Separating sources and analysing connectivity in EEG/MEG using probabilistic models

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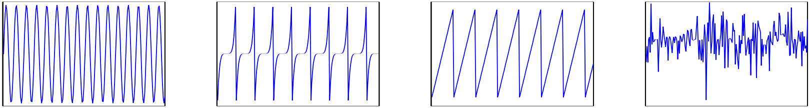
Abstract

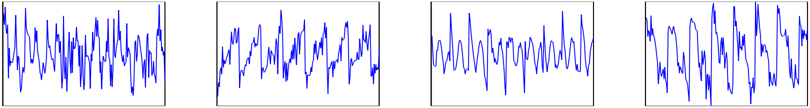
- Introduction to ICA
  - Problem of blind source separation
  - Importance of non-Gaussianity
  - Fundamental difference to PCA
- Motivation of resting-state analysis
- Improving ICA of spontaneous EEG/MEG
  - Applying ICA on time-frequency decompositions
  - Spatial version of independent component analysis (ICA)
- Testing components: Are they just random effects?
  - Intersubject consistency provides an plausible null hypothesis
- Causal analysis / effective connectivity
  - Structural equation models better estimated using non-Gaussianity

Problem of blind source separation

There is a number of “source signals”:



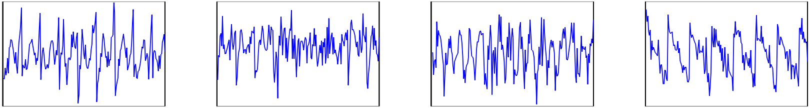
Due to some external circumstances, only linear mixtures of the source signals are observed.



Estimate (separate) original signals!

A solution is possible

PCA does not recover original signals



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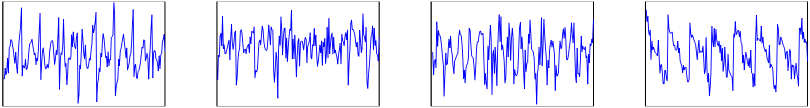
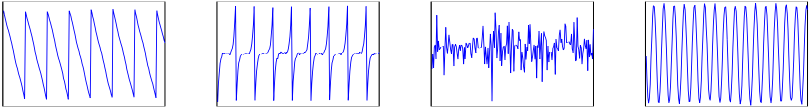


Use information on statistical independence to recover:



Independent Component Analysis

(Hérault and Jutten, 1984-1991)

- Observed random variables x_i are modelled as linear sums of hidden variables:

$$x_i = \sum_{j=1}^{m} a_{ij} s_j, \qquad i = 1...n \tag{1}$$

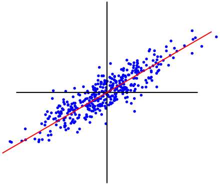
- Mathematical formulation of blind source separation problem
- Not unlike factor analysis
- Matrix of a_{ij} is parameter matrix, called "mixing matrix".
- The s_i are hidden random variables called "independent components", or "source signals"
- Problem: Estimate both a_{ij} and s_j, observing only x_i.

When can the ICA model be estimated?

- Must assume:
  - The s_i are mutually statistically independent
  - The s_i are nongaussian (non-normal)
  - (Optional:) Number of independent components is equal to number of observed variables
- Then: mixing matrix and components can be identified (Comon, 1994)
  A very surprising result!

Reminder: Principal component analysis

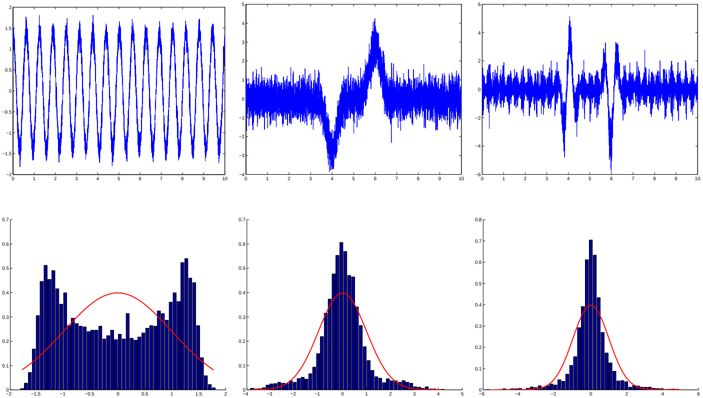
- Basic idea: find directions $\sum_i w_i x_i$ of maximum variance
- We must constrain the norm of $\mathbf{w}$: $\sum_i w_i^2 = 1$, otherwise solution is that w_i are infinite.
- For more than one component, find direction of max var orthogonal to components previously found.
- Classic factor analysis has essentially same idea as in PCA: explain maximal variance with limited number of components



Comparison of ICA, factor analysis and principal component analysis

- ICA is nongaussian FA with no noise or specific factors.
  So many components that all variance is explained by them.
- No factor rotation left unknown because of identifiability result
- In contrast to FA and PCA, components really give the original source signals or underlying hidden variables
- Catch: only works when components are nongaussian
  - Many "psychological" hidden variables (e.g. "intelligence") may be (practically) gaussian because sum of many independent variables (central limit theorem).
  - But signals measured by sensors are usually quite nongaussian

Some examples of nongaussianity



Why classic methods cannot find original components or sources

- In PCA and FA: find components y_i which are uncorrelated

$$\text{cov}(y_i, y_j) = E\{y_i y_j\} - E\{y_i\}E\{y_j\} = 0 \tag{2}$$

  and maximize explained variance (or variance of components)
- Such methods need only the covariances, $\text{cov}(x_i, x_j)$
- However, there are many different component sets that are uncorrelated, because
  - The number of covariances is $\approx n^2/2$ due to symmetry
  - So, we cannot solve the n^2 factor loadings, not enough information!
    ("More variables than equations")

Nongaussianity, with independence, gives more information

- For independent variables we have

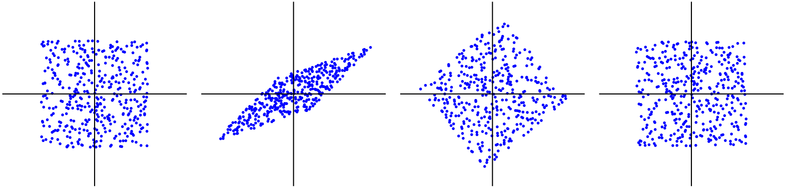
$$E\{h_1(y_1)h_2(y_2)\} - E\{h_1(y_1)\}E\{h_2(y_2)\} = 0. \qquad (3)$$

- For nongaussian variables, nonlinear covariances give more information than just covariances.
- This is not true for multivariate gaussian distribution
  - Distribution is completely determined by covariances
  - Uncorrelated gaussian variables are independent, and their
  - distribution (standardized) is same in all directions (see below)

$\Rightarrow$ ICA model cannot be estimated for gaussian data.

Illustration

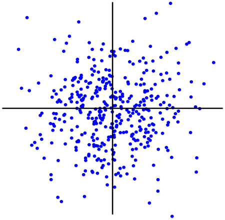
Two components with uniform distributions:
Original components, observed mixtures, PCA, ICA

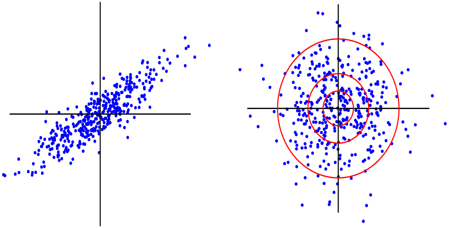


PCA does not find original coordinates, ICA does!

Illustration of problem with gaussian distributions

Original components, observed mixtures, PCA



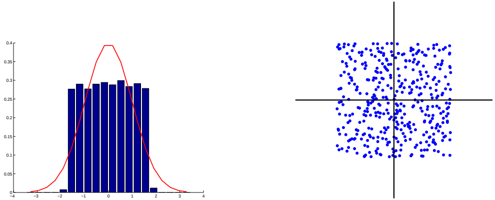


Distribution after PCA is the same as distribution before mixing!
"Factor rotation problem" in classic FA

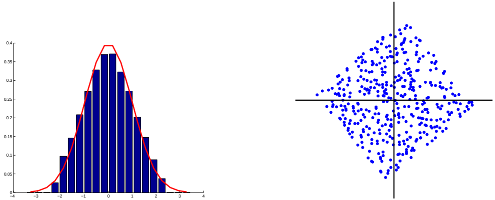
Basic intuitive principle of ICA estimation

- Inspired the Central Limit Theorem:
  - Average of many independent random variables will have a distribution that is close(r) to gaussian
  - In the limit of an infinite number of random variables, the distribution tends to gaussian
- Consider a linear combination $\sum_i w_i x_i = \sum_i q_i s_i$
- Because of theorem, $\sum_i q_i s_i$ should be more gaussian than s_i.
- *Maximizing the nongaussianity* of $\sum_i w_i x_i$, we can find s_i.
- Also known as projection pursuit.
- Cf. principal component analysis: maximize variance of $\sum_i w_i x_i$.

Illustration of changes in nongaussianity



Histogram and scatterplot, original uniform distributions

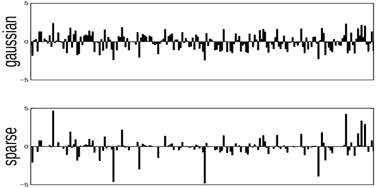


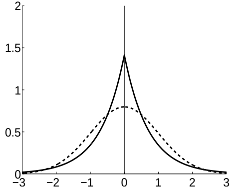
Development of ICA algorithms

- Nongaussianity measure: Essential ingredient
  - Kurtosis: global consistency, but nonrobust.
  - Differential entropy: statistically justified, but difficult to compute.
    - Essentially same as likelihood (Pham et al, 1992/97) or infomax (Bell and Sejnowski, 1995)
  - Rough approximations of entropy: compromise
- Optimization methods
  - Gradient methods (e.g. natural gradient; Amari et al, 1996)
  - Fast fixed-point algorithm, FastICA (Hyvärinen, 1999)

Sparsity is the dominant form of non-Gaussianity

- Sparsity = probability density has heavy tails and peak at zero:





- (Another form of non-Gaussianity is skewness or asymmetry)

Combining ICA with factor analysis or PCA

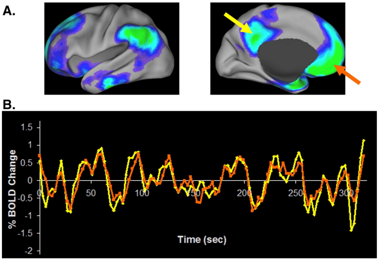
- In practice, it is useful to combine ICA with classic PCA or FA
  - First, find a small number of factors with PCA or FA
  - Then, perform ICA on those factors
- ICA is then a method of factor rotation
- Very different from varimax etc. which do not use statistical structure, and cannot find original components (in most cases)
- Reduces noise in signals, reduces computation

The brain at rest

- The subject's brain is being measured while
  - the subject has no task
  - the subject receives no stimulation
- Measurements by
  - functional magnetic resonance imaging (fMRI)
  - electroencephalography (EEG)
  - magnetoencephalography (MEG)
- Why is this data so interesting?
  - Not dependent on subjective choices in experimental design (e.g. stimulation protocol, task)
  - Not much analysis has been done so far
  - Completely new viewpoint: rich internal dynamics

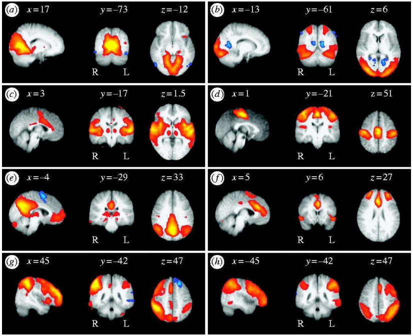
Is anything happening in the brain at rest?

- Some brain areas are actually more active at rest
- "Default-mode network(s)" in PET and fMRI (Raichle 2001)
- Brain activity is "intrinsic" instead of just responses to stimulation
- How to analyse resting state in more detail?



(Raichle, 2010 based on Shulman et al 1997)

ICA finds resting-state networks in fMRI



(Beckmann et al, 2005)

a) Medial and
b) lateral visual areas,
c) Auditory system,
d) Sensory-motor system,
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f) Executive control,
g) Dorsal visual stream

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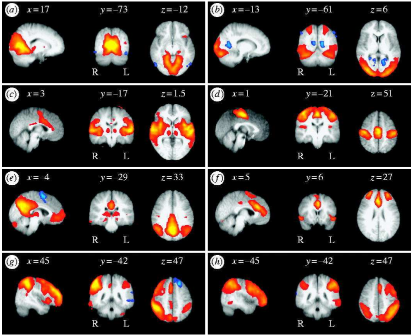

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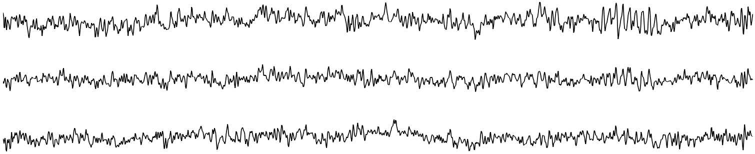
Very similar results obtained if subject watching a movie!

How about EEG and MEG?

- Very high temporal accuracy (millisecond scale)
- Not so high spatial accuracy (less than in fMRI)
- Spontaneous activity vs. evoked responses
- Typically characterized by oscillations, e.g. at around 10 Hz
- Up to 306 time series (signals), $10^4 \dots 10^5$ time points.



- Information very different from fMRI

Different sparsities of EEG/MEG data

- ICA finds components by maximizing sparsity, but sparsity *of what*?
  Depends on preprocessing and representation
- Assume we do wavelet or short-time Fourier transform
- We have different sparsities:

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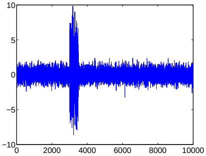
Sparsity in time:

Temporally modulated



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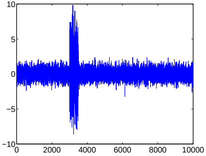
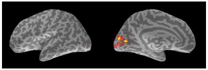


Sparsity in space:
Localised on cortex



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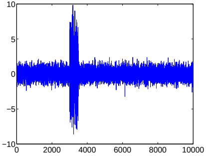

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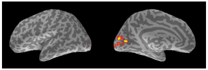
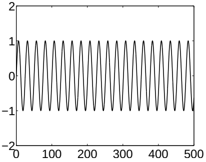


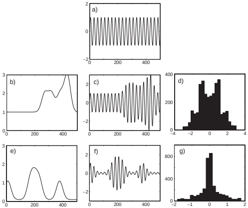
Sparsity in frequency:
narrow-band signals



Spectral sparsity: Fourier-ICA

- Problem: Rhythmic sources (oscillations) may not be sparse

Modulation of oscillations



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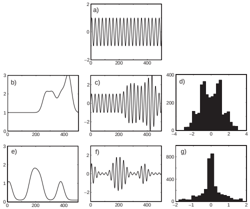
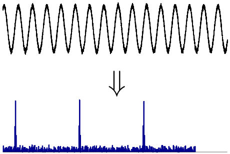
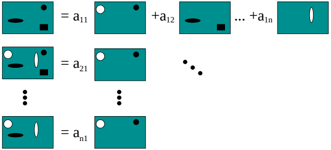


- Solution: Perform ICA on short-time Fourier transforms:
  - Divide each channel into time windows e.g. 1 sec long
  - Fourier transform each window
  - Joint sparsity in time and frequency (NeuroImage, 2010).

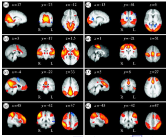


Spatial sparsity (spatial ICA)

- Images observed at different time points are linear sums of "source images"

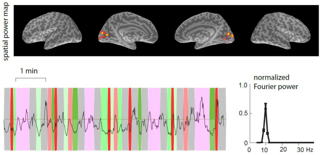


- Reverses the roles of observations and variables
- Maximizes spatial sparsity alone
- Almost always used in fMRI



Spatial ICA in MEG

- Spatial ICA possible for MEG by projecting data on the cortex
- We combine this with short-time Fourier transforms
- Maximizes sparsity spatially and spectrally
- No assumption on temporal independence



(Ramkumar et al, Human Brain Mapping, 2012.
Here, not resting data but with "naturalistic stimulation")

Testing ICs: motivation

- ICA algorithms give a fixed number of components and do not tell which ones are reliable (statistically significant)
- How do we know that an estimated component is not just a random effect?
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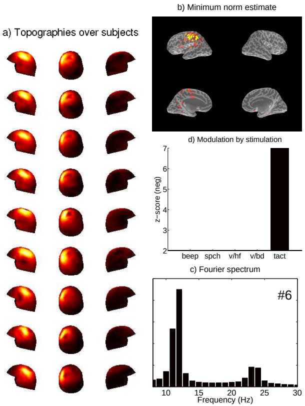
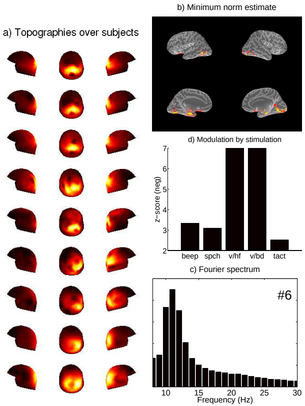
- ICA algorithms give a fixed number of components and do not tell which ones are reliable (statistically significant)
- How do we know that an estimated component is not just a random effect?
- Algorithmic artifacts also possible (local minima)
- We develop a statistical test based on inter-subject consistency:
  - Do ICA separately on several subjects
  - A component is significant if it appears in two or more subjects in a sufficiently similar form
  - We formulate a rigorous null hypothesis to quantify this idea (NeuroImage, 2011)

Testing ICs: results

One IC



Another IC



Causal analysis: Introduction

- Model connections between the measured variables
- Two fundamental approaches
  - If time-resolution of measurements fast enough, we can use autoregressive modelling (Granger causality)
  - Otherwise, we need structural equation models
- If measured variables are raw EEG/MEG, we should first localize sources
- After blind source separation, sources are uncorrelated
  $\Rightarrow$ More meaningful to model dependencies of envelopes (amplitudes, variances)

Structural equation models

- How does an externally imposed change in one variable affect the others?

$$x_i = \sum_{j \neq i} b_{ij} x_j + e_i$$

- Difficult to estimate, not simple regression
  - Classic methods fail in general

Structural equation models

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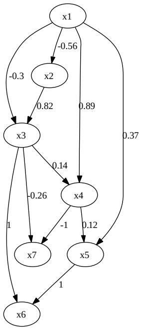
- Can be estimated if (Shimizu et al., JMLR, 2005)
  1. the $e_i(t)$ are mutually independent
  2. the $e_i(t)$ are non-Gaussian, e.g. sparse
  3. the b_{ij} are acyclic: There is an ordering of x_i where effects are all "forward"



Simple measures of causal direction

- The very simplest case: choose between regression models

$$y = \rho x + d \tag{4}$$

  where d is independent of x, and symmetrically

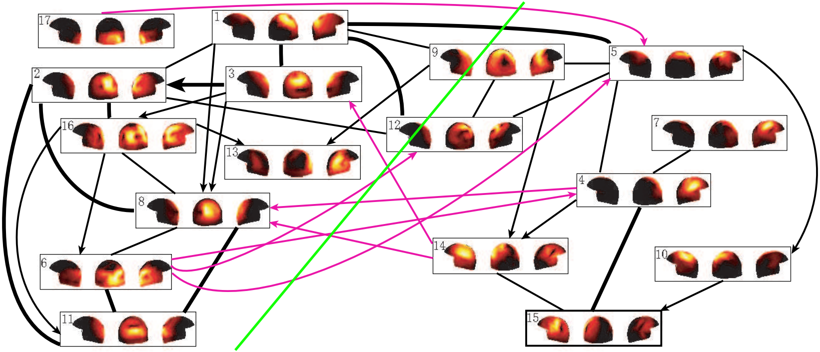
$$x = \rho y + e \tag{5}$$

- If data is Gaussian we can estimate $\rho = E\{xy\}$
  BUT : Both models have same likelihood!
- For non-Gaussian data, approximate log-likelihood ratio as

$$R = \rho E\{x\,g(y) - g(x)y\} \tag{6}$$

  where g is a nonlinearity similar to those used in ICA: $g(u) = u^3$ or $g(u) = -\tanh(u)$ (ACML2010).
- Choose direction based on sign of R!

Sample of results on MEG



Black: positive influence, red: negative influence.
Green: manually drawn grouping.
Here, using GARCH model (Zhang and Hyvärinen, UAI2010)

Discussion

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  - Analyzing their effective connectivity:
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  - Finding sources by different variants of ICA
    - Spatial ICA, time-frequency decompositions, etc.
  - Analyzing their effective connectivity:
    - Non-Gaussian versions of SEM
- At some point, intersubject consistency should be analyzed
  - Makes significance tests possible