Network Models of Functional Brain Connectivity

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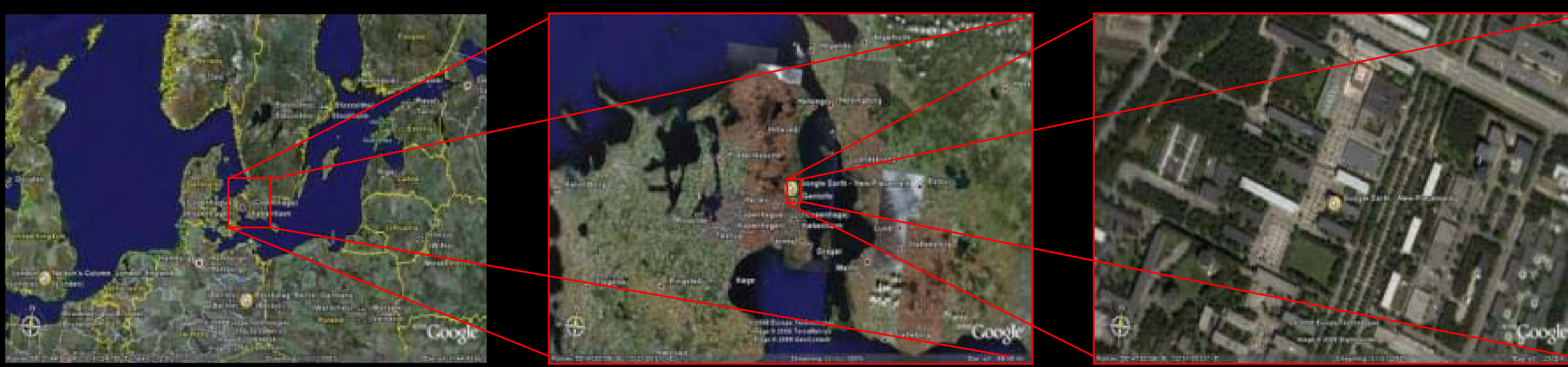


This is joint work with

Kristoffer Hougaard Madsen

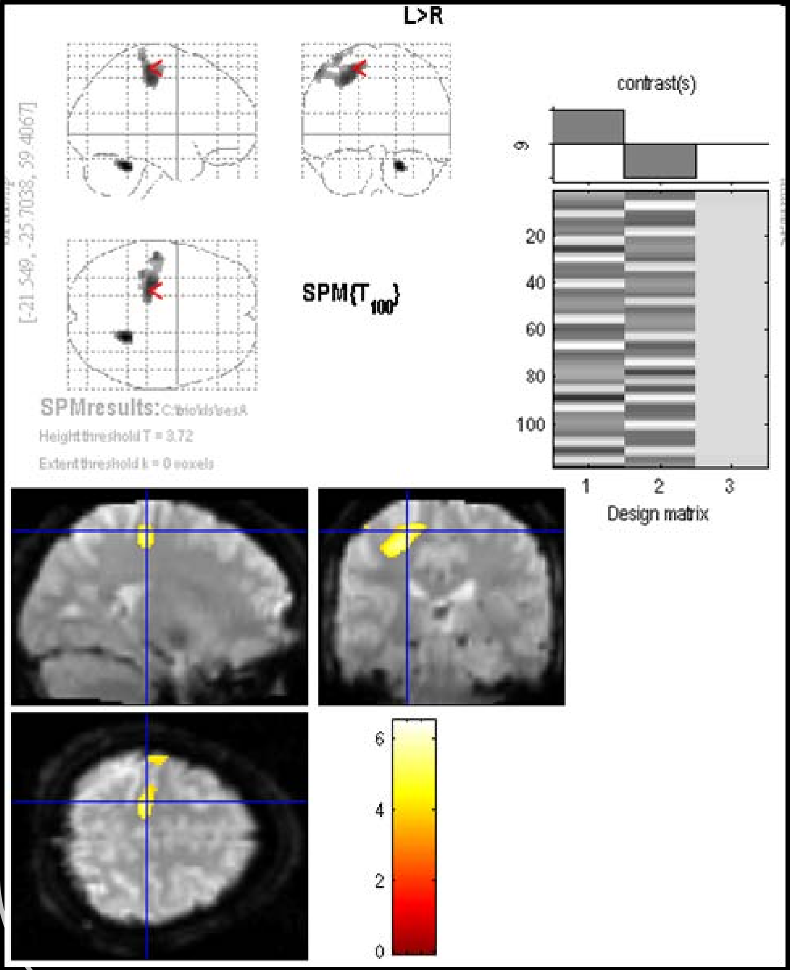
Anne-Marie Dogonowski

Lars Kai Hansen

Hartwig Siebner

(Mørup, Hougaard, Dogonowski, Siebner, Hansen NIPS 2010)

Univariate statistical analysis in NeuroImaging



Problems:

1) **Multiple comparisons, i.e. many voxels tested.**

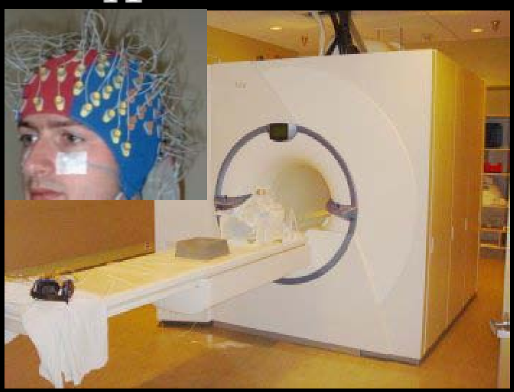
2) **What is the true number of independent tests, i.e. voxels are highly correlated**

3) **Data extremely noisy, i.e. low SNR rendering tests insignificant.**

Need for advanced multivariate methods that can efficiently extract the underlying sources in the data

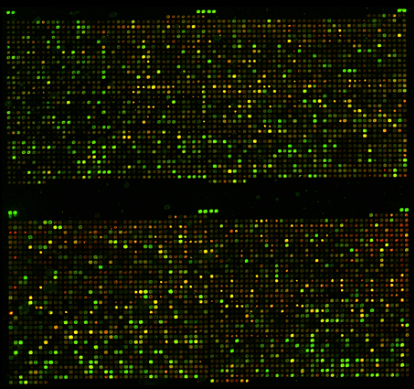
This problem is no different than the problems encountered in general in Modern Massive Datasets (MMDS)

$\mathbf{X}^{Space \times Time}$



NeuroInformatics

$\mathbf{X}^{Gene\ seq. \times Samples}$



BioInformatics

$\mathbf{X}^{Webpages \times Webpages}$

ComplexNetworks

$\mathbf{X}^{Term \times Document}$

WebDataMining

Unsupervised Learning attempts to find the hidden causes and underlying structure in the data.

(Multivariate exploratory analysis – driving hypotheses)

Goal of unsupervised Learning

(Ghahramani & Roweis, 1999)


- Perform dimensionality reduction
- Build topographic maps
- Find the hidden causes or sources of the data
- Model the data density
- Cluster data

Purpose of unsupervised learning

(Hinton and Sejnowski, 1999)


- Extract an efficient internal representation of the statistical structure implicit in the inputs

2008

WIRED MAGAZINE: 16.07

SCIENCE : DISCOVERIES

The End of Theory: The Data Deluge Makes the Scientific Method Obsolete

By Chris Anderson 06.23.08

Illustration: Marian Bantjes

THE PETABYTE AGE:
Sensors everywhere. Infinite storage. Clouds of processors. Our ability to capture, warehouse, and understand massive amounts of data is changing science, medicine, business, and technology. As our collection of facts and figures grows, so will the opportunity to find answers to fundamental questions. Because in the

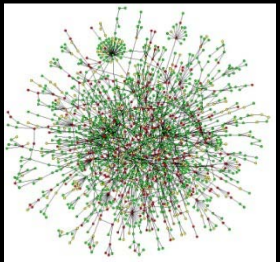
"All models are wrong, but some are useful."

So proclaimed statistician George Box 30 years ago, and he was right. But what choice did we have? Only models, from cosmological equations to theories of human behavior, seemed to be able to consistently, if imperfectly, explain the world around us. Until now. Today companies like Google, which have grown up in an era of massively abundant data, don't

Analysis of massive amounts of data will be the main driving force of all sciences in the future!!

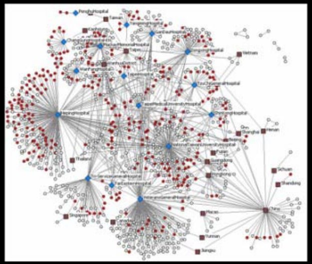
Within Unsupervised learning the analysis of complex network has lately emerged as an important field of research

- Biology:



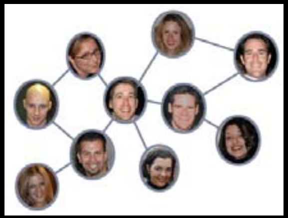
Protein Interaction

Food web



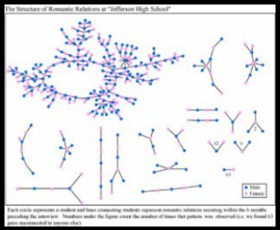
Epidemic Spread

- Social sciences:



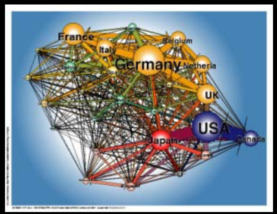
Friendship network

Collaboration network

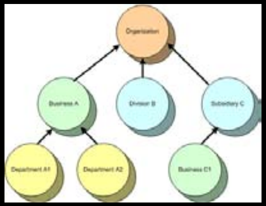


Sexual relations

- Economics:



Trade network



Business Organization

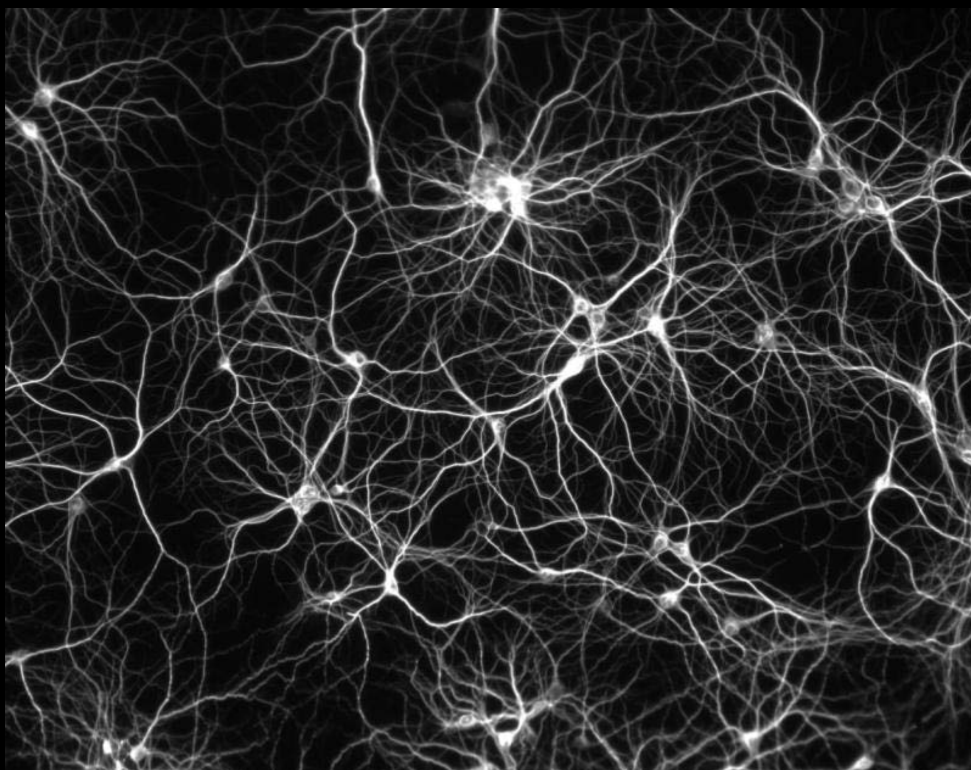
- Technology:

Tele communication network

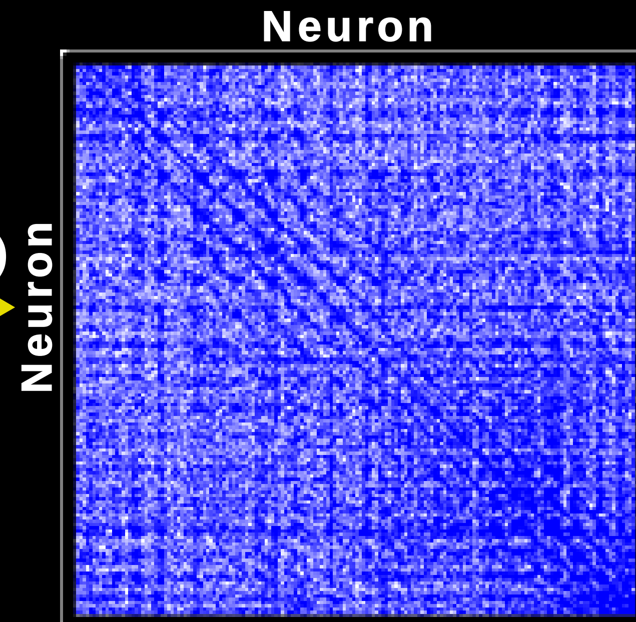
Airline connections

The internet

The perhaps most formidable and fascinating of all networks is the complex network of neurons constituting our mind, i.e. our connectome!



G(E,V)

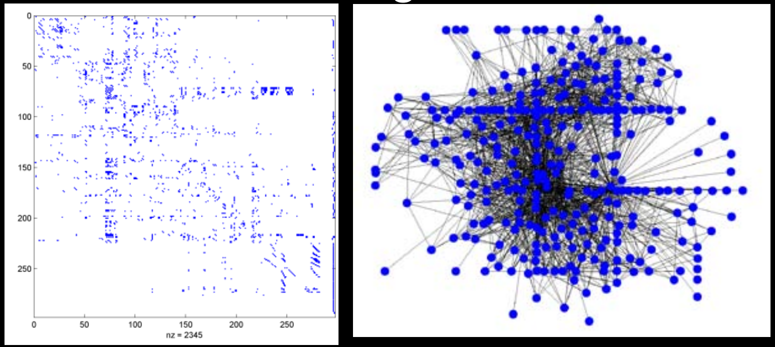


This can be represented as a complex network
~10^{11} neurons,
~ 10^{15} connections

(Sporns et al. 2005, Murre et. al. 1995, Braitenberg et al. 1991)

- Micro-scale (units; single neurons)

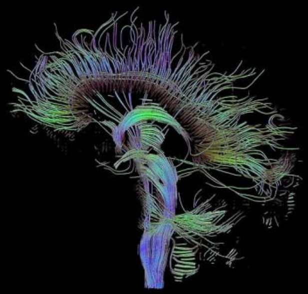
C. Elegans



- Macro scale (units; voxels in mm^3)

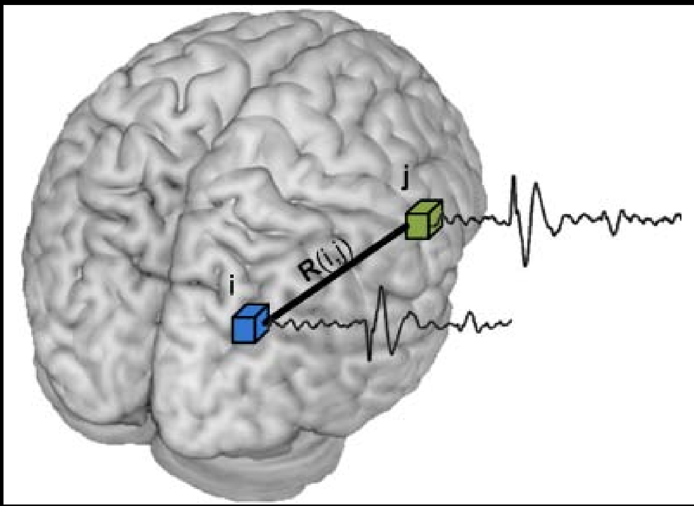
  Structural connectivity: Diffusion Tensor Imaging (DTI)

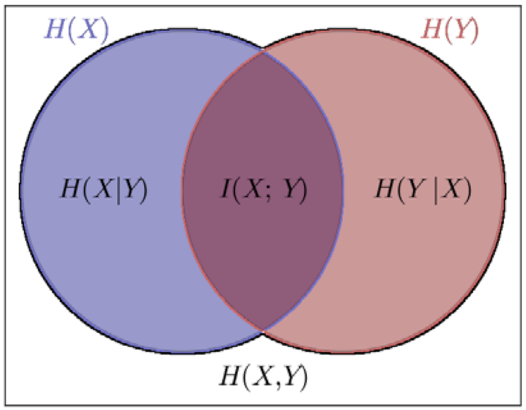
  Functional connectivity: functional Magnetic Resonance Imaging (fMRI)



Estimating the functional communication in the brain at a macro scale from fMRI.

Assumption: If a region in the brain is functionally connected to another region of the brain they consume energy at the same time.
Functional connectivity measured by the information theoretic quantity Mutual information





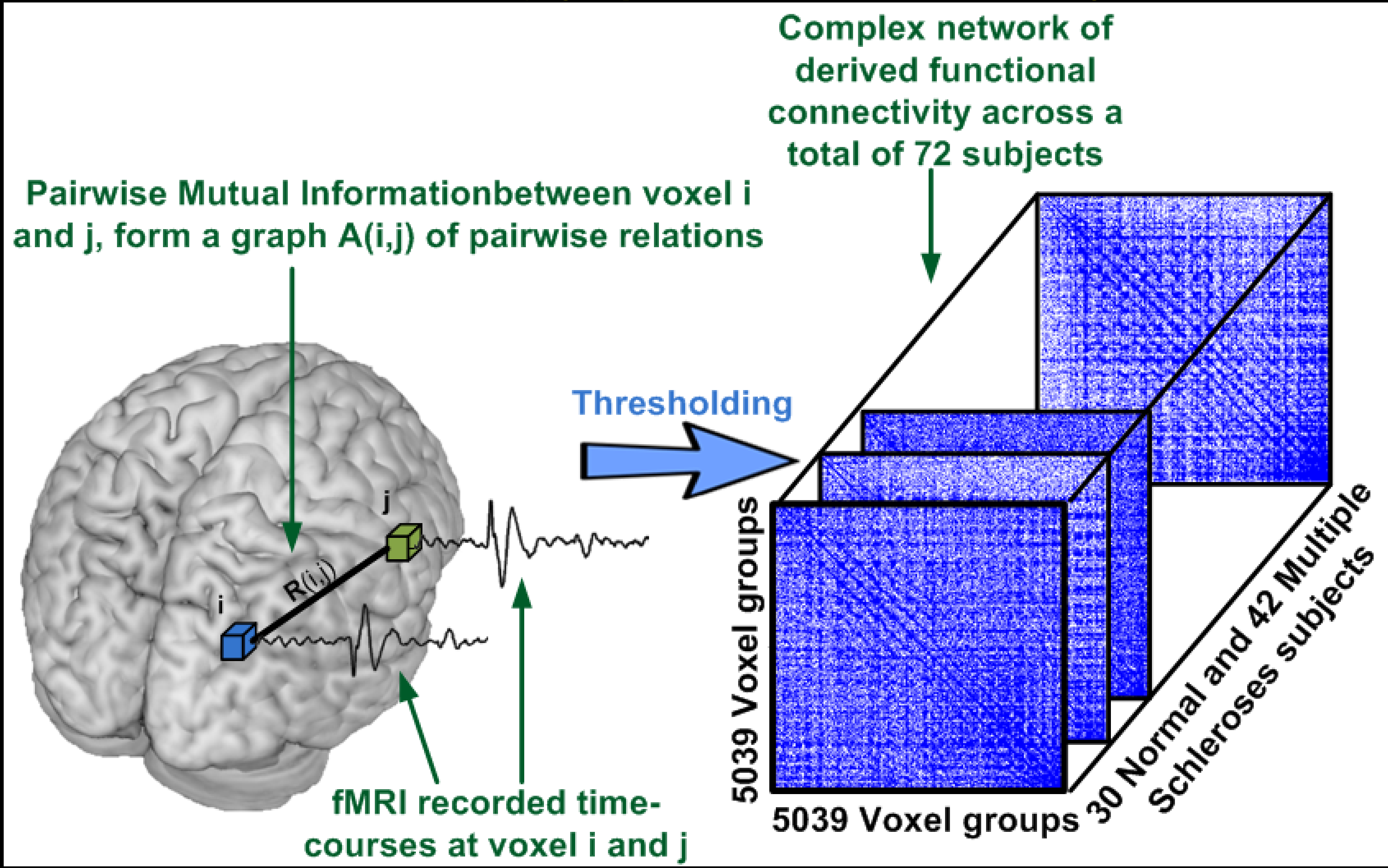
Claude E. Shannon (1916-2001)

Correlation: Linear dependency between time-series.

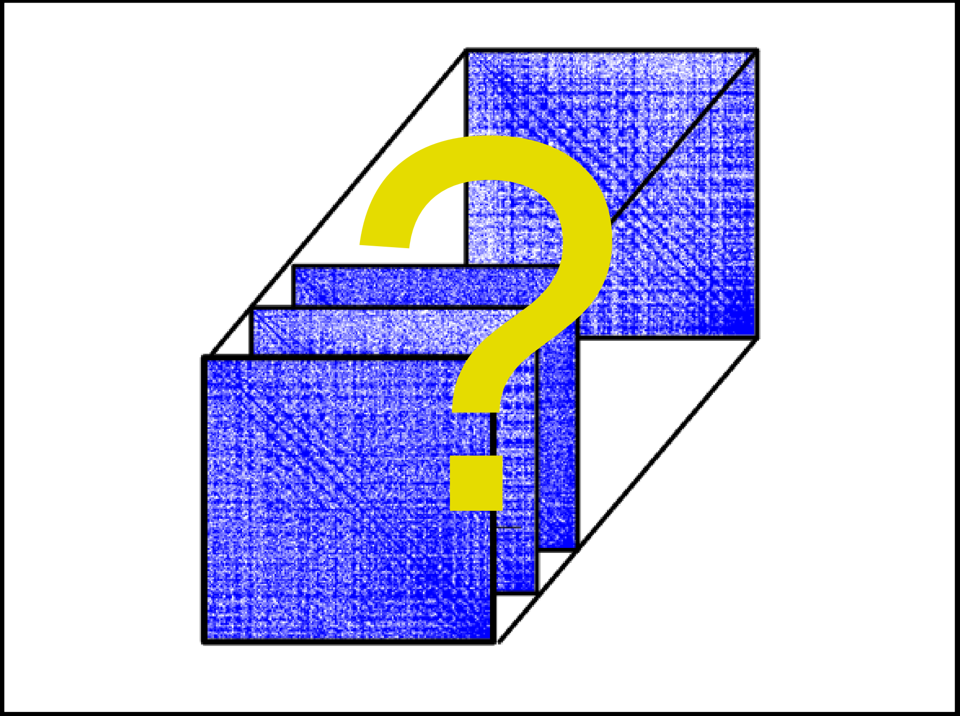
Mutual Information: Both linear and non-linear dependencies between time series.

$$
\begin{aligned}
H(X) &= -\sum_X p(X)\log(p(X)) \\
H(Y) &= -\sum_Y p(Y)\log(p(Y)) \\
H(X,Y) &= -\sum_{X,Y} p(X,Y)\log(p(X,Y)) \\
I(X,Y) &= H(X)+H(Y)-H(X,Y) = \sum_{X,Y} p(X,Y)\log\frac{p(X,Y)}{p(X)p(Y)}
\end{aligned}
$$

Functional connectivity graphs derived from resting state fMRI



How should we comprehend the complex dynamics of the derived functional networks?



Complex Network analysis– The Classic analysis approach:

Compare network properties to those of random graphs.

These analysis have all shown that brain dereived networks are far from random (Sporns et al. 2010,)

	t_c	$\langle L \rangle$	$\langle C \rangle$	γ	G
Normal	0.0164	2.77	0.1116	1.40	0.8587
MS	0.0163	2.70	0.0898	1.36	0.8810
Random	-	2.73	0.0079	0.88	1
P-value(Normal vs. MS)	0.9964	0.4509	0.9954	0.7448	0.7928
P-value(Normal and MS vs. Random)	-	0.6764	$p \leq 0.001$	$p \leq 0.001$	$p \leq 0.001$

tc: Median threshold values

L: Shortest path

C: Clustering coefficient

γ: degree distribution exponent

These measures give however little information as to the intrinsic properties and structure of the networks, nor do they differentiate MS from Normal.

Aim of analysis of brain networks: *To capture large brain systems that can be parcellated into anatomically distinct modules (areas, parcels or nodes), each having a distinct pattern of connectivity*

(Sporns et al. 2005, 2010, Wallace, 2004)

What we would like to identify

- *Functional units* (distinct modules), i.e. groups of voxels that *communicate in the same manner* with the rest of the network (distinct patterns of connectivity)

The Infinite Relational Model

(A statistical framework of modeling the structure of complex networks)

Learning Systems of Concepts with an Infinite Relational Model (AAAI2006)


Charles Kemp


Josh Tenenbaum


Thomas Griffith


Takeshi Yamada


Naonori Ueda

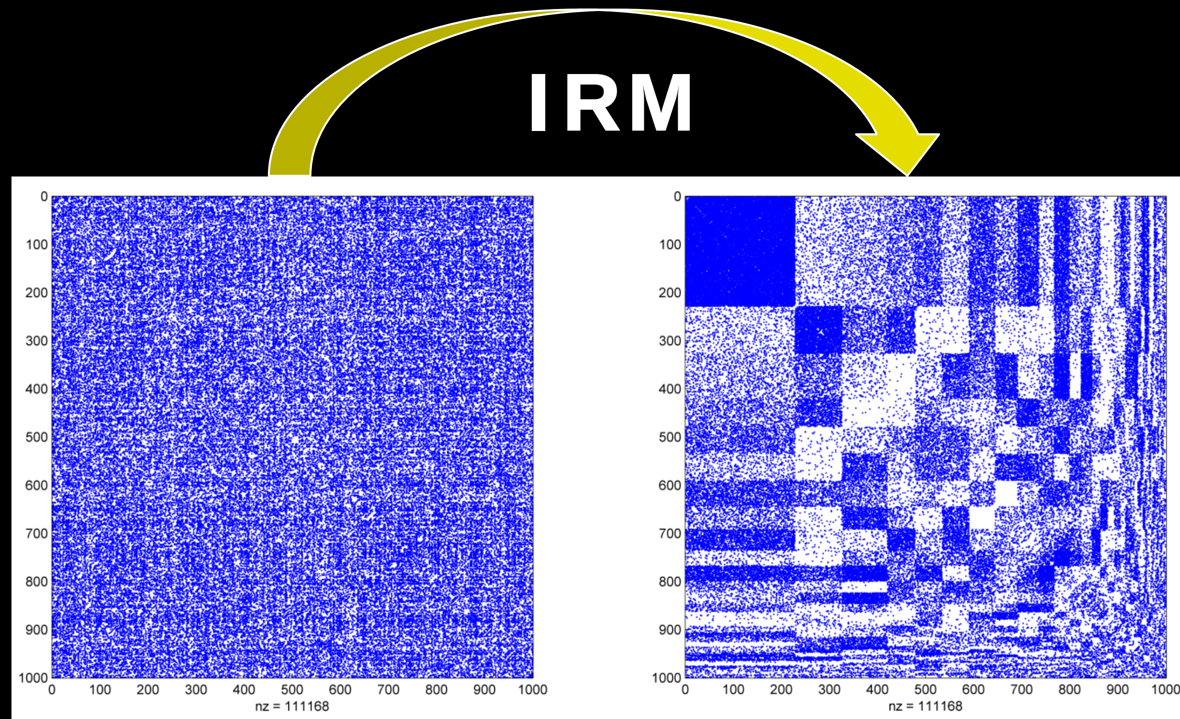
Infinite Hidden Relational Model (UAI 2006)


Zhao Xu

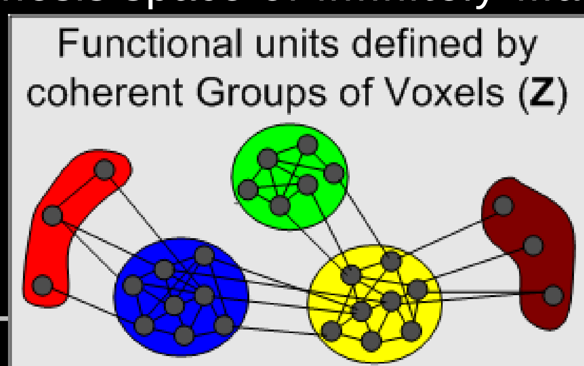

Kai Yu

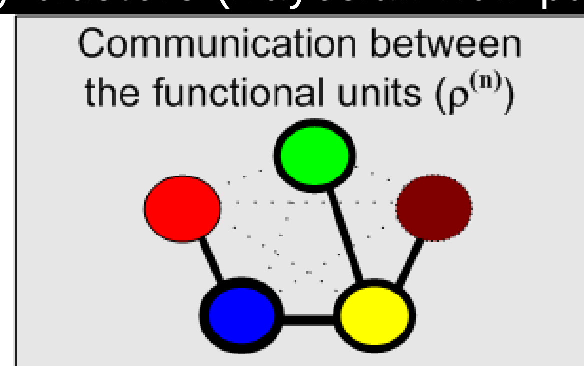

Volker Tresp


Hans-Peter Kriegel

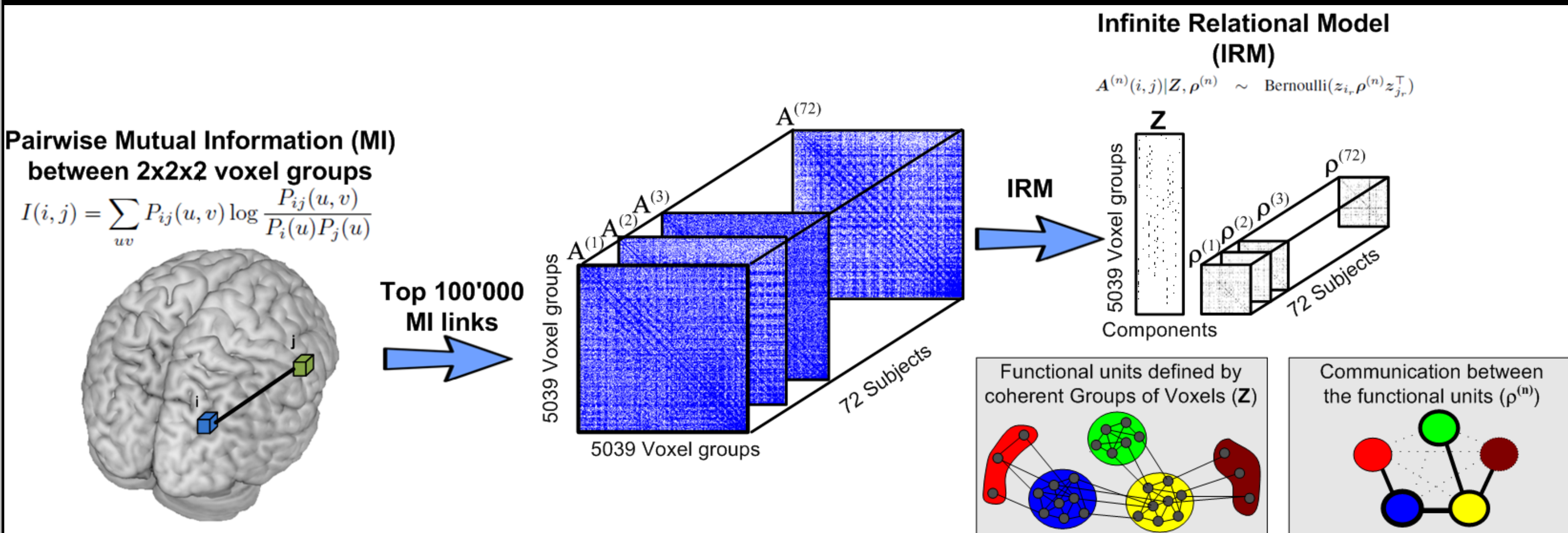


IRM identifies groups of voxels (i.e. functional units) that share the same communication pattern with the rest of the networks. Number of groups inferred from a hypothesis space of infinitely many clusters (Bayesian non-parametrics)





Outline of the analysis

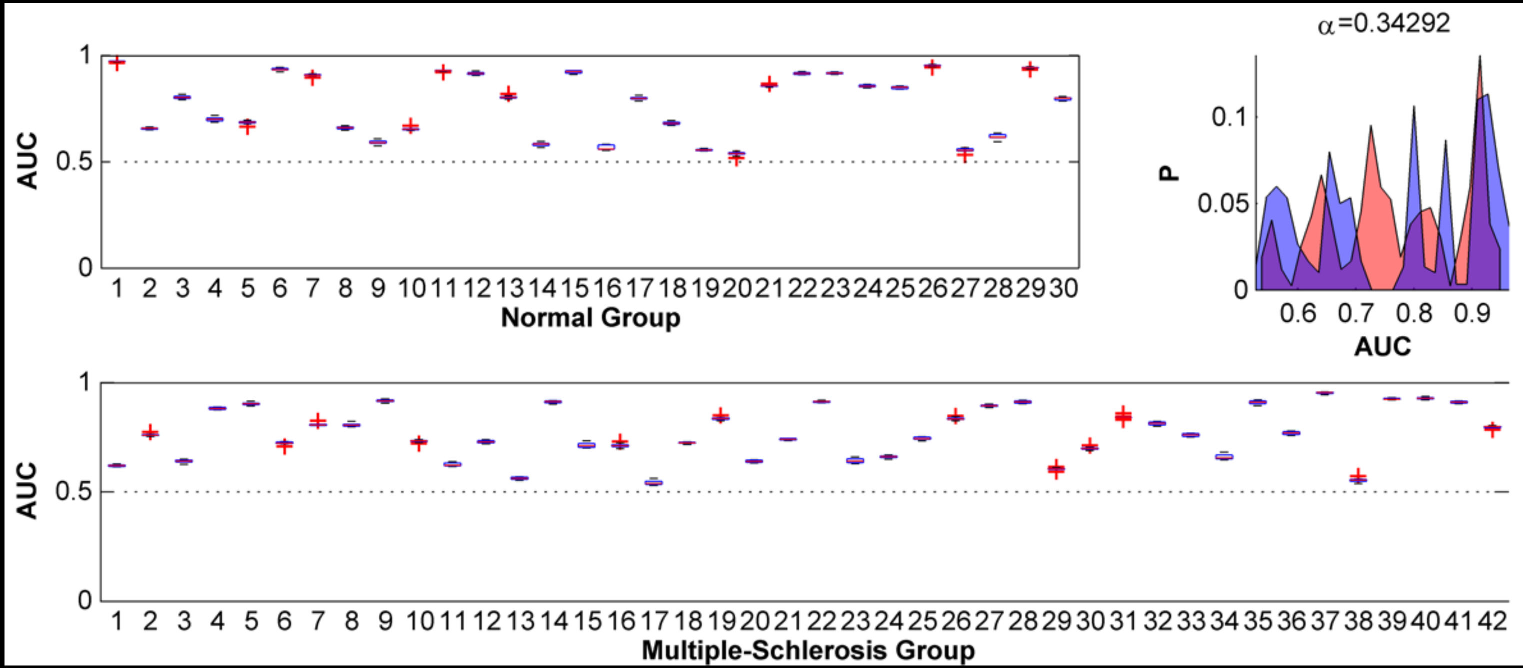


IRM automatically infer the functional units as well as their subject specific interactions (Unsupervised Learning)

How do the proposed framework differ from traditional Unsupervised learning approaches such as ICA/PCA and clustering?

- The graph derived by mutual information can also take non-linear interactions into account.
- Functional units are by the IRM defined by having similar interaction with the remaining network, and as such ***does not need to have a strong degree of self-similarity***. I.e. what defines a group is not necessarily strong communication within the group but that the group of voxels communicate similarly to the remaining network, i.e. IRM specifically extracts consistent patterns of interaction/communication between groups.

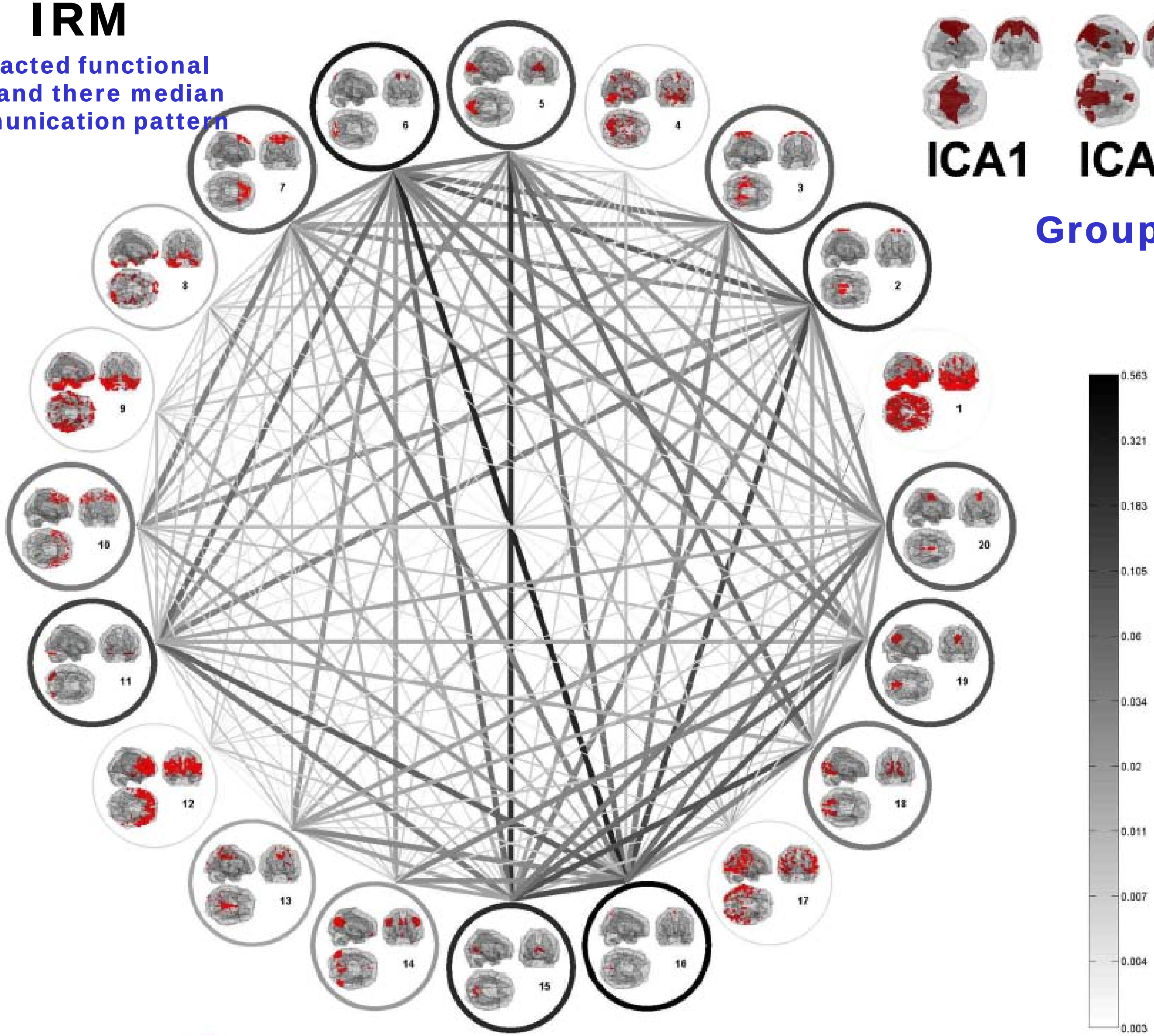
IRM model evaluation by link-prediction of hold out links and non-links in the graph

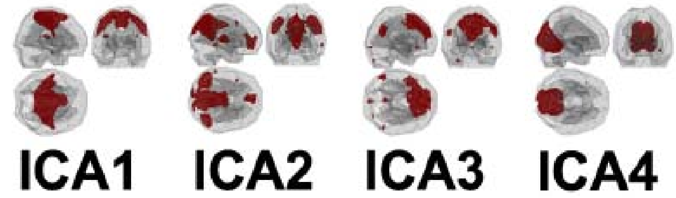


The IRM model predicts communication patterns significantly better than random while there is no significant difference in the models ability to predict structure in Normal and MS group.

IRM

Extracted functional units and there median communication pattern

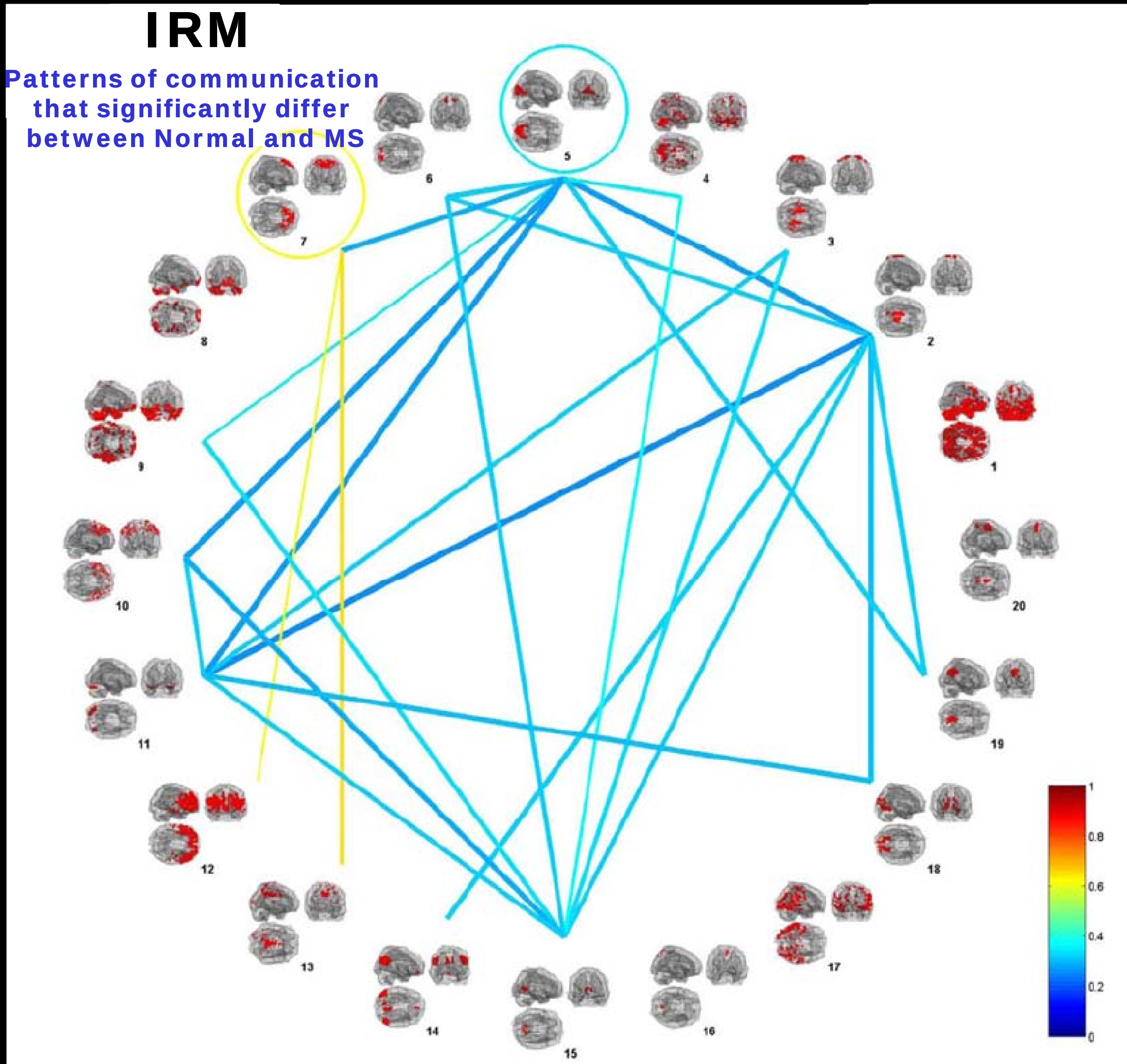




Group ICA analysis

IRM

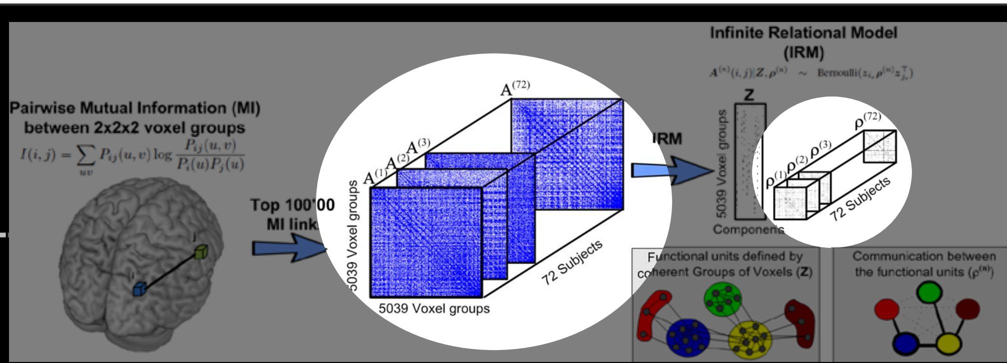
Patterns of communication that significantly differ between Normal and MS



Discriminating MS and Normal subjects based on extracted communication patterns

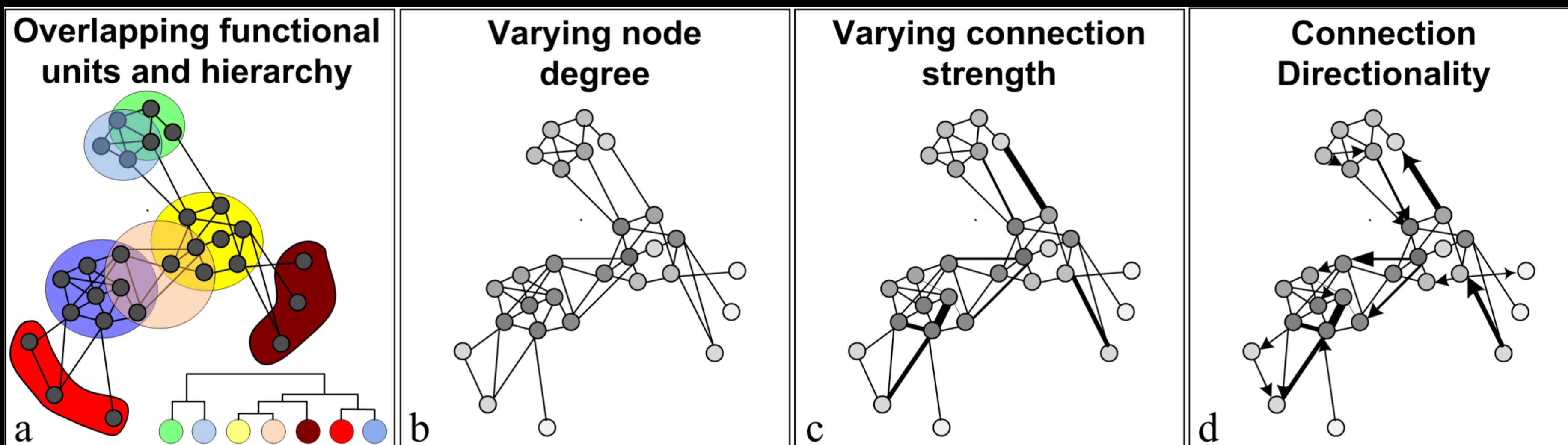
Table 1: Leave one out classification performance based on support vector machine (SVM) with a linear kernel, linear discriminant analysis (LDA) and K-nearest neighbor (KNN). Significance level estimated by comparing to classification performance for the corresponding classifiers with randomly permuted class labels, bold indicates significant classification at a $p \leq 0.05$.

	Raw data	PCA	ICA	Degree	IRM
SVM	51.39	55.56	**63.89** ($p \leq 0.04$)	59.72	**72.22**($p \leq 0.002$)
LDA	59.72	51.39	**63.89** ($p \leq 0.05$)	51.39	**75.00**($p \leq 0.001$)
KNN	38.89	58.33	56.94	51.39	**66.67**($p \leq 0.01$)



Future Research

- Functional Connectivity changes during tasks, neurological disorders, intervention (TMS)
- Structural Connectivity by Diffusion Tensor Imaging.
- Combining structural and functional connectivy in unified analysis



Imporved Statistical Modeling of Complex Networks

- Multiple functional roles, latent feature models
- Hierarchy, tree structured relational modeling
- Functional authority, degree corrected modeling
- Importance, weighted graphs
- Influence, directed graphs