the dynamical systems themselves, etc.

Constructing a Multilayer Network to Study Motor Chunking



- N. F. Wymbs, D. S. Bassett, P. J. Mucha, MAP, & S. T. Grafton [2012], “Differential recruitment of the sensorimotor putamen and frontoparietal cortex during motor chunking in humans”, *Neuron*, **74**(5): 936–946

Challenges and Conclusions

Some Challenges
(some hinted at earlier)

- Too many choices for how to do things
  - Choices of parameter values, such as for interlayer coupling
  - Different choices for what layers encode
- Approach to methods like community detection
  - Modularity maximization is old-fashioned and not statistically principled, but statistically principled methods like inference using stochastic block models require assumptions on probability distributions of edge weights
    - Need more mathematical studies of random-graph models with edge weights
  - Development of random-graph null models and analysis of these models

Some More Challenges
(some hinted at earlier)

- How do to multilayer core–periphery detection?
  - A current project of my PhD student Theo Faust
- Dynamical processes on multilayer networks
  - E.g., oscillations coupled to blood flow, such as in a couple of papers by Alex Arenas and collaborators on a Kuramoto model (i.e., a toy coupled-oscillator model) coupled to a random walk (as a toy model for diffusion of blood)
- How do we define “learning” in the neuroscience experiments?
  - E.g., short-term versus medium-term versus long-term
- I’m sure that many of you see difficulties in these approaches that would be good to think more about and improve.

Summary

- Multilayer network analysis is a flexible framework to study many systems
- There is a rich literature on multilayer network analysis in neuroscience
- The flexibility of multilayer networks is both beneficial and a source of many challenges
  - Including in data analysis, mathematical modeling, and mathematical problems of intrinsic interest (i.e., even if the applications didn't exist)