The analysis of BrainWaves in MCI detection
THE ANALYSIS OF BRAINWAVES IN MCI DETECTION

Nikos A Laskaris
Single-Trial analysis of cognitive ERP Responses
The Clinical problem (simplified):
There are complaints about decline in cognitive performance

Can we distinguish between normal ageing effects and mild cognitive impairment (MCI) / prodromal AD pathology?

A Clinical Approach (just one possibility)

ERPs - auditory oddball paradigm
A waveform-biomarker reflecting the ‘average’ performance in a simple cognitive task

alternatively ...
Preliminaries - Our Motivation

- Discriminative VQ - descriptor
- Cross Frequency Coupling - Biomarker
- Future directions
the synopsis of response dynamics and its variability by means of

**Semantic Maps**

and **Brainwaves Dictionary**

---

IEEE SP Magazine, 2004

[IEEE SP Magazine, 2004](https://ieeexplore.ieee.org)
In a nutshell, **directed queries** are formed in the Single-Trial signals, which are then summarized using a **very limited vocabulary of information granules** (**prototypes**) that are easily understood, accompanied by **well-defined semantics** and help expressing the **inherent data structure**.

The **information abstraction** is accomplished via unsupervised **data-manifold learning** techniques and followed by a suitable **visualization scheme** that can readily **spot interesting events & trends** in the experimental data.

**Semantic Maps**: is a **cartography** of single-trials that results in a **topographical representation** of response variation and enables the **virtual navigation** in the encephalographic database.
Step 1
the spatiotemporal dynamics are decomposed

By designing a **spatial filter** that is used to extract **temporal patterns** conveying the **regional response dynamics**
Step 2

Pattern & Graph-theoretic Analysis of the extracted ST-patterns

- Feature selection
- Dimensionality Reduction
- MAP with semantics attached
- Vector Quantization & Ordering
- Response re-parameterization
- Neural-Gas Codebook design
- Signal Understanding & Machine learning
- Manifold learning
- Embedding in high-D feature space
Can single-trial response dynamics (i.e. the recorded brainwaves) be described/characterized in ways that would help revealing the cognitive impairment better than the averaged response?
Exploiting BrainWaves in aMCI-detection
Part-I. Discriminative VQ - descriptor

auditory oddball paradigm with 20% target tones
Signals were recorded at Cz and Pz sites with \( f_s = 1024 \),
~ 30 responses to target stimulus per subject
25 amnestic MCI patients & 25 non-impaired subjects
from GAADRD
The concept

1. Design the Codebook 
discriminatively

2. Derive semantic map 
based on CodeWaves

3. Embed ST-responses as 
trajectories on the map.

4. Compute distributions 
over the Codebook

5. Compare ‘histograms’
**Training stage**

1. **Laplacian score**
   - Select brain rhythm(s) of interest
   - Select latencies of interest (LOIs)

2. **Neural Gas**
   - Derive the Codebook for N200-related LOIs
   - Derive the Codebook for P300-related LOIs

3. **MCI_score**
   - Merge the two distinct codebooks
   - Rank the **CodeWaves** based on their propensity to reflect MCI

**Group analysis**

- **MCI**
  - Trials
  - \( x_1(t) \)
  - \( x_2(t) \)
  - \( x_{30}(t) \)
  - Patient #1

- **NI**
  - Trials
  - \( x_1(t) \)
  - \( x_2(t) \)
  - \( x_{30}(t) \)
  - Subject #1

- Bandpass filtering
- Laplacian Score & randomization (LOIs)
- Extracting trial-segments around peaks
- **N200**
  - Neural Gas prototyping
  - discriminative codebooks
- **P300**
  - Neural Gas prototyping

**Using MCI_score for Ranking Prototypes**

- Organized Codebook
The temporal patterning in δ-rhythm showed the most prominent differences between NI and aMCI single-trial cognitive responses.

Two distinct temporal segments (LOIs) were identified, associated with the N200 and P300 (averaged) response.
Using randomization,
Based on the detected LOIs
Classification stage

Feature Extraction
- Filtering within δ-band
- Forming single-trial trajectories

DVQ-descriptor
- Encoding trajectories based on composite Codebook
- Derive a response profile reflecting (probabilistically) the similarity of temporal patterning with the CodeWaves

Classification
- Diagnosis is based on subject’s response profile and a given set of profiles with known classification

Single subject analysis

MCI ?

trials

x1(t)  x2(t)  x30(t)

Filtering within δ band

Extracting consecutive signal segments from every trial and building the overall trajectory matrix T_ALL

Deriving DVQ response profile

Nearby neighbor rule

p = 71

MCI  NI
The **semantic map** of the overall CodeBook (a) with single-trial response trajectories sketched within (b & c).
single subject data

- MCI #3
- NI #5

code vector rank
Comparing with Signal Averaging

MDS-based scatterplot for the **DVQ-profiles** (left) and the **Signal-Averaging representation** (right)
By means of **5-fold cross-validation** for CodeBook design & **leave-one-out cross-validation (LOOCV)** for the **knn-classifier**

<table>
<thead>
<tr>
<th></th>
<th>1NN</th>
<th></th>
<th>3NN</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DVQ-profile</td>
<td>Averaged Signal</td>
<td>DVQ-profile</td>
<td>Averaged Signal</td>
</tr>
<tr>
<td>ACC</td>
<td>0.90</td>
<td>0.80</td>
<td><strong>0.93</strong></td>
<td>0.83</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.87</td>
<td>0.73</td>
<td><strong>0.93</strong></td>
<td>0.80</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.93</td>
<td>0.87</td>
<td><strong>0.93</strong></td>
<td>0.87</td>
</tr>
</tbody>
</table>
Brain Waves in MCI detection

PART- II
Can the study of **interactions** among **distinct brain rhythms** (i.e. brainwaves of different prominent frequency jointly analyzed) offer alternative / additional ways for detecting cognitive impairment?
A novel biomarker of amnestic MCI based on dynamic cross-frequency coupling patterns during cognitive brain responses

CFC is a key mechanism for the integration of distinct processes mediated by the distinct brain rhythms, and there is rapidly accumulating experimental evidence about its role in cognition.
Method's outline

1. A PAC-estimator is employed across trials. For each pair of brain rhythms, a time-varying profile of interaction is estimated by means of PLV(low, high).

2. Distinct CFC events associated with the ERP components are detected.

3. Rhythm-pairs and latencies of high discriminative power are detected and wrapped in a multifaceted biomarker.
Using Band-Pass filtering and Hilbert transform

\[
x(t) \overset{\text{1}}{\to} \text{HF}_{\text{filter}}(x(t)) \overset{\text{2: Hilbert}}{\to} \text{envelope} \overset{\text{3: LF}_{\text{filter}}(\text{envelope})}{\to} \text{inst. phase} \]

\[
x(t) \overset{\text{5}}{\to} \text{LF}_{\text{filter}}(x(t)) \overset{\text{6: Hilbert}}{\to} \text{inst. phase} \]
by integrating across trials and within a temporal window

\[
TV_{PLV_{LF \rightarrow HF}}(t') = \left| \frac{1}{N(2w + 1)} \sum_{t' = t-w}^{t+w} \sum_{j=1}^{N} e^{i \Delta \phi_j(t')} \right|
\]
The instantaneous PLV measurements can be tabulated in a $[7 \times 7]$ Matrix or more compactly in a 21-tuple vector. The corresponding 3D/2D array encapsulated the temporal evolution of CFC associated with the response generation.
Single-subject (NI) example

Averaging across pairs

Picking the maximal interaction
Group-averaged results for healthy participants: contrasting CFC from responses to Target and Nontarget stimuli.

(a) Grand Averaged responses - NI subjects

(b) PAC-connectivity patterns of relative increase
Group-averaged results
aMCI vs. NI subjects

studying the PAC evolution - III
Class-Separability Analysis

The dynamic PAC profiles from aMCI and NI subjects are statistically compared.

(a) Wscore* vs msec

(b) Network diagram with nodes labeled θ, α1, α2, δ, γ, β1, β2 and Wscore*

(c) Graph with nodes at 50 msec, 150, 210, 270, 430, 490, 770, 830, and 870 msec, with color indicating Relative Difference.
### Biomarker performance in aMCI detection

<table>
<thead>
<tr>
<th>%</th>
<th>LOOCV</th>
<th>2-CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy</td>
<td>97.5</td>
<td>95.0</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>100.0</td>
<td>96.0</td>
</tr>
<tr>
<td>Specificity</td>
<td>93.3</td>
<td>93.0</td>
</tr>
</tbody>
</table>

SVM operating on TVPAC characteristics.
Future Directions

**ERPs**
- Multichannel signal
- Functional connectivity

**Resting State**
- BrainWaves VQ-characterization
- CFC

**Interventions**
- Restoring brainwaves distribution
- Restoring CFC

---

**HOW A NEW TREATMENT FOR ALZHEIMER’S COULD WORK**

1. Lights flash at 40 times a second.
2. Brain cells in the visual cortex fire at the same rate as the flashes.
3. The brain wave pattern stimulates the brain’s own ‘macrophage cells’ - microglia - to eat the plaques that disrupt the brain.

---

*Nature* International weekly journal of science

Gamma frequency entrainment attenuates amyloid load and modifies microglia

*Nature* 540, 230–235 (08 December 2016) | doi:10.1038/nature20587
acknowledgements

http://neuroinformatics.gr/

M. Tsolaki, I. Tarnanas & coworkers

S. Dimitriadis, M. Bitzidou & coworkers