II. Searching for fingerprints of brain cognitive activity.

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BRANDY, 26-27 June, Val del Sol
On the threshold of a dream ...

How to recognize specific activity changes of the brain networks?

- Simulation of brain networks.
- EEG/MEG microstates.
- Spectral fingerprints.
- Simulation of brain networks.
- Conclusions.

Final goal: Use your brain to the max!
Optimization of brain processes?

Possible form of Brain Fingerprints

**fMRI:** BFP is based on $V(X,t)$ voxel intensity of fMRI BOLD signal changes, contrasted between task and reference activity or resting state.

**EEG:** spatial, spatio-temporal, ERP maps/shapes, coherence, various phase synchronization indices.

1. **Spatial/Power:** direct localization/reconstruction of sources.
2. **Spatial/Synch:** changes in functional graph network structure.
3. **Spectral fingerprinting** (MEG, EEG), localized power distributions.
4. **EEG** microstates, sequences & transitions, dynamics in ROI space.
5. **Frequency/Power:** ERS/ERD smoothed patterns $E(X,t,f)$.
6. **EEG decomposition into components:** ICA, CCA, tensor, RP ...
7. **ERP power maps:** spatio-temporal averaged energy distributions.
8. **Model-based:** The Virtual Brain, integrating EEG/neuroimaging data.

Neuroplastic changes of connectomes and functional connections as results of training for optimization of brain processes.
Dynamic functional brain networks
Correlation matrix representing resting-state functional connectivity between selected brain regions. Shows stronger connectivity for 7 large-scale brain networks: default mode (DM), dorsal attention (DAT), executive control network (FPN, CON), salience (SAL), sensorimotor (SOM), visual (VSN), auditory (ASN). Switching DMN $\Leftrightarrow$ Salience $\Leftrightarrow$ FPN.

Correlations of 6 canonical networks.
Perception,
Action-attention
DMN (Default Mode Network)
Each has up to 10 different network connectivity states (NC-states), rather stable for single subjects, ex. DMN has usually 7-9.
**DMN time-averaged baseline.**
Between-network allegiances (prob. that nodes are in the same community). Rim colors = canonical networks, rim length = greater allegiance to other networks, size of connections = strength of between-network allegiances.
DMN1: weak within-network allegiance strong to DAT, SAL, and VIS.
Global Neuronal Workspace Theory (Deahene et al. 1998): brain processes underlying effortful tasks require two main computational spaces:

- a set of specialized and modular perceptual, motor, memory, evaluative, and attentional processors;
- a unique global workspace composed of distributed and heavily interconnected neurons with long-range axons.

Workspace neurons are mobilized in effortful tasks for which the specialized processors (Kahneman’s System 1) do not suffice (System 2), mobilize or suppress contribution of specific processor neurons.

1. Can the whole-brain network properties change during performance?
2. Do modularity, path length, global, local efficiency and other network measures dependent on the cognitive load?

Cognitive load on whole-brain network

35 participants (17 females; Mean age = 22.6 ± 3.1; 19-31).

**Letter n-back task**

1-back

<table>
<thead>
<tr>
<th>1-back</th>
<th>1-back</th>
<th>2-back</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>B</td>
<td>A</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>D</td>
</tr>
</tbody>
</table>

Instruction

2-back

<table>
<thead>
<tr>
<th>2-back</th>
<th>2-back</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>B</td>
<td>A</td>
</tr>
</tbody>
</table>

Low cognitive effort

High cognitive effort

30 s block

10 blocks x 3 sessions

5:30 min per session

2-back Target: same or different?

Finc et al, Human Brain Mapping, 2017
Human connectome and MRI/fMRI

Structural connectivity

Functional connectivity

Graph theory

Whole-brain graph

Binary matrix

Correlation matrix

Node definition (parcelation)

Signal extraction

Correlation calculation

Many toolboxes available for such analysis.

Bullmore & Sporns (2009)
Two experimental conditions: 1-back, 2-back

Node definition
- Anatomical parcellation (90 nodes)
- Functional parcellation (264 nodes)

Weighted correlation matrices

Binary correlation matrices

Fisher’s z-scores
- Threshold (0.01 - 0.6)

global efficiency | local efficiency | modularity
Network neuroscience is focused on identifying network structures. Hubs, rich club and core of the network. Hubs connect modules via long-distance connections. Hubs are also often densely interconnected forming so called ’rich club’ or integrated core.

Brain modules and cognitive processes

Simple and more difficult tasks, requiring the whole-brain network reorganization.

Left: 1-back
Right: 2-back

Average over 35 participants.

Left and midline sections.

Brain modules and cognitive processes

Simple and more difficult tasks, requiring the whole-brain network reorganization.

Left: 1-back local hubs
Right: 2-back local hubs

Average over 35 participants.

Dynamical change of the landscape of attractors, depending on the cognitive load. Less local (especially in DMN), more global binding (especially in PFC).

Brain modules and cognitive processes

Simple and more difficult tasks, requiring the whole-brain network reorganization.

Left: 1-back connector hubs  
Right: 2-back connector hubs

Average over 35 participants.

Dynamical change of the landscape of attractors, depending on the cognitive load – System 2 (Khaneman).  
DMN areas engaged in global binding!

Changes in modularity

Modularity metric: fraction of within-community edges in the network minus such fraction for randomly connected network with unchanged community structure.

Finc et al, Human Brain Mapping, 2017

Modularity for both parcellations significantly decreases for thresholds ~0.1. Coarse parcellation washes out many effects, especially strong correlations.

Finc et al, Human Brain Mapping, 2017
Changes in efficiency

Global efficiency ~ inverse of characteristic path length
Local efficiency ~ clustering coefficient (Latora & Marchiori, 2001).

Finc et al, Human Brain Mapping, 2017
Cognitive load

**Low cognitive effort**
- Segregated network
- Locally specialized processing

**High cognitive effort**
- Integrated network
- Distributed processing

Parcellation into 264 regions (10 mm spheres) shows subnetworks more precisely than for 90 regions; only a small subgroup of neurons in each ROI is strongly correlated.
Network modularity $\Leftrightarrow$ higher working memory capacity and performance. High connectivity within modules and sparse connections between modules increases effective cooperation of brain regions, is associated with higher IQ.

6-week training, dual n-back task, changes in module allegiance of fronto-parietal and default-mode networks. Each matrix element represents the probability that the pair of nodes is assigned to the same community. Segregation of task-relevant DMN and FPN regions is a result of training and complex task automation.
Working memory training

Recruitment changes from the ‘Naive’ to the ‘Late’ stage of training. Both control and experimental groups exhibited increase of the DMN recruitment but FPN recruitment only increased in experimental group. No consistent changes in FPN-DMN networks integration was noticed.
Deaf vs. Control

Edge-wise functional network differences visualized in the brain space (A). Connections that are significantly stronger (red) or weaker (blue) in deaf adults. Edge thickness reflects t-test statistic strength. (B) Chord diagram representing the number of significant edges between different large-scale networks. Red bands represent edges with stronger functional connectivity in the deaf compared to hearing control, while blue bands represent edges with weaker functional connectivity. (Bonna, Finc, Szwed et al, in review).
Modular organization of mean functional networks in deaf (left) vs control group (right) and reference network division into large-scale brain systems (Power et al., 2011). Salience nodes (black) are part of fronto-parietal (FP) module in deaf group but fall into multi-system (MS) module in control group. Also ventral-attention nodes (dark green) are part of MS module in control group but in deaf group they are part of default mode module (DM).
EEG/MEG Microstates
Microstates

Lehmann et al. EEG microstate duration and syntax in acute, medication-naïve, first-episode schizophrenia. Psychiatry Research Neuroimaging, 2005

Khanna et al. Microstates in Resting-State EEG. Neuroscience and Biobehavioral Reviews, 2015

4-7 states 60-150 ms Symbolic dynamics.
8 large networks from BOLD-EEG

DMN, FP (frontoparietal)-left, right, sensorimotor, ex, control, auditory, visual (medial), (H) visual (lateral). Yuan ... Bodurka (2015)
14 networks from BOLD-EEG

Checkerboard reversal, 5 microstates

M1 => V1
M2 => V2
M3 => Para-hippocampal
M4 => BA7, left PC, precuneus
M5 => dACC

EEG localization and reconstruction


\[ \hat{d}_j = \text{argmin} \| \phi - \sum_j \mathcal{K}_d d_j \|_2^2 \]

Rotating dipole
- Moving
- Rotating
- Fixed

\[ \hat{f} = \text{argmin} \| \psi f \|_1 + \alpha \| f \|_1 \]

S.T. \( \| \phi - \mathcal{K} f \|_2 \leq \varepsilon \)

IRES

\[ \hat{w}_r = \text{argmin} \| w_r \| + \alpha \| w_r \|_1 \]

S.T. \( \mathcal{K}_r w_r = \xi_1 \); \( w_r^T w_r = 1 \)

Beamformer (VBB)

\[ \hat{\mathbf{f}}_{mn} = \mathbf{T}_{mn} \phi \]

\[ S_j = (\mathbf{K} \mathbf{K}^T + \alpha \mathbf{I})^{-1} \mathbf{K} \]

\[ \hat{\mathbf{f}}_{st} = \mathbf{f}_{mn}(\mathbf{f})^T (S_j)^{-1} \mathbf{f}_{mn}(\mathbf{f}) \]

sLORETA

MN (\( \ell_2 \) family)

\[ \hat{f}_m = \text{argmin} \| \phi - \mathcal{K} f \|_2^2 + \lambda \| f \|_2^2 \]

\[ \hat{f}_m = \mathbf{T} \phi = \mathbf{K}^T (\mathbf{K} \mathbf{K}^T + \lambda \mathbf{I})^{-1} \phi \]

MN

Nonlinear post hoc normalization

Beamforming and scanning algorithms

Spatial filters

LCMV (Linearly Constrained Minimum Variance), classical reconstruction filter is a solution to the following problem:

$$\Phi = K(\theta)j + n, \quad j \approx W \Phi, \quad WK(\theta) \approx I$$

LCMV has large error if:
• sources are correlated,
• SNR (signal to noise ratio) is low, or
• forward problem is ill-conditioned.


$$W = \bigcap_{j \in Y} \arg \min_{\hat{W} \in X_r} \left\| \hat{W}K(\theta) - I_j \right\|_2^2$$

where $X_r$ is a set of all matrices of rank at most $r$, and set $Y$ denotes all unitary norms. We use 15000 vertex FreeSurfer brain tessellation together with brain atlases that provide parcellation of the mesh elements into 100-240 cortical patches (regions of interest, ROIs).
SupFunSim

SupFunSim: our library/Matlab toolbox, direct models for EEG/MEG.
Provides many spatial filters for reconstruction of EEG sources: linearly constrained minimum-variance (LCMV), eigenspace LCMV, nulling (NL), minimum-variance pseudo-unbiased reduced-rank (MV-PURE) ...

Source-level directed connectivity analysis: partial directed coherence (PDC), directed transfer function (DTF) measures.

Works with FieldTrip EEG/MEG software. Modular, object-oriented, using Jupyter notes, allowing for comments and equations in LaTeX.

\[
\begin{align*}
A &:= H_{Src,R} := R^{-1/2} H \\
B &:= H_{Src,N} := N^{-1/2} H
\end{align*}
\]

Functional connectivity changes

Influence of brain games on functional connectivity: **Phase Locking Value** (Burgess, 2013; Lachaux 1999), phase differences between signals measured at each electrode. PLV => synchronization maps, info flow.

\[
PLV(a, b) = \frac{1}{T} \sum_{t=1}^{T} e^{i\Phi(t)}
\]
Spectral Fingerprints
A. Keitel i J. Gross, „Individual human brain areas can be identified from their characteristic spectral activation fingerprints”, *PLoS Biol* 14(6), e1002498, 2016
Reliability of ROI identification

Rank one means that ROI is uniquely identified (blue).
Some errors are due to homologous ROIs (left-right) and have mean rank <2.
Most reliable ROI, midline structures

MEG data from the Human Connectome Project (HCP) for 1200 subjects.
ROI that we can recognize quite reliably. Colors – ROI 1-6
33 1 Cingulum_Mid_L, 34 2 Cingulum_Mid_R, 35 3 Cingulum_Post_L,
36 4 Cingulum_Post_R, 51 5 Occipital_Mid_L, 110 6 Vermis_3
Most reliable ROI, midline structures

MEG data from the Human Connectome Project (HCP) for 1200 subjects. ROI that we can recognize quite reliably. Colors – ROI 1-6
3 Cingulum_Post_L,
5 Occipital_Mid_L
Some errors are due to homologous ROIs (left-right) and have mean rank <2. Number of ROIs that can be reliably identified this way is much larger. Some regions are hard to identify: S/N is different depending on cortex folding and MEG/EEG measures. MEG can see cingulate cortex activity, EEG is better for flat cortex on the surface.
Most reliable ROI, homologous \( \leq 1.5 \)

MEG data from the Human Connectome Project (HCP) for 1200 subjects. Some ROI can be recognized quite reliably. If homologues are not distinguished we have 29 ROIs, many sub-cortical.
Least reliable ROI

<table>
<thead>
<tr>
<th>iROI</th>
<th>key</th>
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<tbody>
<tr>
<td>5</td>
<td>Frontal_Sup</td>
</tr>
<tr>
<td>9</td>
<td>Frontal_Mid</td>
</tr>
<tr>
<td>37</td>
<td>Hippocampus</td>
</tr>
<tr>
<td>39</td>
<td>ParaHippocam</td>
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</table>
Simulations of brain networks
Neuropsychiatric phenomics

2008: The Consortium for Neuropsychiatric Phenomics

“... categories, based upon presenting signs and symptoms, may not capture fundamental underlying mechanisms of dysfunction” (Insel et al., 2010).

New approach: RDOC NIMH.

Description of organisms at different levels will help to answer different types of questions.

Network level is in the middle and can be connected to the mental level via computational models.
Emergent neural simulator:

3-layer model of reading:
oesthesia, phonology, semantics, or
distribution of activity over
**140 microfeatures** defining concepts.
In the brain: microfeature=subnetwork.
Hidden layers OS/OP/SP_Hid in between.

Learning: mapping one of the 3 layers to the other two.
Fluctuations around final configuration = attractors representing concepts.
How to see properties of their basins, their relations?
Model in **Genesis**: more detailed neuron description.
Computational Models

Models at various level of detail.

• Minimal model includes neurons with 3 types of ion channels.

Models of attention:

• Posner spatial attention;
• attention shift between visual objects.

Models of word associations:

• sequence of spontaneous thoughts.

Models of motor control.

Critical: control of the increase in intracellular calcium, which builds up slowly as a function of activation. Initial focus on the leak channels, 2-pore $K^+$, looking for genes/proteins.
Nasz Viser toolbox (Dobosz, Duch) do wizualizacji szeregów czasowych w wielu wymiarach różnymi technikami.
Transitions to new patterns that share some active units (microfeatures) shown in recurrence plots.
Probability of recurrence may be computed from recurrence plots, allowing for evaluation how strongly some basins of attractors capture neurodynamics.
Attention is focused only for a brief time and then moved to the next attractor basin, some basins are visited for such a short time that no action may follow, corresponding to the feeling of confusion and not being conscious of fleeting thoughts.
Trajectory visualization

Wavelet decomposition, Recurrent Quantification Analysis, feature ranking and machine learning. Nonlinear features are critical to achieve good results, and their correlation with ASD depends on age.
EEG of 3 to 36-month old babies, 19 electrodes selected from 64 or 128. Daubechies (DB4) wavelets transform EEG signal into 6 bands. 7 features from Recurrence Quantitative Analysis (RQA): RP entropy, recurrence rate, laminarity, repetition, max/mean line length, trapping time. In addition sample entropy and Detrended Fluctuation Analysis was used. Nonlinear features were computed from EEG signals and used as input to statistical learning methods. Prediction of the clinical diagnostic outcome of ASD or not ASD was highly accurate. SVM classification with 9 features gave high specificity and sensitivity, exceeding 95% at some ages. Prediction using only EEG data taken as early as 3 months of age was strongly correlated with the actual measured scores.
EEG non-linear features

Features: not only structure, but also dynamics.

Nonlinear invariant measures of a time series and their physical interpretation, recurrence quantification analysis (RQA).

For example:
1. Sample Entropy (SampE)
2. Entropy derived from recurrence plot (L_entr).
3. Recurrence rate (RR), probability of recurrence.
4. Determinism (DET), repeating patterns in the system.
5. Laminarity (LAM), frequency of transitions between states.
6. Trapping time (TT), time in a given state.
Probability of recurrence may be computed from recurrence plots, or from clusterization of trajectory points, allowing for evaluation how strongly some basins of attractors capture neurodynamics. Our Viser Toolbox is used for all visualizations.
ASD vs Low Risk Healthy

RR = recurrence rate

L_max = max line length, related to Lyapunov exponent

TT = trapping time
Developmental trajectories for SampE in the left temporal region (T7 sensor) in higher frequencies (beta+gamma) for ASD, LRC-, and HRA-

LRC low risk controls
HRA high risk for ASD
- no ASD
Developmental trajectories for SampE in the right temporal-parietal region (T8 +P4+P8 sensors) in frequencies theta through gamma for ASD, LRC-, and HRA-.
Trajectories may be visualized either using recurrence plots that shows relative changes of the trajectory or some form of visualization showing absolute positions of points on trajectories (MDS/FSD/SNE). Visualization shows transitions between microstates, or attractor states.
Depth of attractor basins

Variance around the center of a cluster grows with synaptic noise; for narrow and deep attractors it will grow slowly, but for wide basins it will grow fast. Jumping out of the attractor basin reduces the variance due to inhibition of desynchronized neurons.
All plots for the flag word, different values of $b_{\text{inc}\_dt}$ parameter in the accommodation mechanism. $b_{\text{inc}\_dt} = 0.01$ & $b_{\text{inc}\_dt} = 0.005$

$b_{\text{inc}\_dt} = \text{time constant for increases in intracellular calcium building up slowly as a function of activation, controls voltage-dependent leak channels.}$

[Link](http://kdobosz.wikidot.com/dyslexia-accommodation-parameters)
Typical Development vs ADHD

All plots for the flag word, different values of b_inc_dt parameter in the accommodation mechanism. b_inc_dt = 0.01 & b_inc_dt = 0.02. 
b_inc_dt = time constant for increases in intracellular calcium which builds up slowly as a function of activation.
http://kdobosz.wikidot.com/dyslexia-accommodation-parameters
Rapid Serial Visual Presentation

Any RSVP applications for fast reading.
Simulation: showing series of words, looking for attention/associations.
star => flea => tent => lock => tart => hind
RSVP: typical brain

Normal speed
associations, context=>understanding
Some shallow microstates, no associations

too fast, speed 5x
microstates get blurred,
few associations
High functioning ASD case (HFA):

- normal presentation
- long dwelling times
- fast presentation
- enforced quick resynchronization
- more internal stimuli.
RSVP simulations in deep autism

Normal speed
skipping some words,
no associations

fast presentation
more internal states
some associations arise
Conclusions

- Many brain states are now linked to specific mental states, and can be transformed into signals that we can understand: motor intentions, plans, images, inner voices ...

- Neuroimaging ⇔ models of whole brain (TVB) ⇔ networks, neurodynamics ⇔ interpretation, mental states: S(B) ⇔ S(M).

- Neurodynamics is the key to understanding mental states; it creates dynamical forms, changing states of functional connectomes without rearranging physical elements. Influence of other phenomics levels on mental states may be understood indirectly, via changes in neurodynamics.

- AI/ML draws inspirations from brain research, but also neural network models and learning algorithms (CNN, recurrence networks, reinforcement learning) help to interpret information processing in the brain.

- Many neurocognitive technologies are coming, helping to diagnose, repair and optimize brain processes.
INCF PL

International Neuroinformatics Coordination Facility (INCF) goal: integrate and analyze diverse data across scales, techniques, and species to understand the brain and positively impact the health and well-being of society.

Polish INCF Node, established in Warsaw at Nencki Institute, since 2017 at the Nicolaus Copernicus University in Toruń.


Neuroimaging, computational neuroscience, artificial intelligence.

Speakers

Jan Bjaalie, University of Oslo
Rafal Bogacz, University of Oxford
Andrzej Cichocki, RIKEN CBS
Maureen Clerc, Inria
Carole Goble, University of Manchester
William Grisham, UCLA
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Pedro Valdes-Sosa, Cuban Neuroscience Center, University of Electronic Science and Technology China
Kirstie Whitaker, University of Cambridge
Alexander Woodward, RIKEN CBS
Thank you for synchronization of your neurons

Google: W. Duch
=> talks, papers, lectures, Flipboard …