Computational and visual analysis of brain data

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http://www.cs.rug.nl/svcg/
Imaging Modalities

Spatial resolution in mm

- brain lobe
- column
- neuron
- synapse

Temporary resolution in sec

- millisecond
- second
- minutes
- ∞

- EEG/MEG
- SPECT
- PET
- fMRI
- MRI
- LM
- EM

- structural
- functional
Prediction of Neurodegenerative Diseases

GLIMPS ("GLucose IMaging in ParkinsonismS")

Joint work with the Department of Neurology
University Medical Center Groningen
GLIMPS

• Creation of a database of FDG (fluoro-deoxyglucose) PET scans of the brain
• Contributing clinical centers: Netherlands (11-15), Germany (2), Spain (1)
• Identify structural and functional brain patterns which display statistically significant differences in healthy subjects and patients
• Purpose is to improve patient care directed at early differential diagnosis of patients with neurodegenerative diseases

Mathematical classification model

- Principal Component Analysis (PCA) and Scaled Subprofile Model (SSM)
- Extract disease-specific FDG-PET patterns (GIS: group-invariant subprofiles) for PD, MSA, PSP, etc.
- **Subject score** for each pattern measures how strongly this pattern is expressed in the subject
- Decision tree classification (C4.5, Quinlan 1993)

D Eidelberg, Trends in Neurosciences 32(10), 548 - 557, 2009
PG Spetsieris, Y Ma, v Dhawan, D Eidelberg, NeurolImage 45(4), 1241 - 1252, 2009
PCA and subject scores

(a) Preprocessed FDG-PET scans.

(b) The first four component images.

<table>
<thead>
<tr>
<th></th>
<th>PC1</th>
<th>PC2</th>
<th>PC3</th>
<th>PC4</th>
<th>...</th>
<th>Class</th>
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<tbody>
<tr>
<td>Scan 1</td>
<td>-625</td>
<td>826</td>
<td>-1164</td>
<td>149</td>
<td>...</td>
<td>HC</td>
</tr>
<tr>
<td>Scan 2</td>
<td>186</td>
<td>1395</td>
<td>135</td>
<td>207</td>
<td>...</td>
<td>HC</td>
</tr>
<tr>
<td>Scan 3</td>
<td>1273</td>
<td>-1420</td>
<td>-1070</td>
<td>947</td>
<td>...</td>
<td>MSA</td>
</tr>
<tr>
<td>Scan 4</td>
<td>-1331</td>
<td>-159</td>
<td>887</td>
<td>-1501</td>
<td>...</td>
<td>MSA</td>
</tr>
<tr>
<td>Scan 5</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Scan 6</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

(c) Subject scores are computed as the projection of each scan onto each principal component image.
PD group vs healthy controls (HC)

20 PD patients, 18 healthy controls
Differentiating Early and Late Stage Parkinson’s Patients from Healthy Controls

- Data set University Medical Center Groningen (UMCG):
  - 20 Parkinson’s patients (early stage), 18 Healthy Controls
- Data set Clinica Universidad de Navarra (CUN):
  - 49 Parkinson’s patients (later stage), 19 Healthy Controls
- Decision tree approach with various choices for training and test sets
- Compare with other Machine Learning methods
  - GMLVQ: Generalized Matrix Learning Vector Quantization
  - SVM: Support Vector Machine
Performance of classifiers

<table>
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<tr>
<th></th>
<th>GMLVQ</th>
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<th>SVM</th>
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<th>DT</th>
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<tr>
<td></td>
<td>HC</td>
<td>PD</td>
<td>HC</td>
<td>PD</td>
<td>HC</td>
<td>PD</td>
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<tr>
<td>HC (37 subjects)</td>
<td>35</td>
<td>2</td>
<td>32</td>
<td>5</td>
<td>24</td>
<td>13</td>
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<tr>
<td>PD (40 subjects)</td>
<td>4</td>
<td>36</td>
<td>4</td>
<td>36</td>
<td>10</td>
<td>30</td>
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<tr>
<td>Class accuracy (%)</td>
<td>94.6</td>
<td>90</td>
<td>86.5</td>
<td>90</td>
<td>64.9</td>
<td>75</td>
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<tr>
<td>Overall performance (%)</td>
<td>92.2</td>
<td></td>
<td>88.3</td>
<td></td>
<td>70.1</td>
<td></td>
</tr>
</tbody>
</table>

Performance (leave-one-out cross-validation) of classifiers on combined datasets CUN-UMCG
PD: Parkinson’s patients. HC: Healthy Controls
Confusion matrix and overall performance.

Mudali et al. Journal of Biomedical Engineering and Medical Imaging, 3(6), 2016
Enhanced decision tree diagrams

- For each non-leaf node:
  - scatterplot of subject scores
  - thumbnail of the PC image overlaid on a context image

- For each leaf node:
  - thumbnail of typical pattern of incoming instances
    (a linear combination of PC images encountered when traversing the tree to that node)
Enhanced decision tree diagrams

D. Williams et al. Journal of Biomedical Engineering and Medical Imaging 3(3), 2016
GLIMPS: long term

Long term: 5 years

- Clinical follow-up
- Increasing the number of clinical centers
- Improved machine learning methods
- Improved classification of disease types
- Integrated visual analytics system
Multichannel EEG coherence network visualization

Joint work with Department of Neurology (UMCG) & Department of Experimental and Work Psychology (RUG)
EEG coherence

- Synchronous electrical activity between brain regions is assumed to imply functional relationships between these regions

- Measure for this synchrony: EEG coherence as a function of frequency

- Conventional visualization is hypothesis-driven

- New method: data-driven graph visualization method

M. Ten Caat, N. Maurits, J. Roerdink
Conventional data-driven visualization

1-3 Hz

<table>
<thead>
<tr>
<th>significance threshold</th>
<th>coh &gt; 0.15</th>
</tr>
</thead>
<tbody>
<tr>
<td>top 10%</td>
<td>coh &gt; 0.37</td>
</tr>
<tr>
<td>top 1%</td>
<td>coh &gt; 0.91</td>
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</table>

All electrodes and all significant coherences
Result: visually cluttered edges
• **Functional Unit (FU):** a set of spatially connected electrodes which record pairwise significant coherent signals in an EEG coherence network.
• Combination of spatial structure and connectivity property.

• at a more global scale for a lower EEG frequency
• at a more local scale for a higher EEG frequency

Similarly, we observe less connections for higher frequency
**Application: Mental Fatigue**

<table>
<thead>
<tr>
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<th>Participants</th>
<th>Freq (Hz)</th>
<th>Participants</th>
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<td><img src="image1" alt="Non-fatigued" /></td>
<td>1-3</td>
<td><img src="image2" alt="Fatigued" /></td>
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<tr>
<td>4-7</td>
<td><img src="image3" alt="Non-fatigued" /></td>
<td>4-7</td>
<td><img src="image4" alt="Fatigued" /></td>
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<tr>
<td>8-12</td>
<td><img src="image5" alt="Non-fatigued" /></td>
<td>8-12</td>
<td><img src="image6" alt="Fatigued" /></td>
</tr>
<tr>
<td>13-23</td>
<td><img src="image7" alt="Non-fatigued" /></td>
<td>13-23</td>
<td><img src="image8" alt="Fatigued" /></td>
</tr>
<tr>
<td>24-35</td>
<td><img src="image9" alt="Non-fatigued" /></td>
<td>24-35</td>
<td><img src="image10" alt="Fatigued" /></td>
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<tr>
<td>36-70</td>
<td><img src="image11" alt="Non-fatigued" /></td>
<td>36-70</td>
<td><img src="image12" alt="Fatigued" /></td>
</tr>
</tbody>
</table>

Lorist, Bezdan, ten Caat, Span, Roerdink and Maurits: Brain Research 1270, 95-106, 2009
Dynamic EEG Coherence Networks

Dynamic FU

- FU whose members (i.e., included electrodes) are evolving over time as a result of the changing coherences.
- They may appear and disappear in time.
- Detected by graph similarity algorithm.

Synthetic example with five dynamic Fus D1, …, D5: Red, D1; Blue, D2; Cyan, D3; Green, D4; Magenta, D5.
**Color Encoding and Ordering of Electrodes**

- LT (Left Temporal), Fp (Fronto polar), F (Frontal), C (Central), P (Parietal), O (Occipital), RT (Right Temporal). (Robert & Peter. Clinical Neurophysiology 112, 4(2008): 713-719.)
- The vertices are ordered based on their location. Within each FU, vertices are ordered based on the brain parts to which they belong.
- Vertices from the same region are placed together, and they are ordered as follows: LT, Fp, F, C, O, RT.
Visualization of Dynamic Coherence Networks

- Lines represent electrodes, block of lines represents dynamic FU
- FUs are ordered by barycenter; within each FU brain regions are ordered based on the EEG electrode placement system
Augmented timeline representation

To enhance spatial context, partial FU maps are added: electrodes included in a block are colored black, the others white.

Ji, Van de Gronde, Maurits, Roerdink, VCBM 2017
Visualization of EEG Networks based on Community Structure Analysis

- FU method detects maximal cliques, this makes analysis of local synchronization difficult

- Alternative method, based on network community structure, partitions the set of electrodes into dense groups of spatially connected electrodes recording pairwise significantly coherent signals

- Computation based on optimizing the modularity index of the partition of a network (Blondel et al. 2008)

Ji, Maurits, Roerdink: 6th International Conference on Complex Networks and Their Applications, Lyon, France, 2017
Community Clique:

- Each pair of nodes is significantly connected;
- Nodes are spatially connected;
- Nodes within the same community are more densely connected than electrodes in different communities.

Results

[1, 3]Hz

Young

[4, 7]Hz

Old

[8, 12]Hz
Conclusions and outlook

• Finding brain patterns can be based on many neuroimaging methods (PET, EEG, MEG, fMRI, DTI; separate or simultaneous)
• Machine learning is helpful but not the silver bullet
• Computation and visualization go hand in hand
• Clinical application requires comparison of networks