Brain Connectivity Analysis:
from Unimodal to Multimodal

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joint work with Rene Huster, Terran Lane, Vince Clark, Michael Weisend and Vince D. Calhoun
Definitions and Tools

1. Definitions and Tools
2. Unimodal Connectivity Analysis: EEG
3. Contrasting modalities
4. Data Sharing Fusion
5. Validation through Interventions
Introduction

- Neuroimaging studies brain function
- Advanced techniques produce immense amounts of data
- Each with their strength and weaknesses
- Our goal: causal relations among brain networks
Functional Neuroimaging (fMRI)

- functional Magnetic Resonance Imaging (fMRI)
- Blood Oxygenation Level Dependent (BOLD) response
- 4D data (3D volumes evolving in time)

- **Advantage**: Relatively well localized
- **Disadvantage**: Slow sampling rate
Definitions and Tools

Functional Neuroimaging (MEG)

- **Magneto-EncephaloGraphy (MEG)**
- Electromagnetic phenomenon
  - **Advantage**: Instant reflection of the underlying activity (ms resolution)
  - **Disadvantage**: Uncertain spatial localization
Common Underlying Phenomenon

- Inverse problem
- Functional connectivity

[Diagram showing MEG, fMRI, and neural activity]
Data Fusion: Source Analysis
Definitions and Tools

Single modality: **Connectivity Analysis**

- **MEG**
- **fMRI**
Connectivity Inference: Bayesian Networks

\[ P_\theta(X) = \prod_{i=1}^{n} P(X_i | P_a(X_i); \theta) \]
Comparing the Results: **Graph Characterization**

- in-degree
- out-degree
- degree centrality
- maximum degree
- diameter
- density
- average path length

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Outline

1. Definitions and Tools
2. Unimodal Connectivity Analysis: EEG
3. Contrasting modalities
4. Data Sharing Fusion
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Stop-Go task
What are the nodes?
Contrasted sliding graphs metrics\(^2\)

- Higher clustering coefficient for the stop task: network consolidates for processing?
- Shorter characteristic path-length for the stop task: network becomes more efficient?

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Comparison Pipeline

- collect modalities: same subjects same paradigm
- process modalities: place data in the same ROIs
- pre-process data: align sampling rates and quantize
- infer effective connectivity: Bayesian Nets
- compare results: aggregate metric

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Contrasting modalities

Neuroimaging

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Contrasting modalities

Processing

**MEG**

**fMRI**

**novel**

**target**
Resulting Connectivity

Contrasting modalities

Neuroimaging

marginal distributions of edges

highest scoring networks in transverse view
Comparing the Results
Graph Metrics Distributions

node-degree distribution
Comparing the Results
Graph Metrics Distributions

node-degree distribution
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Why do fusion in dynamical settings?

- temporal resolution affects causality\(^4\)

- fusion helps to avoid temporal inverse problem\(^5\)


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\[
P(R_{t0:TR}, M_{t0:TR}, B_{t0:TR}) = P(R_{t0}) P(B_{t0} | R_{t0}) P(B_{tTR} | R_{tTR}) \prod_{i=1}^{TR} P(R_{ti} | R_{ti-1}) \prod_{i=0}^{TR} P(M_{ti} | R_{ti})
\]

6 Murphy, K. PhD thesis (UC Berkeley, 2002).

- circles - hidden
- squares - observed
Dynamic Bayesian Networks transition model

\[ P(\mathcal{R}_{t_0:t_{TR}}, \mathcal{M}_{t_0:t_{TR}}, \mathcal{B}_{t_0:t_{TR}}) = P(\mathcal{R}_{t_0}) P(\mathcal{B}_{t_0}|\mathcal{R}_{t_0}) P(\mathcal{B}_{t_{TR}}|\mathcal{R}_{t_{TR}}) \prod_{i=1}^{TR} P(\mathcal{R}_{t_i}|\mathcal{R}_{t_{i-1}}) \prod_{i=0}^{TR} P(\mathcal{M}_{t_i}|\mathcal{R}_{t_i}) \]

\[ \mathcal{R}_t = k\mathcal{R}_{t-1} + \sigma_\mathcal{R}_\eta_t \]

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DATA SHARING FUSION

NEUROIMAGING
Data Sharing Fusion  Neuroimaging

Dynamic Bayesian Networks  MEG forward model\(^6\)

\[
P\left(\mathcal{R}_{t_0:t_{TR}}, \mathcal{M}_{t_0:t_{TR}}, \mathcal{B}_{t_0:t_{TR}}\right) = P\left(\mathcal{R}_{t_0}\right) P\left(\mathcal{B}_{t_0} | \mathcal{R}_{t_0}\right) P\left(\mathcal{B}_{t_{TR}} | \mathcal{R}_{t_{TR}}\right) \prod_{i=1}^{TR} P\left(\mathcal{R}_{t_i} | \mathcal{R}_{t_{i-1}}\right) \prod_{i=0}^{TR} P\left(\mathcal{M}_{t_i} | \mathcal{R}_{t_i}\right)
\]

\[
\mathcal{M}_t = \text{MFM}(\mathcal{R}_t) + \sigma \mathcal{M} \eta_t,
\]


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Dynamic Bayesian Networks  

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\[ \mathcal{B}_t = \text{HFM}(\mathcal{R}_t) + \sigma_B \eta_t \]

\[ \mathcal{M}_t \]  

\[ \mathcal{R}_t \]  

\[ \mathcal{B}_t \]

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Dynamic Bayesian Networks inference\textsuperscript{6}

\[
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\]

Particle Filtering

\textbf{circles} - hidden
\textbf{squares} - observed

Demonstration

fMRI only  MEG only  fMRI+MEG

Comparison: fMRI vs. fMRI+MEG

- from sparse to constant activity
- 1000 runs per point

\[ \mathcal{E} = \sum_{i=1}^{1000} \frac{\| T_i - M_i \|_2}{\| T_i \|_2} \]

- Event Related studies
- fusion yields:
  - lower errors
  - stabler estimates
Comparison: fMRI vs. fMRI+MEG

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Speed up and stability

BOLD (% of change)

![Graph showing BOLD estimate variance vs. number of particles]

- X-axis: Number of particles
- Y-axis: BOLD estimate average variance
- Data points for FMRI
Speed up and stability

BOLD (% of change)  neural activity (a.u.)

fusion yields: ○ lower variance and ○ faster computation
Real data

- same paradigm for fMRI and MEG
- 120 trials of an 8 Hz checkerboard reversal

**MEG**
- 1200 Hz
- averaged

**fMRI**
- interpolated to 1200 Hz
- averaged
Real data results

fMRI only
Real data results

fMRI only

MEG only
Real data results

fMRI only

MEG only

fMRI+MEG

BOLD response (arbitrary units)

neural activity (arbitrary units)

0 1 2 3 4 5
0 1 2 3 4 5

time (seconds)

time (seconds)
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Does inferred connectivity reflect brain function?

- Manipulation principle: learn by breaking parts of the system!
- How to alter brain function without subjects complaining too loud?
- Transcranial Direct Current Stimulation (tDCS): a noninvasive low current technique affecting firing thresholds of cortical neurons.
Does inferred connectivity reflect brain function?

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Preliminary Results
Preliminary Results

distribution of edges in likely graphs (right hand stimulation)

- run1
- run2
- run3
- run4
- run5

- sham
- full

- probability (logscale)
- # of children
Summary

- **Goal:** Combine modalities to infer function-induced networks

- **Results so far:**
  - Demonstrated useful results of sliding window treatment
  - Demonstrated pitfalls of single-modality connectivity estimation\(^8\)
  - Demonstrated fMRI+MEG fusion in the DBN framework\(^9\)

- **Future work:**
  - Causal structure fusion
  - Whole brain DBN fusion framework
  - tDCS-based analysis framework for validation

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Thank you!