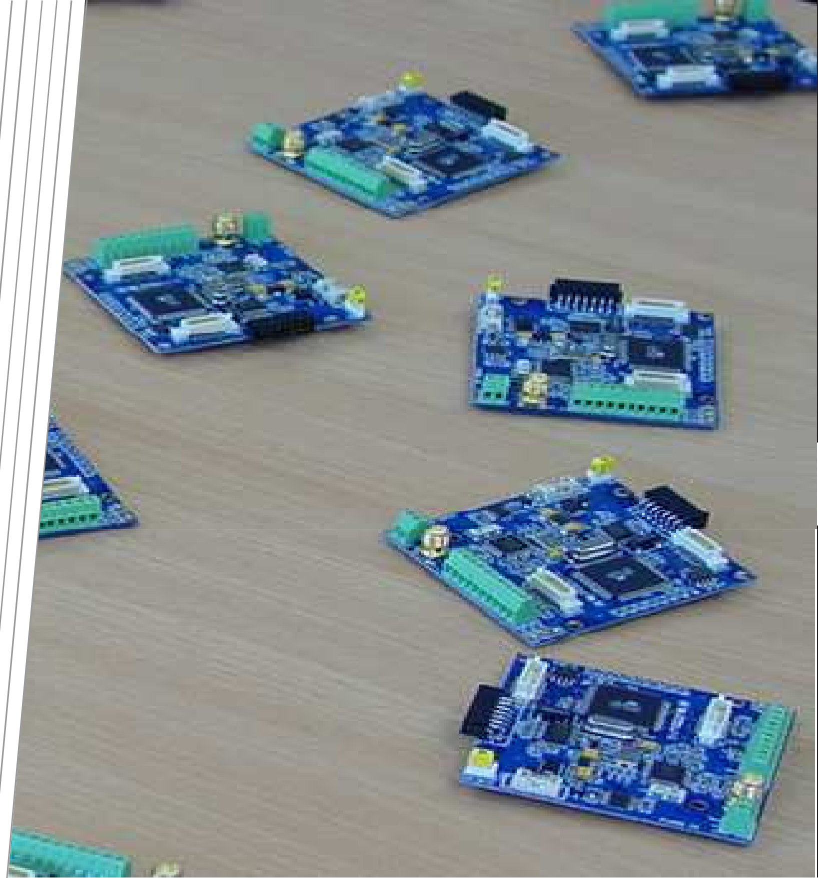

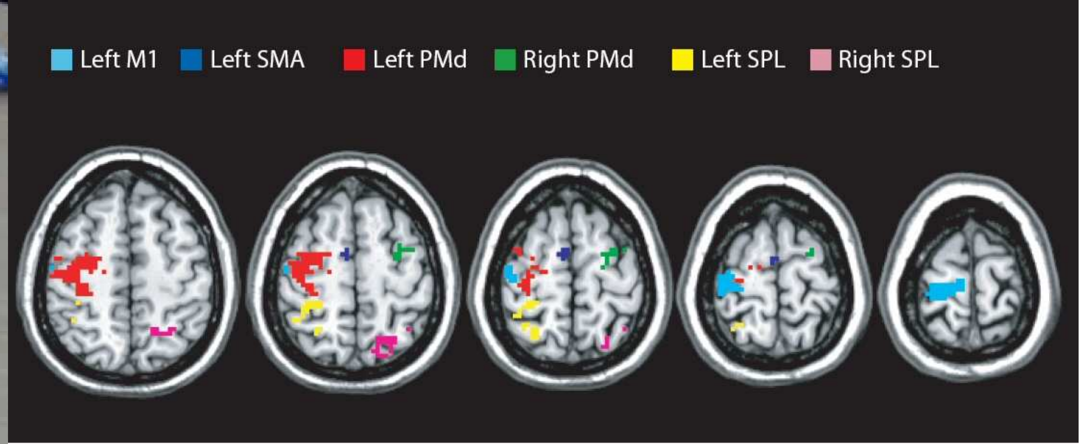

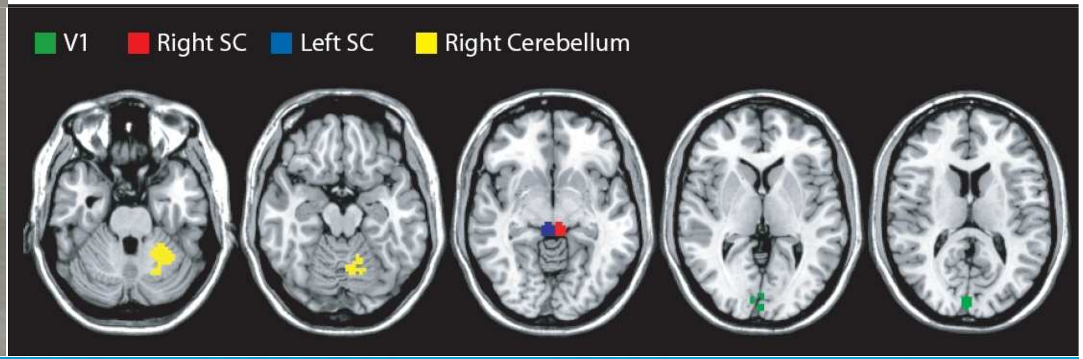

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Multivariate information-theoretic measures reveal directed information structure and task relevant changes in fMRI connectivity

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To Complex Sys. & Centre for Waves + Complex Sys., School of Physics, The University of Sydney on 5/10/2010

Multivariate info-theoretic measures reveal directed information structure in fMRI connectivity: Overview

- Computational neuroscience
  - Computational analysis of brain imaging data
  - Neuroscientist: “How can we analyse data to understand how brain regions interact? What does this tell us about, e.g. disease? ”
  - Computer scientist: “How can we describe computation in the brain? What does this tell us about computation in nature?”
- Task: establish directed information structure from time-series brain imaging data
  - Also known as functional networks
  - Taking into account some particular requirements: capturing multivariate interactions, non-linearity, small amount of data …
- Method: information transfer
  - Plus enhancements including multivariate analysis and statistical significance measurements
- Application: a visuomotor tracking task
  - Directed interregional structure, with movement planning regions driving visual and motor control

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Directed information structure task

- Take a multivariate time series measured across different brain regions during a cognitive task. Each region contains many measured variables (in fMRI these are voxels).
- Infer the directed information structure between the regions that supports this task.

There is much previous work on establishing functional networks, but none meets *all* of the following challenges/requirements:

- Explicitly examines information transfer
- Capture directionality
- Capture non-linear interactions
- Capture collective interactions
- Infer at the regional level
- Handle small amounts of data
- Distinguish a weak relationship from none
- Don't assume an underlying model

Our approach has properties to meet these challenges/requirements:

- Uses transfer entropy
- Asymmetric analysis
- Information-theoretic (i.e. non-linear)
- Multivariate
- Infers at the regional level
- Uses dynamic kernel width (Kraskov)
- Uses statistical significance
- Information-theoretic (i.e. model-free)

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Information-theory: the natural domain

- Shannon entropy

$$H(X) = -\sum_{x \in \mathcal{X}} P(x) \log P(x)$$

- Joint entropy

$$H(X,Y) = -\sum_{x \in \mathcal{X}} \sum_{y \in \mathcal{Y}} P(x,y) \log P(x,y)$$

- Conditional entropy

$$H(Y|X) = \sum_{x \in \mathcal{X}} \sum_{y \in \mathcal{Y}} P(x,y) \ \log \frac{P(x)}{P(x,y)}$$

- Mutual information

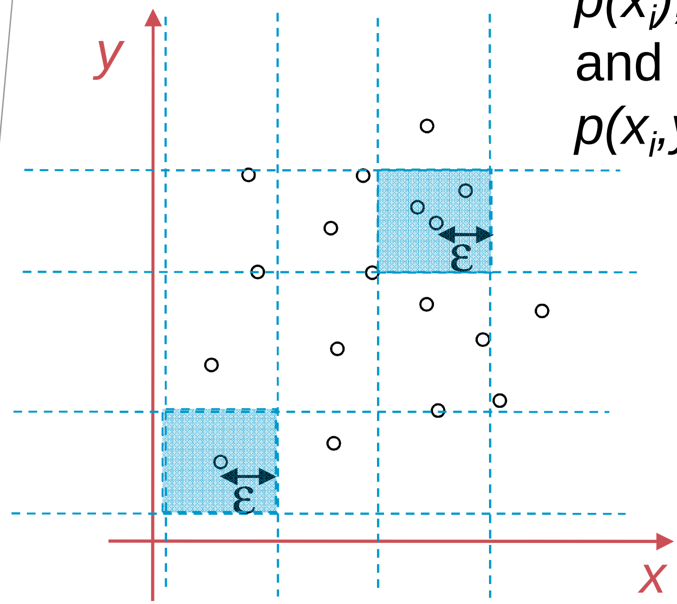
$$I(X;Y) = \sum_{x \in \mathcal{X}} \sum_{y \in \mathcal{Y}} P(x,y) \ \log \frac{P(x,y)}{P(x)P(y)}$$

$$I(X;Y) = H(X) + H(Y) - H(X,Y)$$

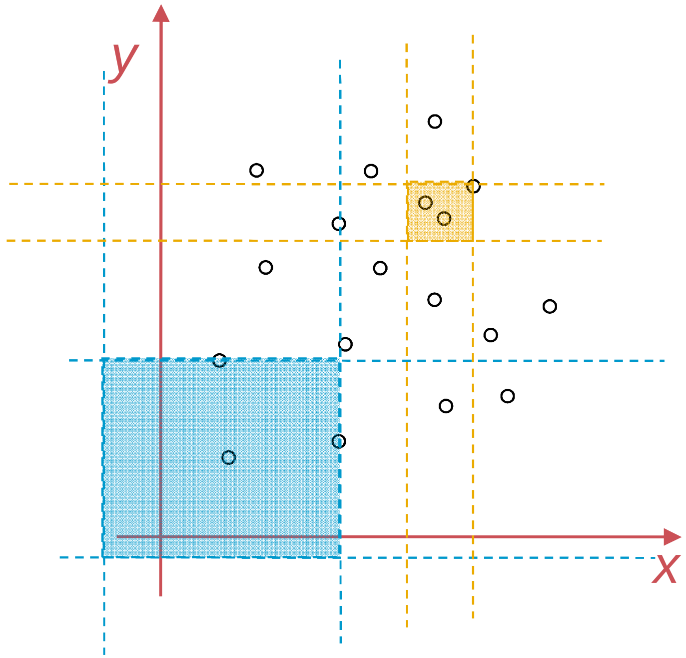
- Conditional mutual information

$$I(X;Y|Z) = H(X|Z) - H(X|Y,Z)$$

Information measures on continuous-valued variables



$p(x_i)$, $p(y_i)$
and
$p(x_i,y_i)$?



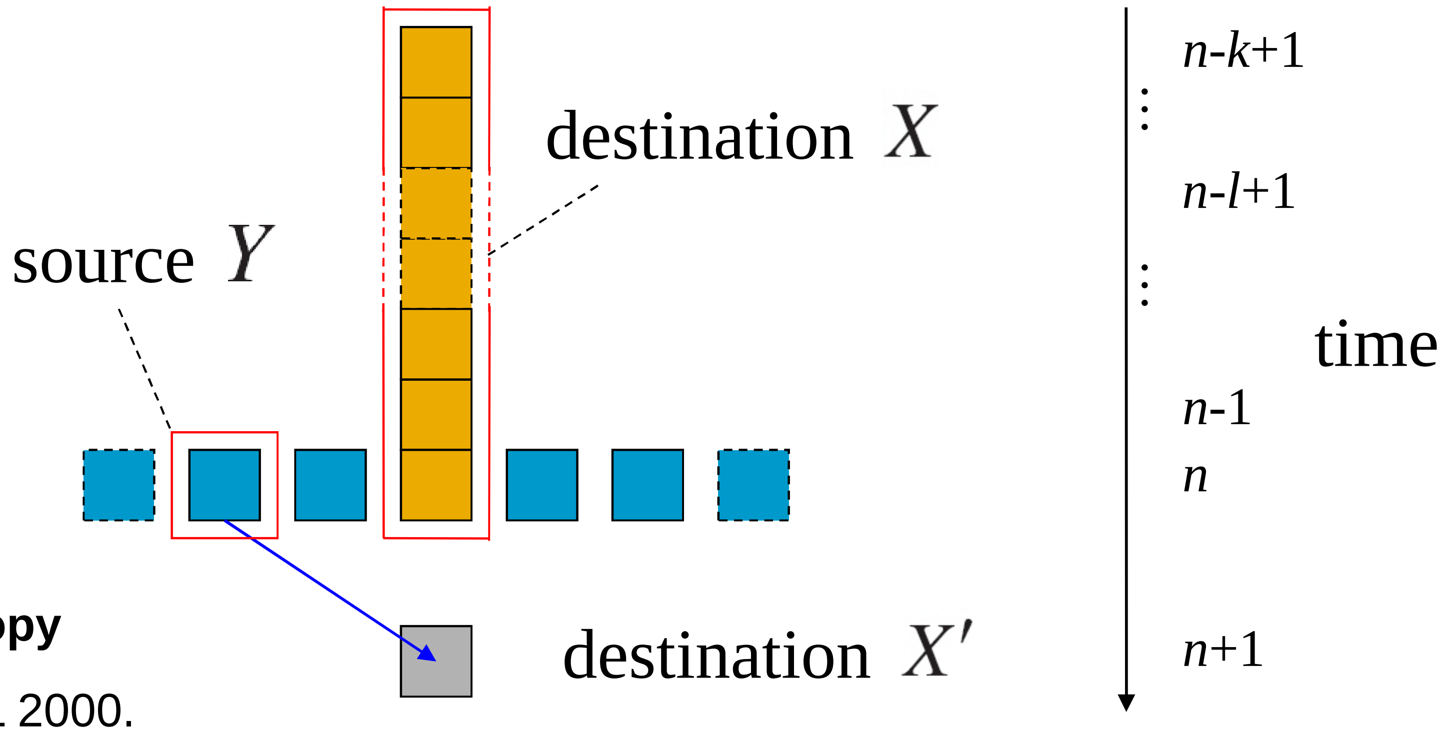
- Kernel estimation
  - Fixed box width
  - "How does knowing *x* within ε help me predict *y* within ε?"

- Kraskov technique
  - Dynamic box width and bias correction
  - "How does knowing *x* within its *k* closest samples help me predict *y* within its *k* closest samples?"

Is useful for small data sets

Information Transfer

$$T_{Y \to X'} = I(Y; X' | X) = H(X'|X) - H(X'|X,Y)$$



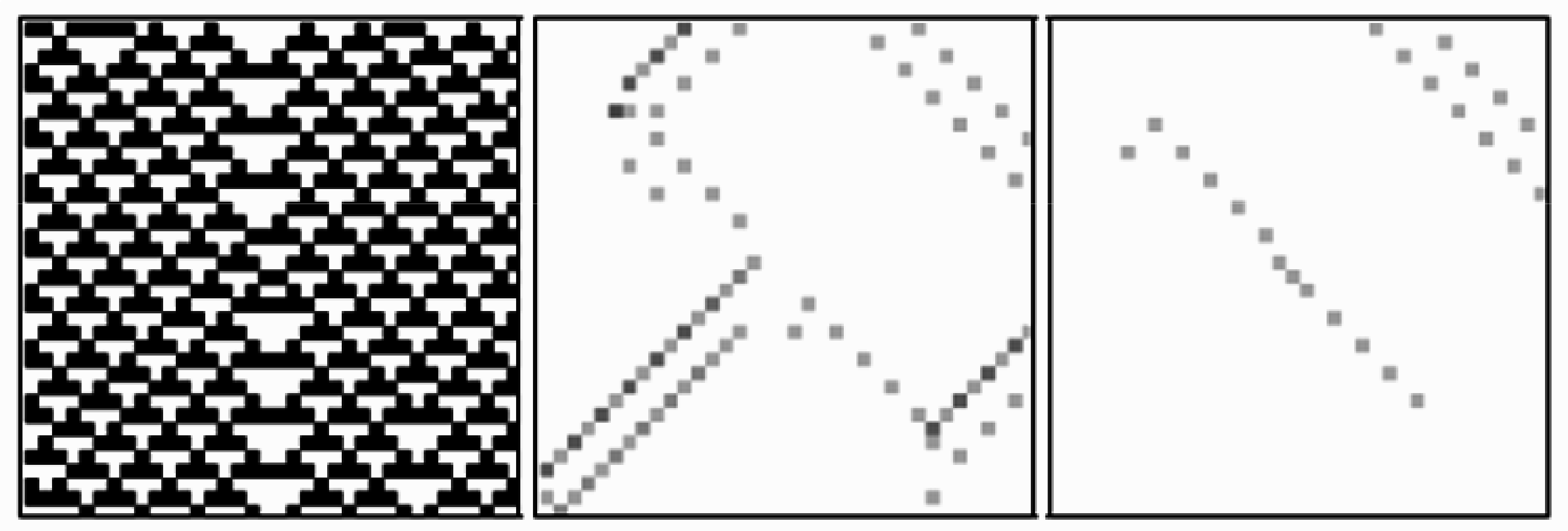
Transfer entropy

Schreiber, PRL 2000.

$$T_{Y \to X} = \frac{1}{N} \sum_{n=1}^{N} \log_2 \frac{p(x_{n+1} | x_n^{(k)}, y_n^{(l)})}{p(x_{n+1} | x_n^{(k)})}$$

Explicitly info transfer, non-linear, directional, model-free

Information transfer in cellular automata



ECA rule 54 | t(i,j=-1,n,k=16) > 0 | t(i,j=-1,n,k=16) < 0

Transfer entropy (on a local scale) confirms the long-held conjecture that gliders in CAs are the dominant information transfer agents in their direction of motion. (Lizier et al, PRE 2008)

→ Transfer entropy aligns with our qualitative understanding of information transfer

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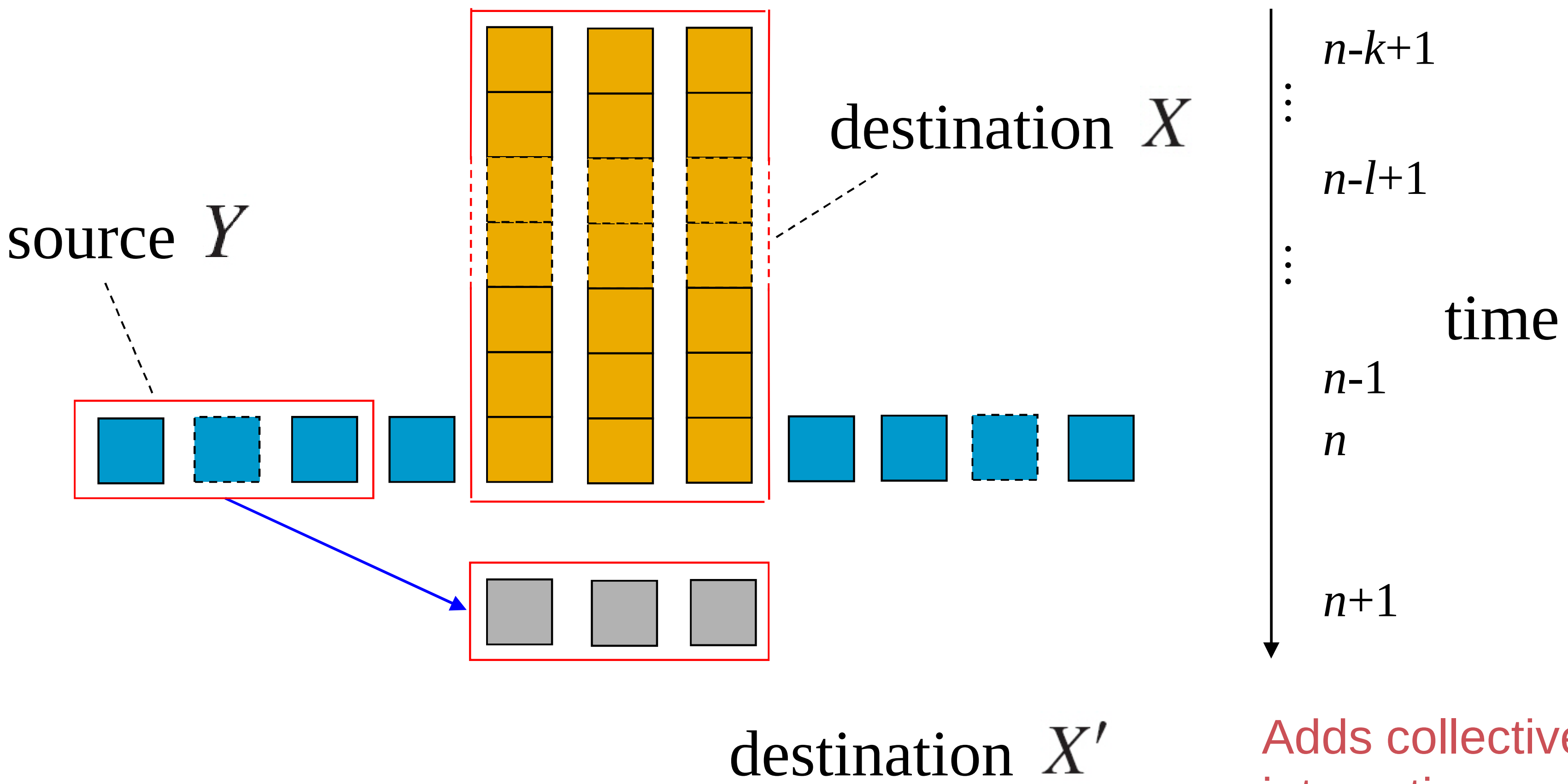
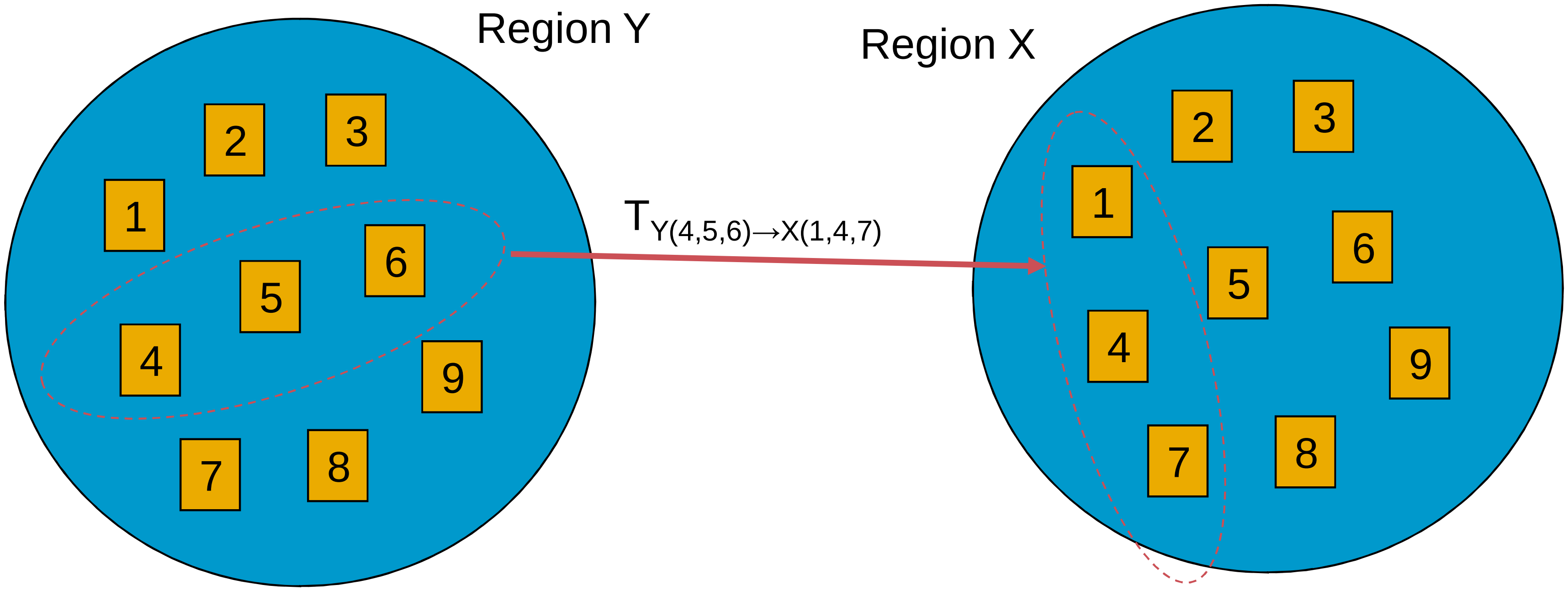
Multivariate Information Transfer

$$T_{Y \to X'} = I(Y; X' | X) = H(X' | X) - H(X' | X, Y)$$



Adds collective interactions

Interregional Multivariate Information Transfer



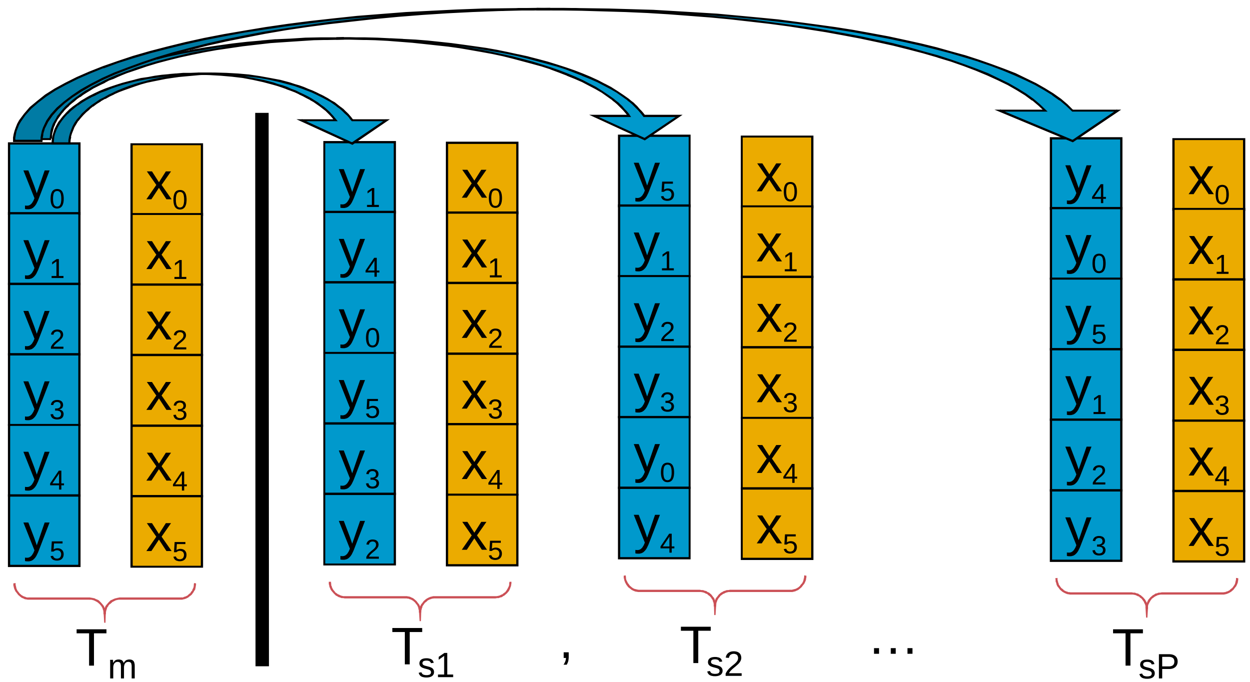
Interregional Transfer is the average Transfer Entropy from each pair *i* of *v* voxels in region *Y* to each pair *j* of *v* voxels in region *X*.

$$T_{k,v}\,(\mathbf{Y} \rightarrow \mathbf{X}) = \langle T_k\,(\mathbf{Y_i} \rightarrow \mathbf{X_j})\rangle_{i,j}$$

Adds interregional level

A method of inferring interregional links for the directed information structure

- Inferring a directional link with transfer entropy (Chávez et al, 2003)
  - Compute the significance of the measured transfer entropy T_m by comparing to a population of surrogate values with relationship between source and destination destroyed.
    Null hypothesis: no temporal relationship b/w source and destination.
  - Compute P surrogate TE values T_s by permuting the source observations y_n with respect to the destination state transitions $x^k_n \rightarrow x_{n+1}$.
  - Conclude a significant link where $p(T_m < T_s) < \alpha$



A method of inferring interregional links for the directed information structure

- Extend inference to multivariate transfer entropy (trivial)
- Extend inference to interregional transfer
  - To generate each sample TE value:
    - Permute **all** of the source variables together against the destination region.
    - Compute $T_{Y_i \rightarrow X_j}$ for each required set (*i,j*) with the same permutation of source variables.
- The method is applicable using both MI or TE as a basis (for undirectional or directional analysis respectively).
- For analysis across group:
  - Use the binomial distribution to infer whether the number of individuals who had a significant link for that region pair was a significant number (with the null hypothesis that individual links may be inferred by chance alone).
- We can analyse modulation of the structure with respect to an experimental variable (by assessing significance of the correlation against surrogate correlations from permuted data sets)

Distinguishes the existence of a relationship from no relationship; adds robustness to small data sets

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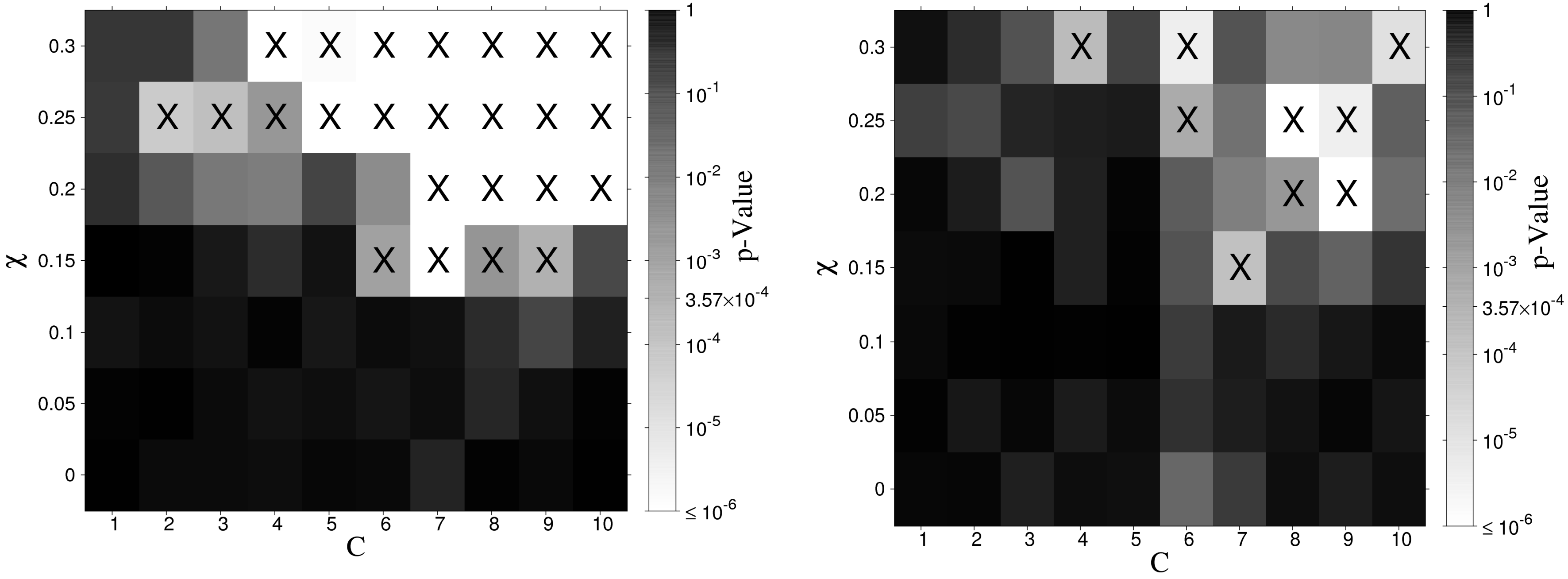
Verification of the technique

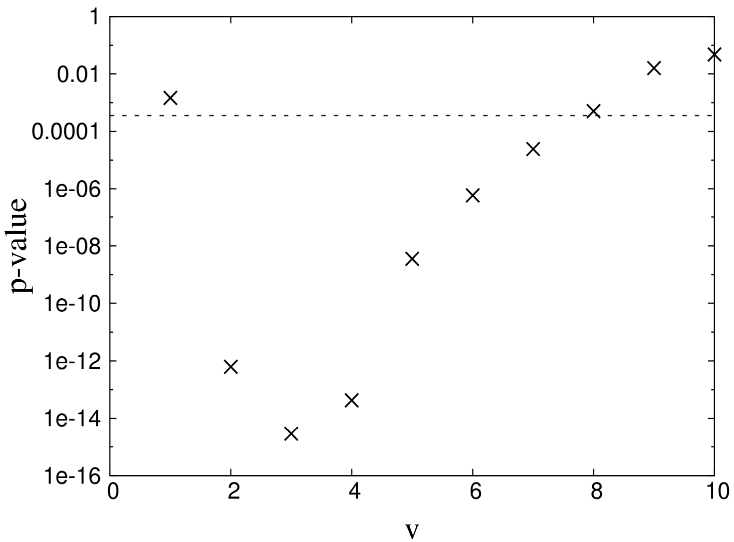
- Performed using coupled Gaussians
  - *C* variables in region **X** depend on non-linear coupling from v=2 variables in region **Y** for a proportion χ of their next state (while a 0.7 proportion is determined from their past and 0.3 – χ proportion from noise)



- TE MI
- The TE-based technique was more consistently able to detect the interregional relationship as weaker couplings.
- No false positives in reverse direction

Verification of the technique (continued)

- Demonstrated that the limitations of the technique when there is insufficient data:
  - Importantly, the technique is robust to this because it simply makes no inferences when there is not enough data



- Demonstrated some robustness to undersampling
- Demonstrated some weakness to false positive situations (pathway structure and common cause) though identified the conditions under which this occurred and suggested techniques to mitigate the effect (future work).

Application to an fMRI data set

- Cognitive task: visuomotor tracking
  - control a mouse with right hand to track a moving target on a computer screen
  - 4 levels of difficulty; changed after 16.8 second blocks.
  - 8 subjects
  - functional Magnetic Resonance Imaging (fMRI) measurements
  - resolution: 3mm, typically hundreds of voxels in each regions.
  - 1 image every 2.8 seconds.
  - 20 blocks of 7 images gives 140 images per difficulty level.
  - data pre-processed (standard motion correction and spatial normalization) and 11 localized regions of interest selected using a general linear model (GLM) and general interest for tracking (F-test) analysis.

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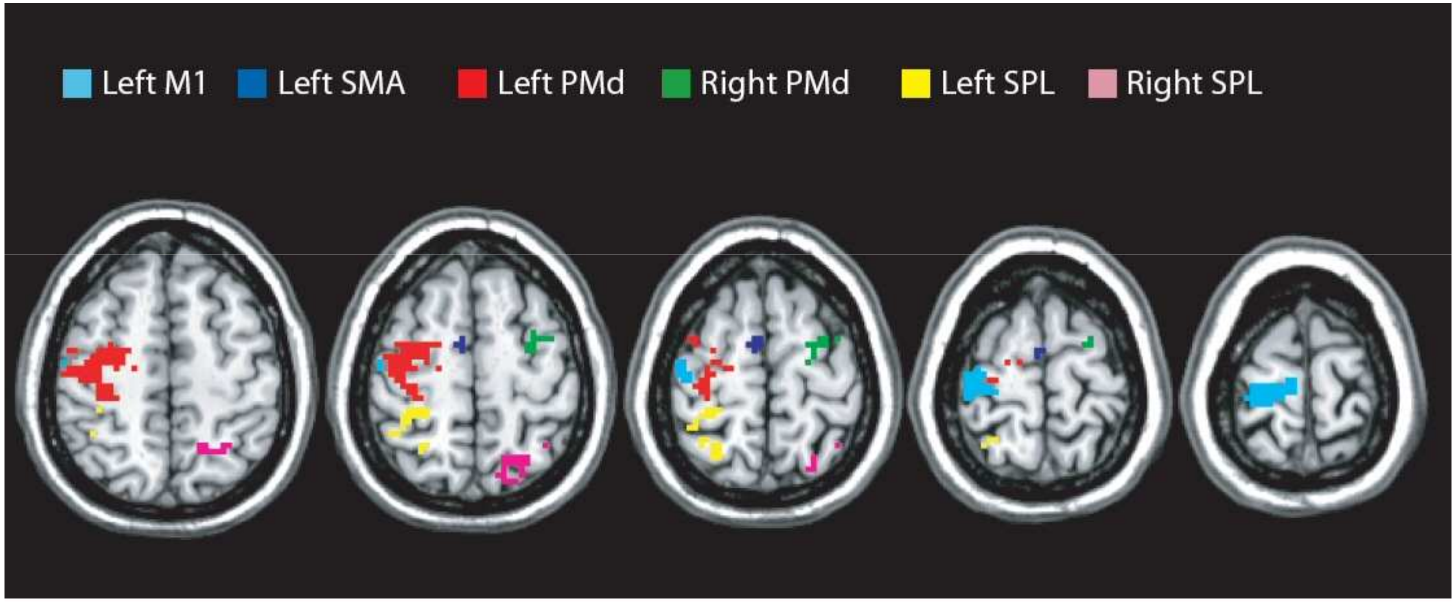
fMRI-BOLD imaging

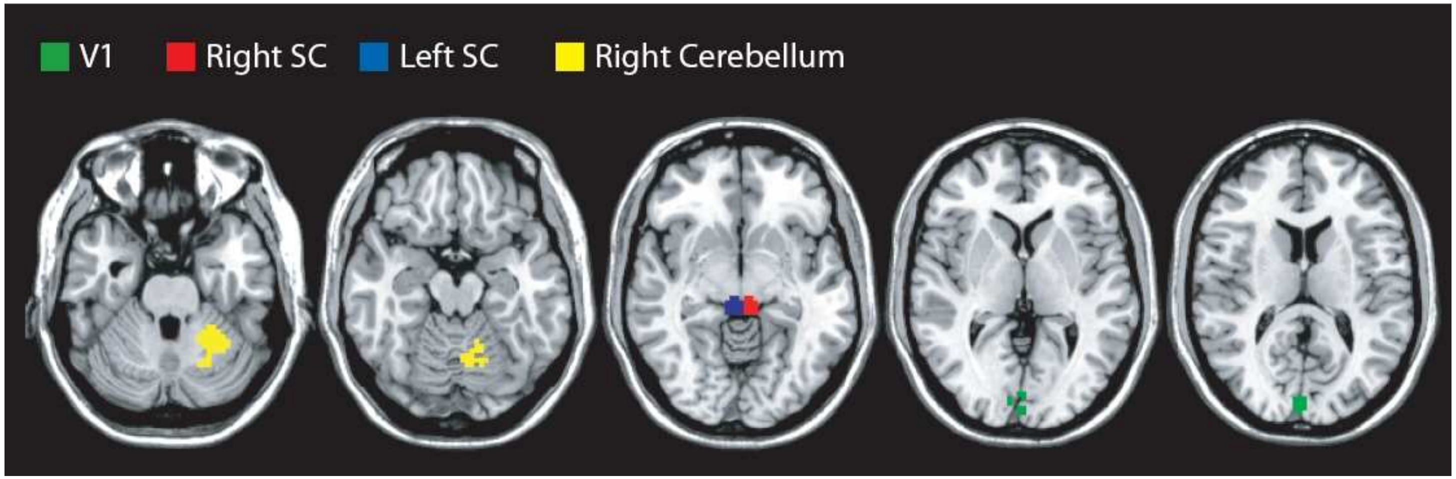


M1 – primary motor cortex

SMA – Supplementary motor area

PMd – pre-motor dorsal

SPL – superior parietal lobule



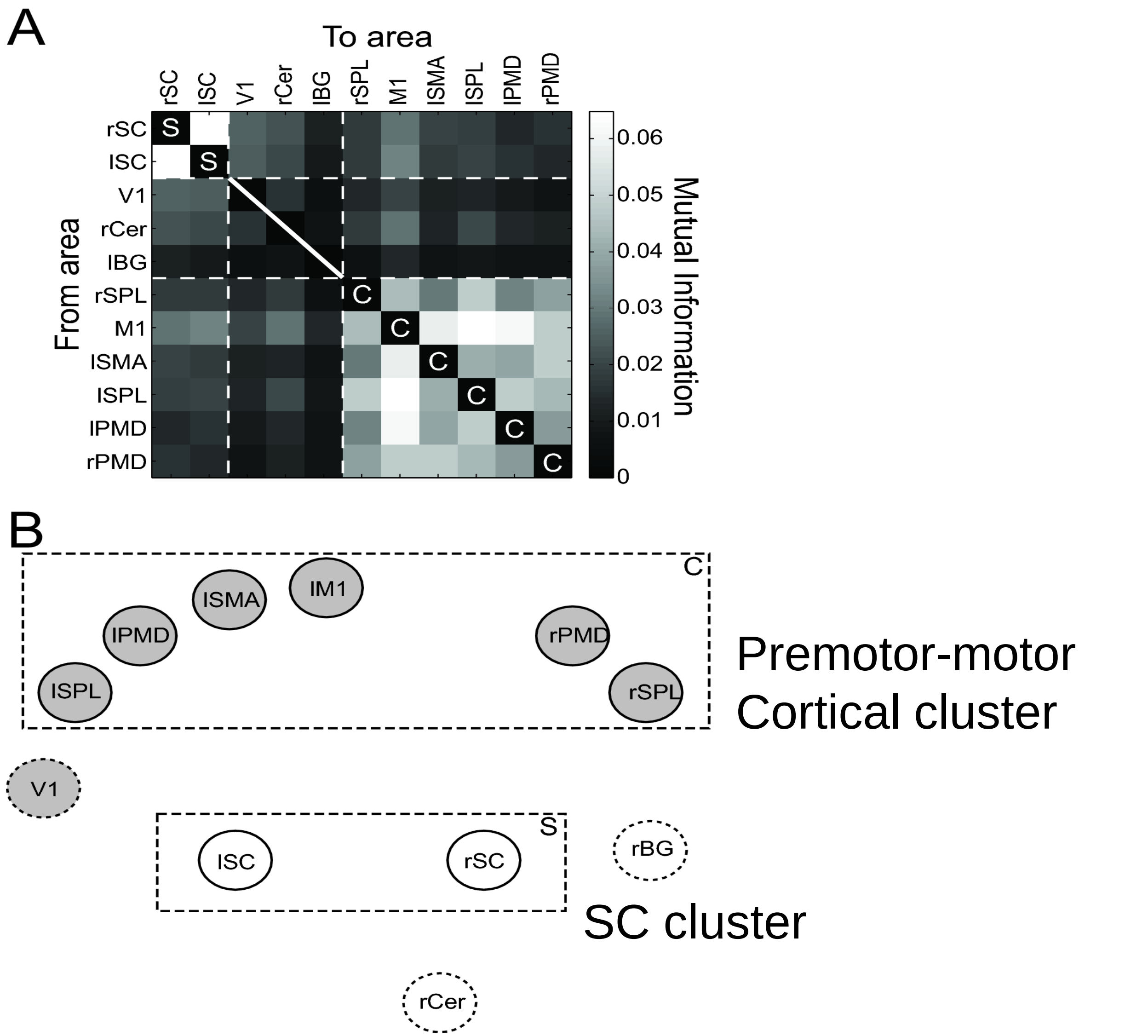
V1 – primary visual cortex

SC – superior colliculus

These regions encompass: Movement planning, visual perception and control, and execution

Undirected structure (inferred by MI technique)

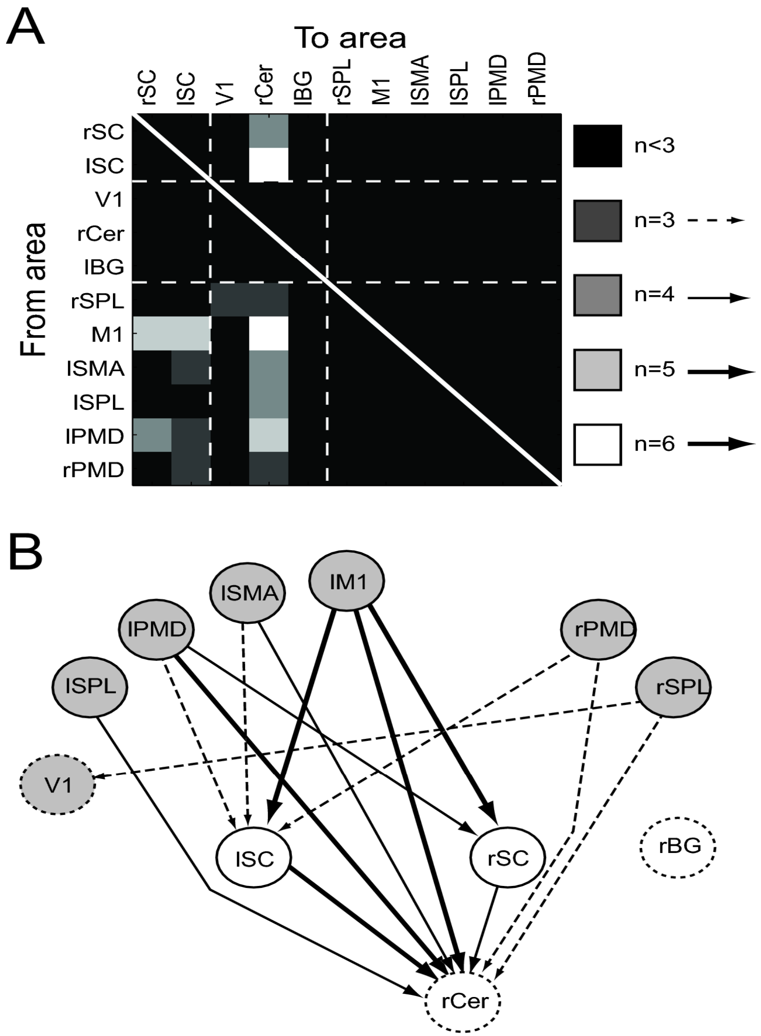
All region pairs had a significant undirected relationship at the group level during the task; but clusters could be identified by spectral reordering



Directed structure (inferred by TE technique)

Fewer region pairs had a significant directed relationship at the group level.

We find an interesting hierarchical structure between the clusters.

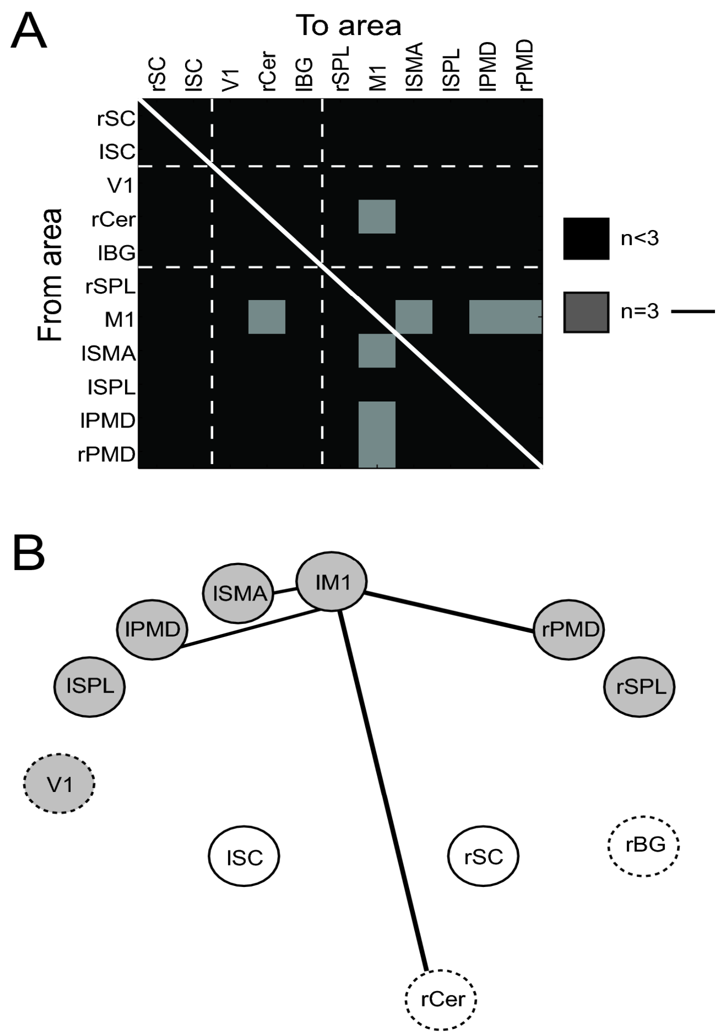


1. Structure correlates well to the experiment

2. Be aware of the influence of the measurement technique, e.g. low sampling rate may be responsible for no bottom-up links detected.

Modulation of the undirected structure

Increased coupling within the cortical cluster and from that cluster to motor execution



1. No significant modulation for directed structure: a change may be missed by the slow temporal resolution of the fMRI measurements.

Summary

- Useful method for investigating interregional information structure demonstrated:
  - Satisfies several key requirements: explicitly measures information transfer, is directional, captures non-linear and collective interactions, works on a regional level, is robust to small data sets, distinguishes weak relationships from none, and is model-free.
- Technique verified using numerical data sets
- Technique inferred an interesting 3-tier inter-regional structure in fMRI data from a visuo-motor tracking task
  - movement planning
  - sensor (visual) processing and control of eye movement
  - motor (movement) execution
- As task becomes more difficult, there is an increased coupling between regions involved in movement planning and execution

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Reference

J.T. Lizier, J. Heinzle, A. Horstmann, J.-D. Haynes, M. Prokopenko, "Multivariate information-theoretic measures reveal directed information structure and task relevant changes in fMRI connectivity", Journal of Computational Neuroscience, 2010, in press.

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