An Introduction to Independent Component Analysis (ICA)

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“Essentially, all models are wrong, but some are useful.”

-George E.P. Box, statistician

In *Empirical Model-Building and Response Surfaces*, 1987
outline

• introduction to ICA

• a group ICA framework

• applications and examples

• practical challenges
Independent Component Analysis

• A blind source separation (BSS) method
• Goal: separate sources from a linear mixture
• Model: $X = AS$

  $X$: Mixture (observed data)
  $A$: Mixing coefficients (estimated)
  $S$: Sources (estimated)

• Estimate: $\hat{S} = WX$, $W = A^{-1}$, based on maximizing statistical independence of $\hat{S}$

• Assumptions
  – Linear mixing
  – Independence of sources
  – Non-Gaussian sources
• With the general linear model (GLM) we can only study the activation that we’ve modeled.
  – ICA requires no explicit temporal model; temporal activations are data-driven.

• Seed-based connectivity uses only pair-wise (bivariate) relationships. It also requires choice of a seed region.
  – ICA is hugely multivariate. It considers the relationships between all voxels simultaneously. Component shapes and “centers” are data-driven.
Comparisons to other models

- With the general linear model (GLM) we can only study the activation that we’ve modeled.
  - ICA requires no explicit temporal model; temporal activations are data-driven.

Comparisons to other models

• Seed-based connectivity uses only pair-wise (bivariate) relationships. It also requires choice of a seed region.
  – ICA is hugely multivariate. It considers the relationships between all voxels simultaneously. Component shapes and “centers” are data-driven.
(not so scary) example

Observations ($X$) = Mixing matrix ($A$) × Sources ($S$)

$X = AS$

- **background**
- **candle out**
- **candle 1**
- **candle 2**
- **candle 3**

**Sources ($S$)**

- candle 1
- candle 2
- candle 3

**Mixing matrix ($A$)**

- time
- candle out

**Observations ($X$)**

- pumpkins

**ICA APPLICATIONS EXTENSIONS CHALLENGES SUMMARY**
FastICA demo: mixtures

Input signals and density
FastICA demo: whitened

Whitened signals and density
FastICA demo (step 1)

Separated signals after 1 step of FastICA
FastICA demo (step 2)

Separated signals after 2 steps of FastICA
Separated signals after 3 steps of FastICA
Separated signals after 4 steps of FastICA
Separated signals after 5 steps of FastICA
ICA applied to fMRI

- We typically perform spatial ICA:
  - the sources are maps that are maximally spatially independent (i.e., non-overlapping)
  - the mixing matrix represents activation time courses of the sources.

\[ X = AS \]

\[ A_1 \quad \hat{S}_1 \]

\[ A_2 \quad \hat{S}_2 \]
group ICA
multi-subject ICA frameworks

combine single subject ICAs

ICA

Subject 1

: 

Subject N

assumptions: variable

ICA

matching/clustering

group ICA with temporal concatenation

ICA

Subject 1

: 

Subject N

assumptions: spatial consistency

tensor ICA

subject

voxels

Subject 1

assumptions: spatial consistency

temporal consistency

ICA

Subject 1

: 

Subject N

assumptions: temporal consistency
ICA (Forward Estimation)

Data

PCA reductions

Subject 1

\[ A_1 \]

\[ A \]

\[ A_N \]

Subject N

\[ S \]

\[ \mathbf{A} \times \mathbf{S} \]

Back-reconstruction through inversion

\[ \mathbf{A_i}^{-1} \times \mathbf{S_i} = \mathbf{A} \times \mathbf{S} \]

Back-reconstruction through spatial-temporal (dual) regression

1) Regress \[ \mathbf{S} \] onto each timepoint of Subject i to generate \[ \mathbf{A_i} \]

2) Regress \[ \mathbf{A_i} \] onto each image of Subject i to generate \[ \mathbf{S_i} \]
benefits of group ICA

Compare single subject ICA with group ICA (5 subjects) and subsequent back-reconstruction
inter-subject variability

simulations

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\sigma_{x,y} = 0$</td>
<td>$\sigma_{x,y} = 2$</td>
<td>$\sigma_{x,y} = 4$</td>
<td>$\sigma_{x,y} = 6$</td>
<td>$\sigma_{x,y} = 8$</td>
</tr>
</tbody>
</table>

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### Table 2

Inter-subject spatial variability reported for functional areas. In all studies subject datasets were spatially normalized prior to group analysis. VOTC = ventral occipito-temporal cortex; LOTC = lateral occipito-temporal cortex; IFJ = inferior frontal junction; BA = Brodmann area; SMA = supplementary motor area; ACC = anterior cingulate cortex; STG = superior temporal gyrus; IFG = inferior temporal gyrus.

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>$n$</th>
<th>Region</th>
<th>Group peak (MNI)</th>
<th>Average distance ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilms et al. (2005)</td>
<td>fMRI</td>
<td>14</td>
<td>Right V5/MT+</td>
<td>51, -72, 10</td>
<td>9.5 ± 7.6 mm</td>
</tr>
<tr>
<td>Wilms et al. (2005)</td>
<td>fMRI</td>
<td>14</td>
<td>Left V5/MT+</td>
<td>-45, -76, 14</td>
<td>8.7 ± 3.9 mm</td>
</tr>
<tr>
<td>Duncan et al. (2009)</td>
<td>fMRI</td>
<td>45</td>
<td>Left VOTC</td>
<td>-42, -50, -20</td>
<td>15.0 ± 5.0 mm</td>
</tr>
<tr>
<td>Duncan et al. (2009)</td>
<td>fMRI</td>
<td>45</td>
<td>Left LOTC</td>
<td>-40, -58, -20</td>
<td>9.0 ± 3.0 mm</td>
</tr>
<tr>
<td>Derrfuss et al. (2009)</td>
<td>fMRI</td>
<td>14</td>
<td>Left IFJ</td>
<td>-39, 2, 32</td>
<td>8.2 ± 3.8 mm</td>
</tr>
<tr>
<td>Xiong et al. (2000)</td>
<td>PET</td>
<td>20</td>
<td>SMA, BA 6</td>
<td>0, 15, 51</td>
<td>9.4 ± 3.4 mm</td>
</tr>
<tr>
<td>Xiong et al. (2000)</td>
<td>PET</td>
<td>20</td>
<td>ACC, BA 32/24</td>
<td>3, 26, 28</td>
<td>9.7 ± 4.4 mm</td>
</tr>
<tr>
<td>Xiong et al. (2000)</td>
<td>PET</td>
<td>20</td>
<td>Left M1, BA 4/6</td>
<td>-44, -7, 18</td>
<td>13.4 ± 5.6 mm</td>
</tr>
<tr>
<td>Xiong et al. (2000)</td>
<td>PET</td>
<td>20</td>
<td>Left STG, BA 22</td>
<td>-54, -35, 10</td>
<td>11.9 ± 5.1 mm</td>
</tr>
<tr>
<td>Xiong et al. (2000)</td>
<td>PET</td>
<td>20</td>
<td>Left IFG, BA 44</td>
<td>-46, 21, 7</td>
<td>11.7 ± 4.7 mm</td>
</tr>
<tr>
<td>Xiong et al. (2000)</td>
<td>PET</td>
<td>20</td>
<td>Left IFG, BA 47</td>
<td>-38, 32, -19</td>
<td>13.1 ± 5.4 mm</td>
</tr>
</tbody>
</table>

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• Group ICA facilitates the estimation of components in single subjects

• Estimation is robust to considerable variability

• Temporal and spatial patterns can be captured at the level of the individual
“How can I trust your information when you’re using such outdated technology?”
Variability in a healthy sample (n=603)

5 minutes of resting-state data from ~600 healthy subjects combined across studies

Datasets decomposed in a single group ICA

28 components (RSNs) selected for analysis

Examined how baseline factors such as age and gender affect functional connectivity

Functional connectivity features

Component spatial maps

Functional network connectivity (FNC)

Time course spectra
univariate models

(1) $H_0: \beta_1 = 0$

\vdots

(\nu) $H_0: \beta_\nu = 0$

Is voxel $i$ affected by age?

multivariate models

$H_0: \beta_1 = \beta_2 = \ldots \beta_\nu = 0$

Are any of these voxels affected by age?
univariate followup examples
applications in disease: spatial maps

subjects with Alzheimer’s disease

healthy elderly subjects

ICA is not the end point: it’s just the beginning!

- ICA provides you with a linear “functional parcellation” of the brain.

- Use time courses for
  - task-based models (GLM)
  - functional connectivity
  - graph construction
  - PPI
  - DCM
  - ...

- Use components for
  - ROI definitions/data-driven seeds
  - artifact removal
challenges
some practical challenges

• How many components should be estimated?

• Which components should be used in feature analysis?

• Should I remove artifacts from the data before performing ICA?
Methods to select model order

**Theoretical**

Information theoretic criteria reward goodness of fit, and penalize the number of estimated parameters.

**Empirical**

Empirical methods consider the stability of components over randomized initial conditions of the ICA algorithm and/or bootstrap resamples of subjects.

Real imaging data may not match theoretic assumptions...

Under- or over-split components may still be stable...
How much does it matter?

How much does it matter?

seasonal affective disorder (SAD) > healthy controls

How much does it matter?

choosing a model order...

- let theoretical estimates guide you
- let empirical estimates inform you
- consider the needs and goals of your study
- consider the quality of your data
- don’t worry too much
component selection
Methods to select components

- Spatial characteristics
  - Overlap with gray matter
  - Similarity with previously defined intrinsic networks

- MRN: mialab.mrn.org/data
- Oxford/San Antonio: fsl.fmrib.ox.ac.uk/analysis/brainmap+rsns
- Stanford: findlab.stanford.edu/functional_ROIs.html

Anterior Insula / Dorsal ACC (Anterior Salience Network)
Methods to select components

How similar will components be in rest and different tasks?
Methods to select components

- Spectral characteristics
  - Intrinsic networks should have very slow oscillations

Methods to select components

- Temporal characteristics
  - Time course correlation with nuisance variables (motion, CSF, respiration)
- TE-dependence of components
  - Requires multi-echo pulse sequence

Artifact removal prior to ICA?

- In general we recommend to leave the data “as is”,
- ICA separates artifact sources well, especially at high model order.
- Filtering or regression of artifacts is always imperfect; residual variance will remain and ICA will have greater difficulty separating the remaining noise.
- One exception might be large movements (which violates spatial stationarity), though this is debated. Note that you will still find motion artifact components even if you have “removed” this variance with regression.
- Other exceptions might be sources of noise that are spatially heterogeneous across subjects.
ICA is not model free (assumes independence & consistency), but may be more flexible and have fewer assumptions than other approaches.

Can provide an alternative to voxel-wise analyses, with interpretable results.

Though a group framework, identifies the features or projection space that can be used to characterize a new subject.
software

• mialab.mrn.org/software

• Group ICA of fMRI Toolbox (GIFT)
  – Single subject/Group ICA
  – Model order estimation
  – ICASSO (clustering/stability)
  – MANCOVA testing framework
  – Dynamic FNC

• Simulation Toolbox (SimTB)
  – Flexible generation of fMRI-like data