Brain Connectivity Analysis: from Unimodal to Multimodal

Sergey M. Plis

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

Contents

1 Definitions and Tools

2 Unimodal Connectivity Analysis: EEG

3 Contrasting modalities

4 Data Sharing Fusion

5 Validation through Interventions

Outline

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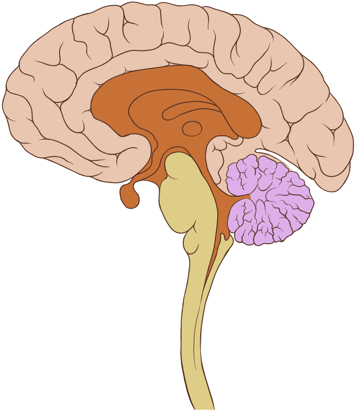
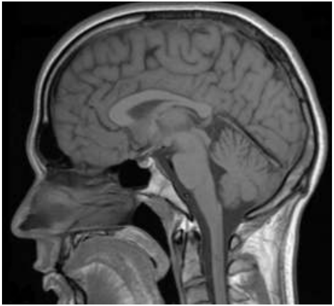
Introduction

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



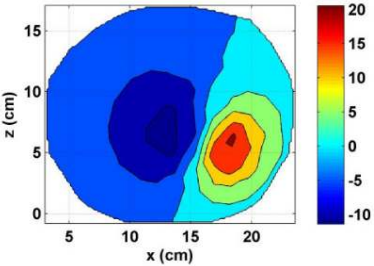
Functional Neuroimaging (fMRI)

- 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



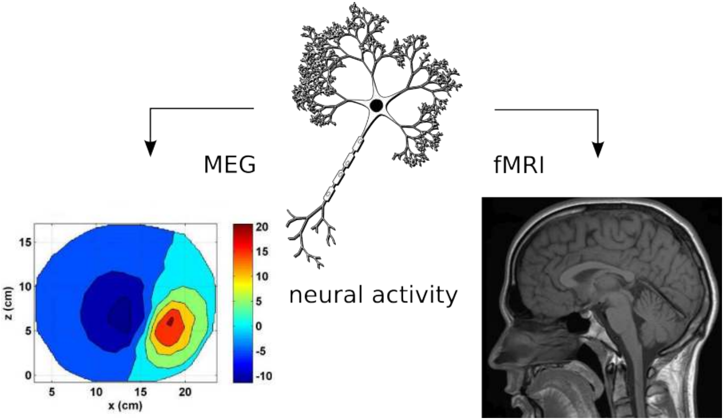
Functional Neuroimaging (MEG)

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

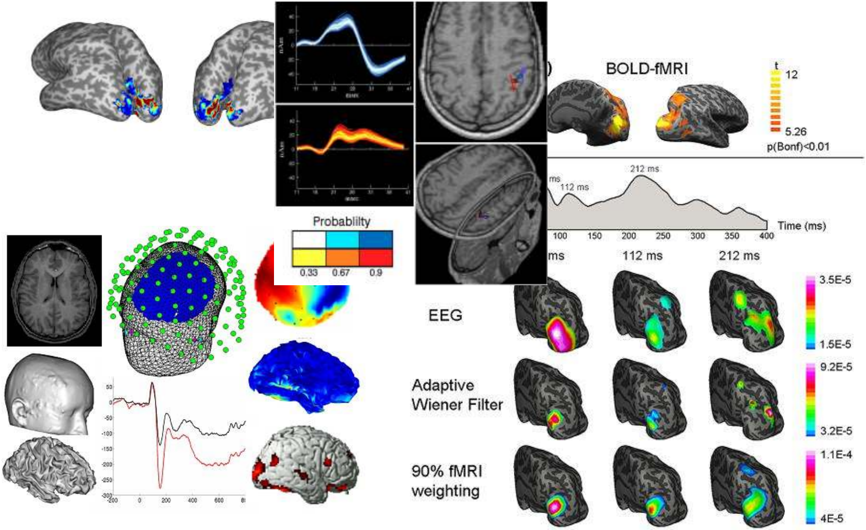


Common Underlying Phenomenon

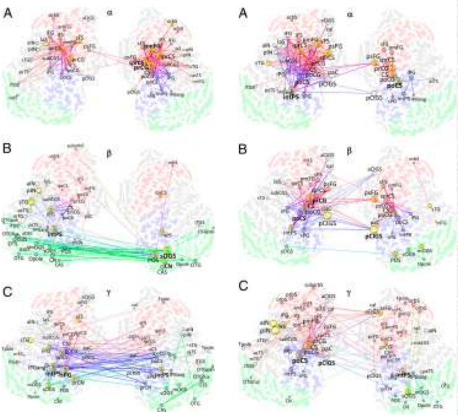
- Inverse problem
- Functional connectivity



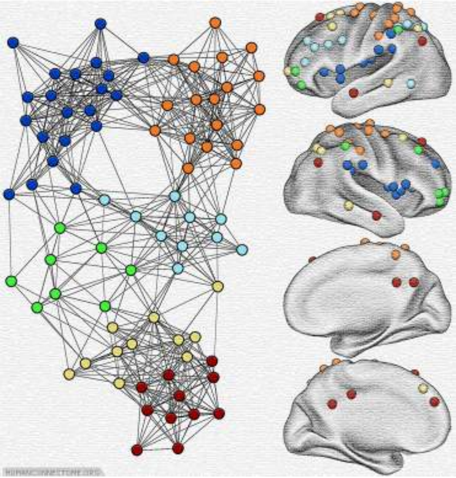
Data Fusion: Source Analysis



Single modality: Connectivity Analysis

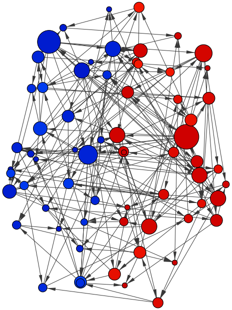


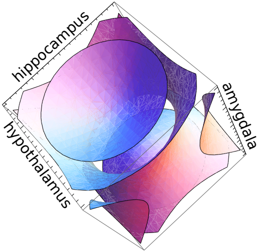
MEG



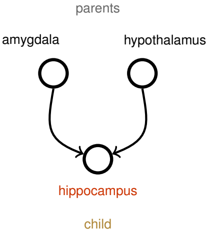
fMRI

Connectivity Inference: Bayesian Networks



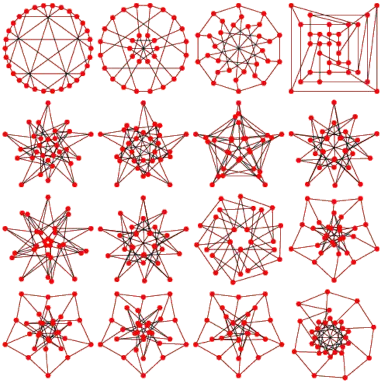


$$P_\theta(\boldsymbol{X}) = \prod_{i=1}^{n} P(X_i | P_a(X_i); \theta)$$



Comparing the Results: Graph Characterization[1]

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



[1] Rubinov, M. *et al. Neuroimage* **52,** 1059–1069 (2010).

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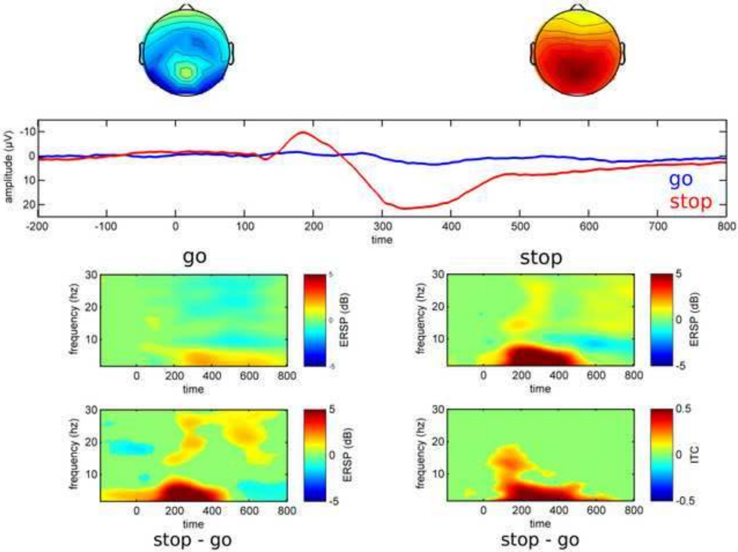
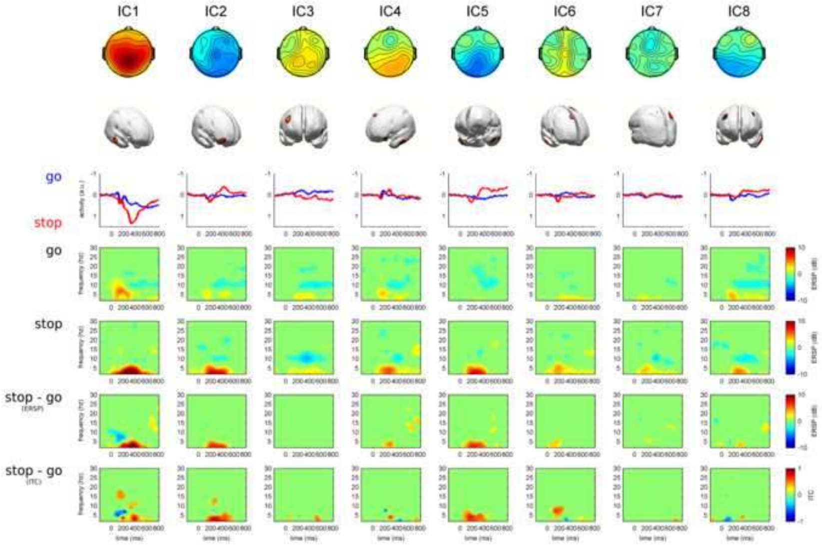
Stop-Go task

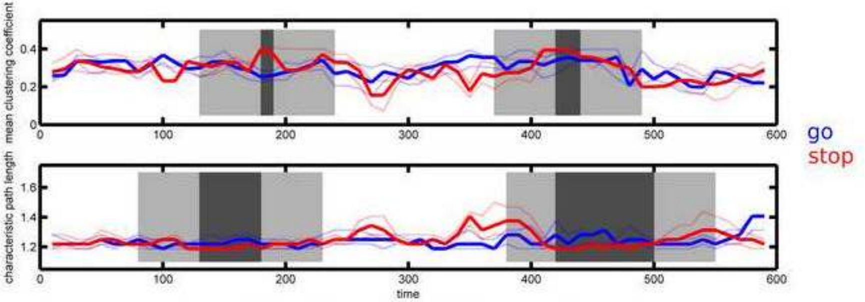


amplitude (μV)
-10
0
10
20
-200
-100
0
100
200
300
400
500
600
700
800
time
go
stop
go
frequency (hz)
30
20
10
0
200
400
600
800
time
ERSP (dB)
stop
5
0
-5
stop - go
ITC
0.5
-0.5

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?

[2] Grzegorczyk, M. *et al. Machine Learning* **71,** 265–305 (2008).

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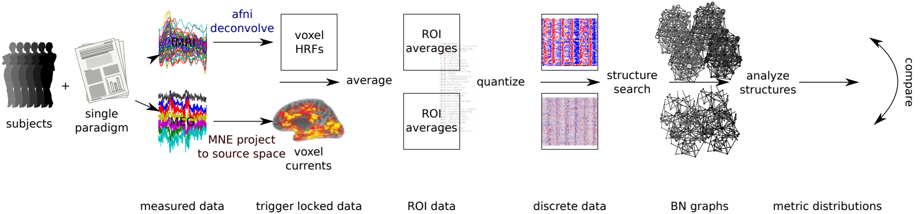
Comparison Pipeline[3]



- 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

[3] Plis, S. M. *et al. Computers in Biology and Medicine* **41,** 1156–1165 (2011).

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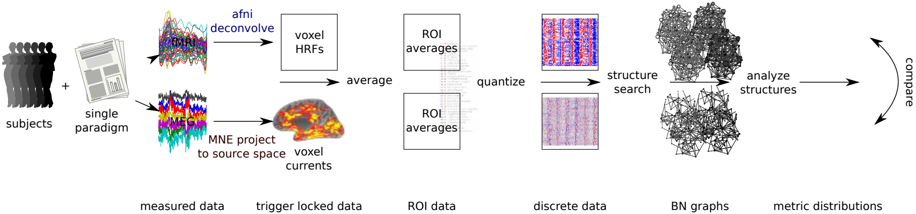

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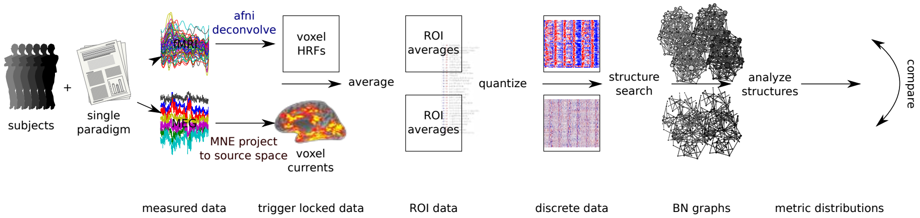

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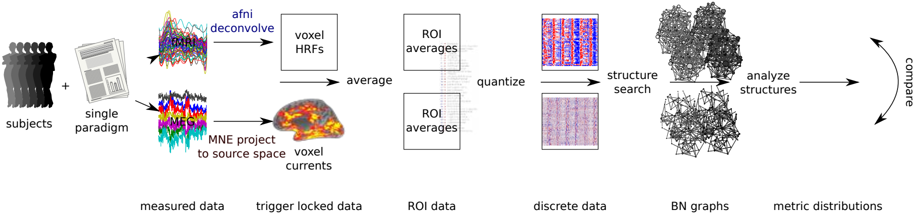

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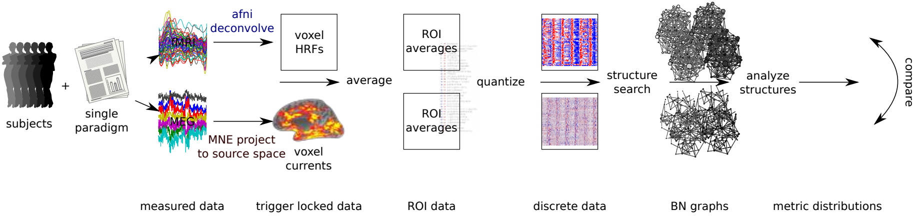

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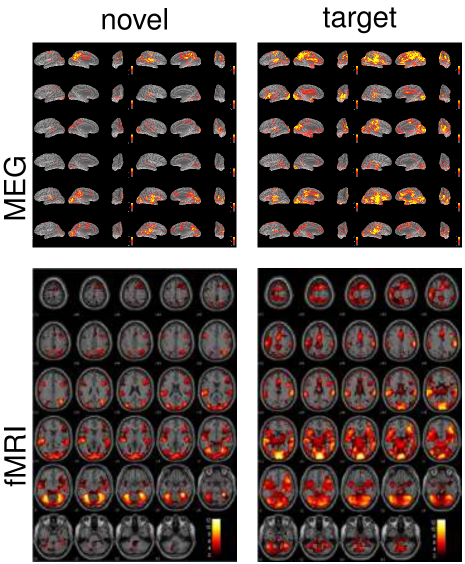
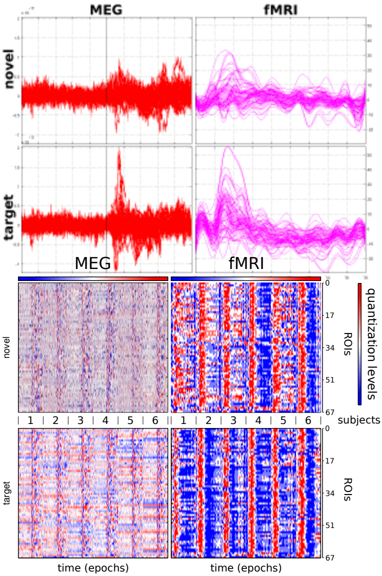
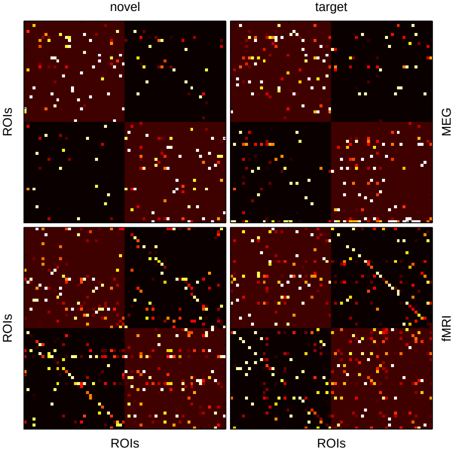
Processing

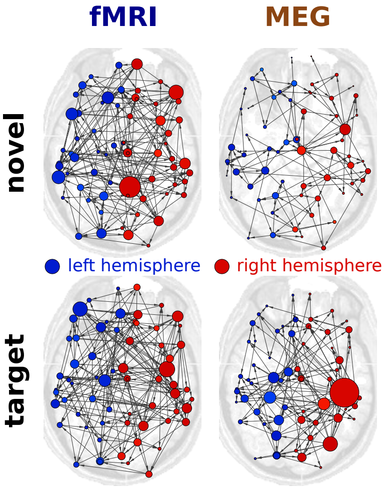

novel
target
MEG
fMRI


MEG
fMRI
novel
target
MEG
fMRI
novel
target
1 2 3 4 5 6
1 2 3 4 5 6
ROIs
ROIs
quantization levels
subjects
0
17
34
51
67
time (epochs)
time (epochs)

Resulting Connectivity

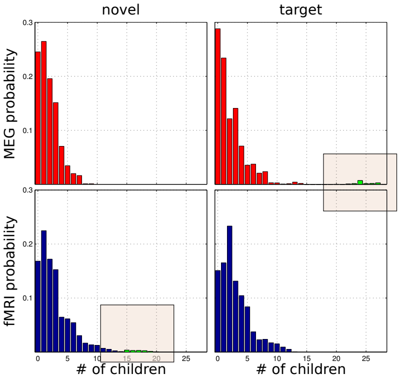


marginal distributions of edges



highest scoring networks
in transverse view

Comparing the Results
Graph Metrics Distributions



node-degree distribution

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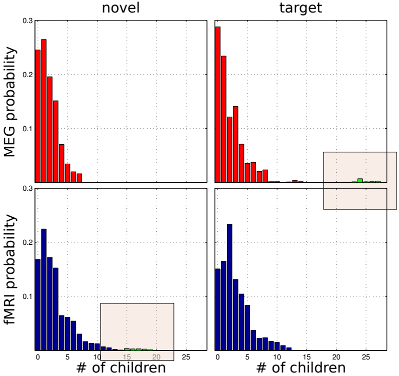
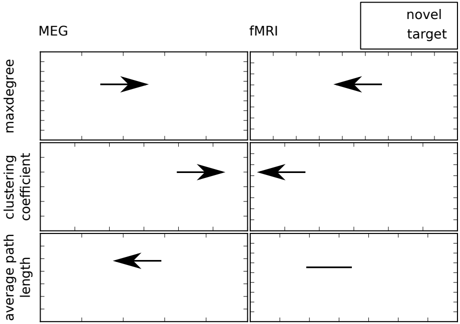


node-degree distribution



graph metrics distributions

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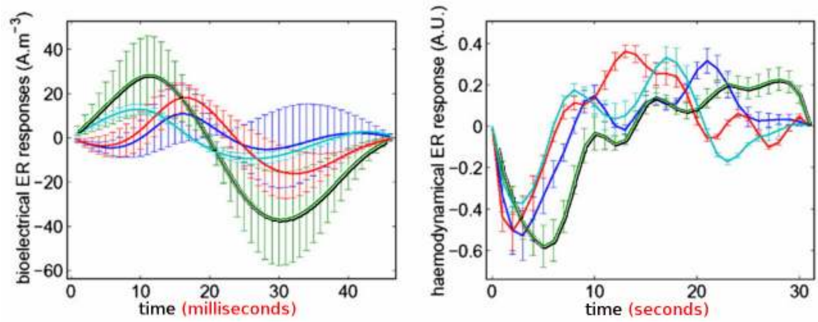
Why do fusion in dynamical settings?

- temporal resolution affects causality[4]



- fusion helps to avoid temporal inverse problem[5]

[4] Daunizeau, J. *et al. Neuroimage* **36,** 69–87 (May 2007).

[5] Riera, J. J. *et al. Neuroimage* **21,** 547–567 (Feb. 2004).

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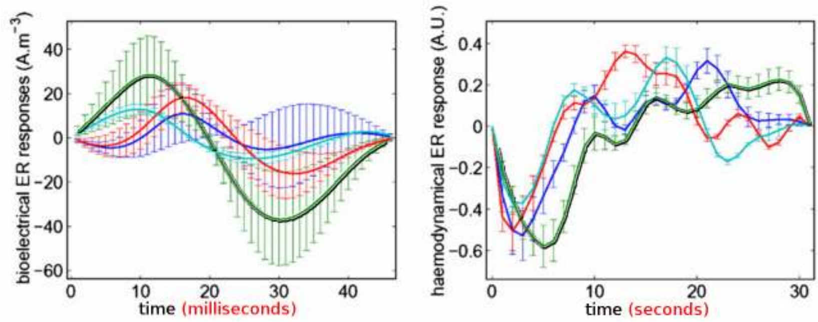

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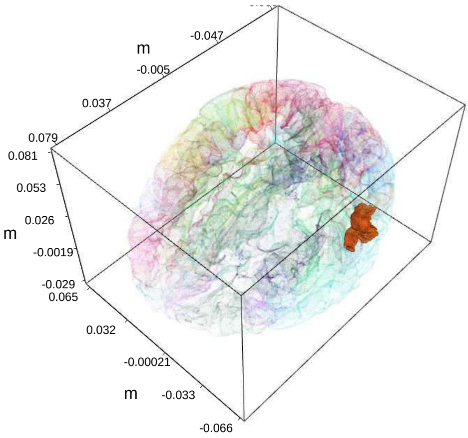
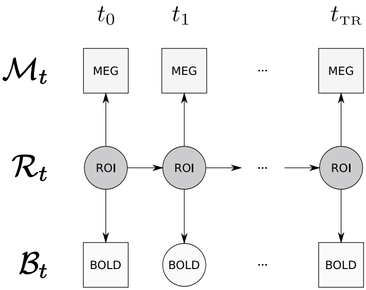
Dynamic Bayesian Networks[6]

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





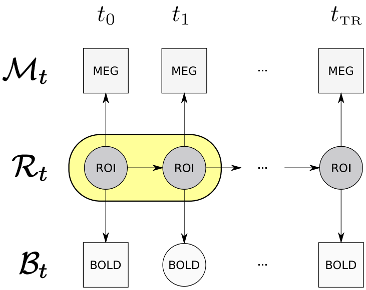
- circles - hidden
- squares - observed

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

Dynamic Bayesian Networks transition model

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

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



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Dynamic Bayesian Networks MEG forward model[6]

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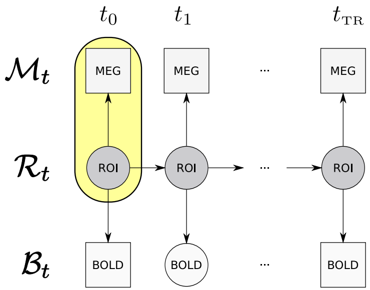
$$\mathcal{M}_t = \mathrm{MFM}(\mathcal{R}_t) + \sigma_{\mathcal{M}}\eta_t,$$



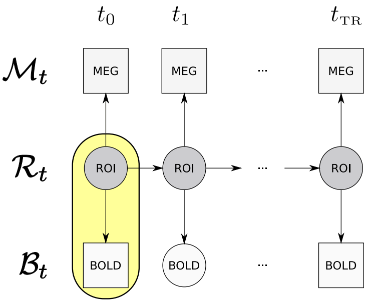
- circles - hidden
- squares - observed

[6] Sarvas, J. eng. *Phys Med Biol* **32,** 11–22 (1987).

Dynamic Bayesian Networks fMRI forward model[6]

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

$$\mathcal{B}_t = \mathrm{HFM}(\mathcal{R}_t) + \sigma_{\mathcal{B}}\eta_t$$



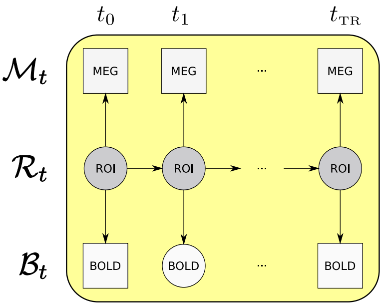
- circles - hidden
- squares - observed

[6] Friston, K. J. *et al. Neuroimage* **12,** 466–477 (2000).

Dynamic Bayesian Networks inference[6]

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

Particle Filtering

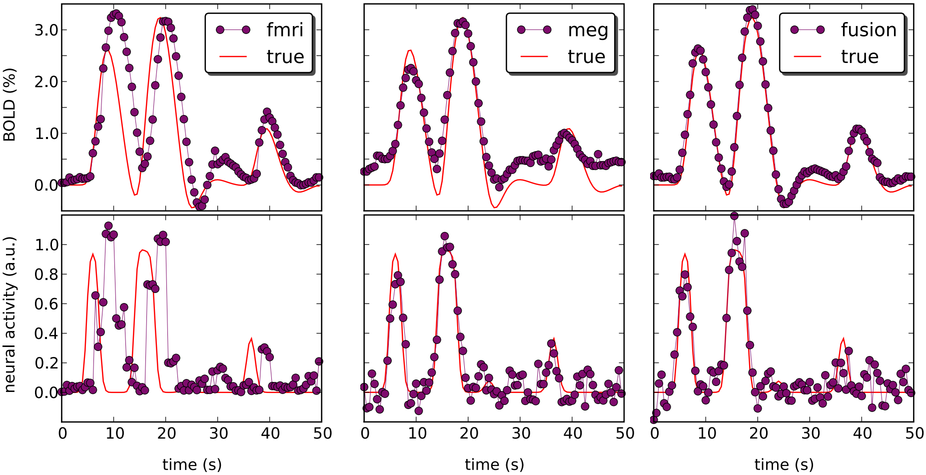


- circles - hidden
- squares - observed

[6] (eds Doucet, A. *et al.*) (Springer-Verlag, Berlin, 2001).

Demonstration[7]

fMRI only | MEG only | fMRI+MEG



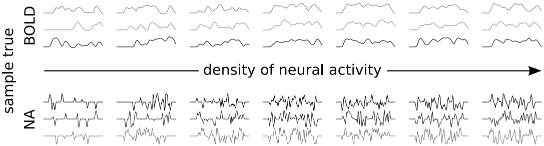
[7] Plis, S. M. *et al. Frontiers in Neuroinformatics* **4,** 12 (2010).

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

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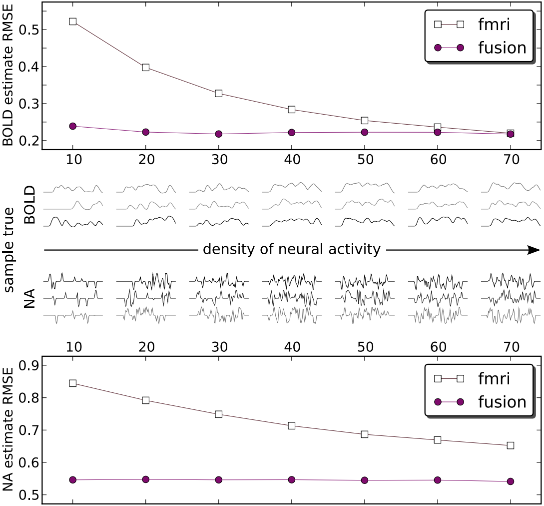

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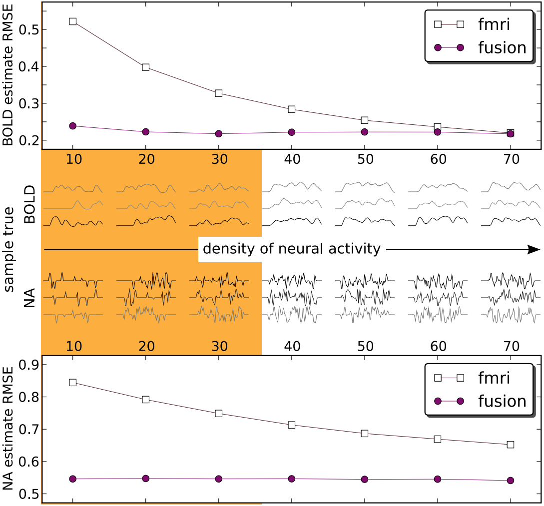

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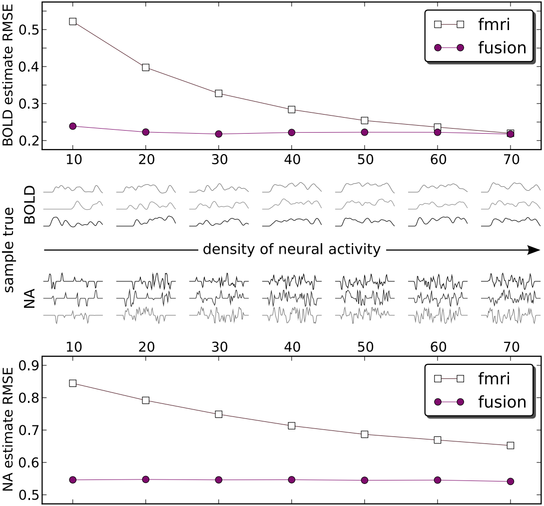

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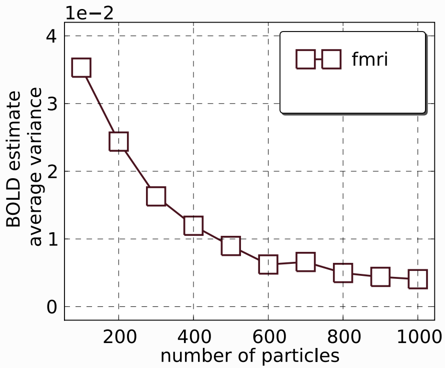
Speed up and stability

BOLD (% of change)



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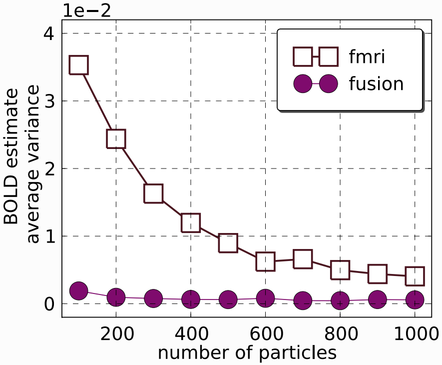
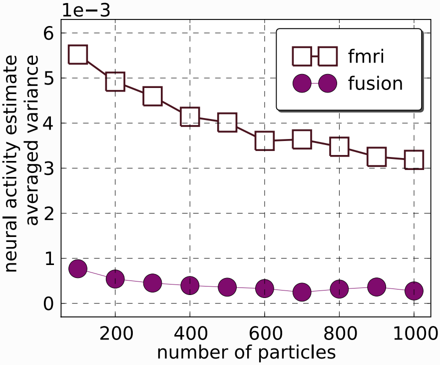


neural activity (a.u.)



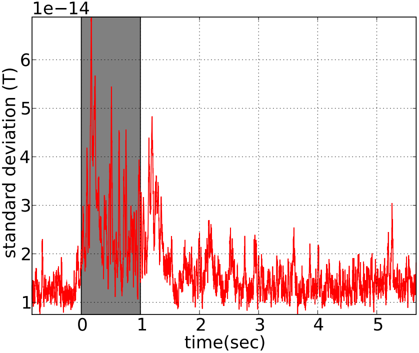
fusion yields: ○ lower variance and ○ faster computation

Real data

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

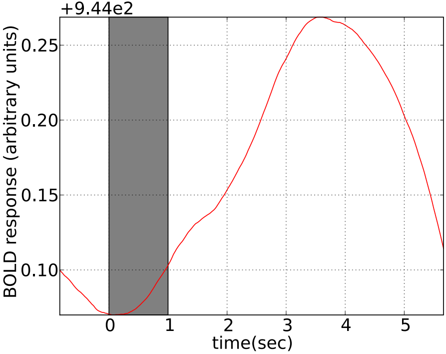
MEG

- 1200 Hz
- averaged



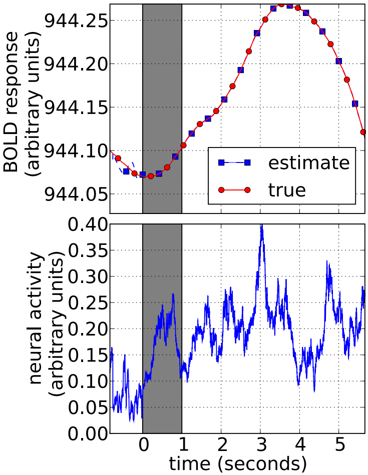
fMRI

- interpolated to 1200 Hz
- averaged



Real data results

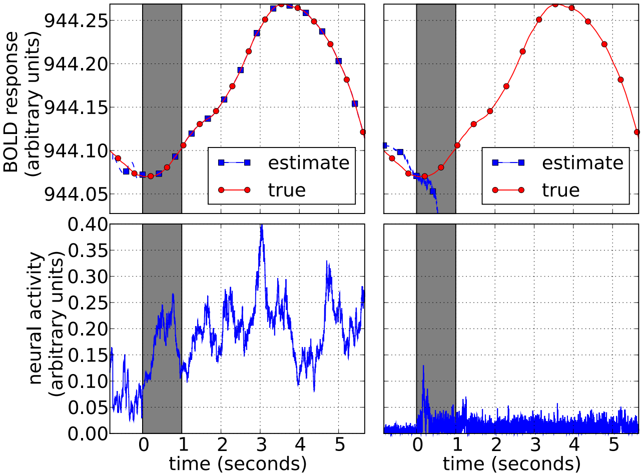
fMRI only



Real data results

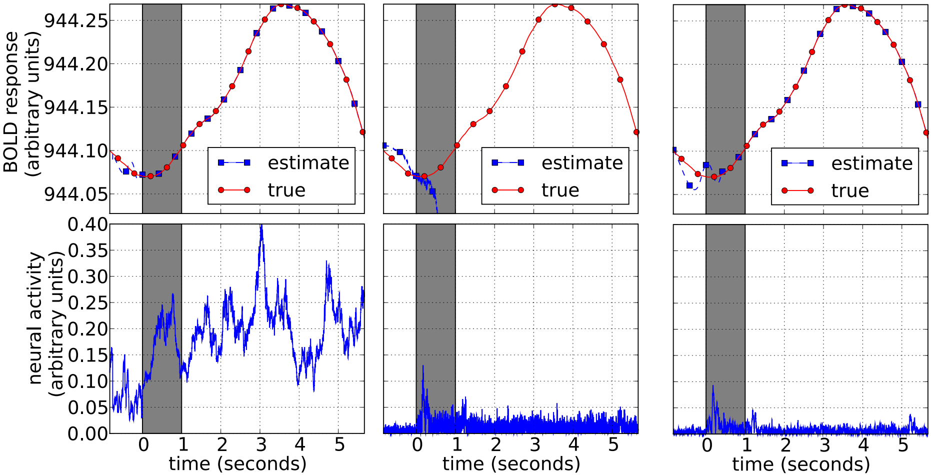
fMRI only

MEG only



Real data results

fMRI only | MEG only | fMRI+MEG



Outline

1 Definitions and Tools

2 Unimodal Connectivity Analysis: EEG

3 Contrasting modalities

4 Data Sharing Fusion

5 Validation through Interventions

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.

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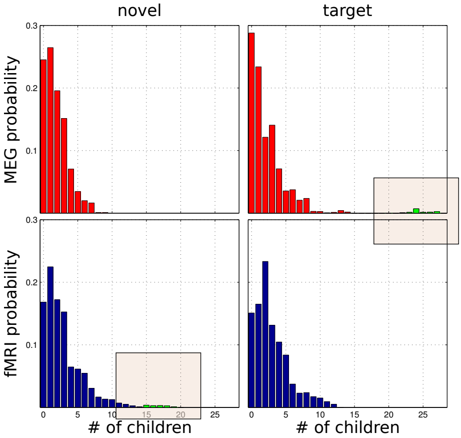

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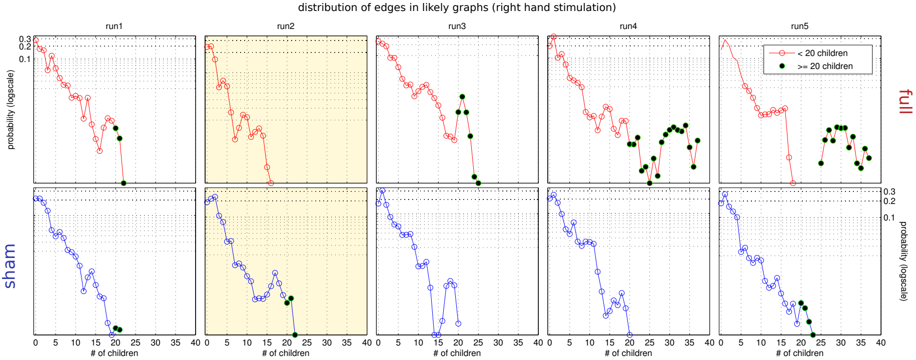

Summary

- 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

[8] Plis, S. M. *et al. Computers in Biology and Medicine* 41, 1156–1165 (2011).

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Thank you!