

Atomic Decomposition of Human EEG Oscillations In Medical Research And Pharmaceutical Trials

Roman Rosipal^{1,2}, Leonardo Jose Trejo¹, Zuzana Rostakova²,
Barbora Cimrova³

¹ Pacific Development and Technology, LLC, Palo Alto, CA, USA

² Slovak Academy of Sciences, Bratislava, Slovakia

³ Comenius University, Bratislava, Slovakia



IPEG, 21 - 25 November, 2018, Zurich

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News from the International
Pharmaco-EEG Society (IPEG)
and its members of research,
including neurophysiology,
predictive work, personalized
medicine.

ipsg-society.org
Joined November 2012
25 Photos and videos



Tomas Ros @neuromediate - Oct 17
Local field potentials primarily reflect inhibitory neuron activity in human and monkey cortex.



IPFG @ihermacewep - Oct 16
Final Program for IPEG Meeting 2018 in Zurich -
mailchi.mp/235d2aa540dc/0...



Program IPEG Meeting Zurich, Switzerland,
November 21-23, 2018

The 20th biennial IPEG Meeting



EEG biomarkers for treatment prediction: More Replication
urgently needed! ipg.psychiatryonline.org/doi/abs/10.1177/0887640118770424
Link to poster at the IPEG meeting in November in Zurich,
Switzerland



Final Abstract Submission 30th September + Preliminary
Program - mailchi.mp/083304258607/c...

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Electroencephalographic Biomarkers for Treatment Response Prediction in Major Depressive Illness: A Meta-Analysis

Alik S. Widge✉, M.D., Ph.D., M. Taha Bilge, Ph.D., Rebecca Montana, B.A., Weilynn Chang, B.A., Carolyn I. Rodriguez, M.D., Ph.D., Thilo Deckersbach, Ph.D., Linda L. Carpenter, M.D., Ned H. Kalin, M.D., Charles B. Nemeroff, M.D., Ph.D.

Published Online: 3 Oct 2018 | <https://doi.org/10.1176/appi.ajp.2018.17121358>

Articles

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Objective:

Reducing unsuccessful treatment trials could improve depression treatment. Quantitative EEG (QEEG) may predict treatment response and is being commercially marketed for this purpose. The authors sought to quantify the reliability of QEEG for response prediction in depressive illness and to identify methodological limitations of the available evidence.

Method:

The authors conducted a meta-analysis of diagnostic accuracy for QEEG in depressive illness, based on articles published between January 2000 and November 2017. The review included all articles that used QEEG to predict response during a major depressive episode, regardless of patient population, treatment, or QEEG marker. The primary meta-analytic outcome was the accuracy for predicting response to depression treatment, expressed as sensitivity, specificity, and the logarithm of the diagnostic odds ratio. Raters also judged each article on indicators of good research practice.

Articles

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Alik S. Widge M.D., Ph.D., M. Taha Bilge, Ph.D., Rebecca Montana, B.A., Welwynn Chang, B.A., Carolyn I. Rodriguez, M.D., Ph.D., Thilo Deckersbach, Ph.D., Linda L. Carpenter, M.D., Ned H. Kalin, M.D., Charles B. Nemeroff, M.D., Ph.D.

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Results:

In 76 articles reporting 81 biomarkers, the meta-analytic estimates showed a sensitivity of 0.72 (95% CI=0.67–0.76) and a specificity of 0.68 (95% CI=0.63–0.73). The logarithm of the diagnostic odds ratio was 1.89 (95% CI=1.56–2.21), and the area under the receiver operator curve was 0.76 (95% CI=0.71–0.80). No specific QEEG biomarker or specific treatment showed greater predictive power than the all-studies estimate in a meta-regression. Funnel plot analysis suggested substantial publication bias. Most studies did not use ideal practices.

Conclusions:

QEEG does not appear to be clinically reliable for predicting depression treatment response, as the literature is limited by underreporting of negative results, a lack of out-of-sample validation, and insufficient direct replication of previous findings. Until these limitations are remedied, QEEG is not recommended for guiding selection of psychiatric treatment.

Articles

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IPEG @pharmacoeeg · Oct 4

EEG biomarkers for treatment prediction: More Replication urgently needed!
[ajp.psychiatryonline.org/doi/abs/10.117...](https://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2018.17121358)

Let's discuss at the IPEG meeting in November in Zurich, Switzerland
ipeg-society.org



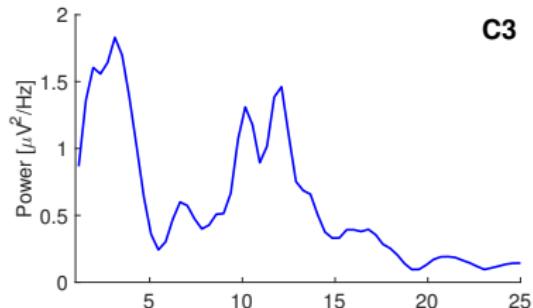
3

- standardization of EEG recording, pre-processing steps, etc.
 - sample size
 - diurnal effects
 - task conditions (beyond EC/EO ?)
 - effects of long-stay at clinic
 - etc.
-

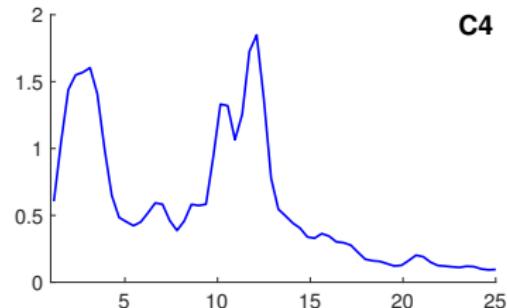
- wider frequency bands vs. individual narrow-oscillatory rhythms
- inter-individual variability
- electrodes space

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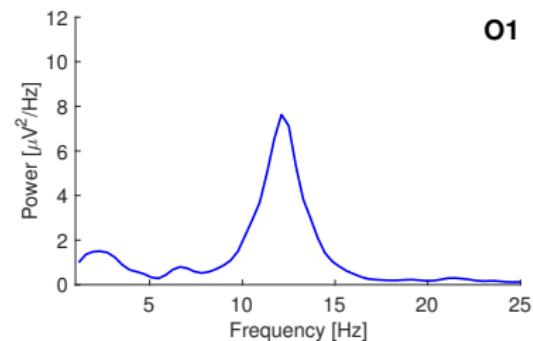
Motivational Examples (frequency)



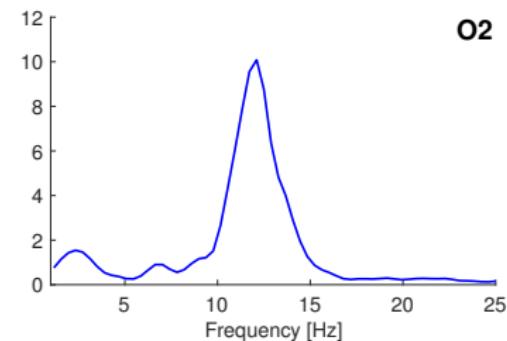
C3



C4

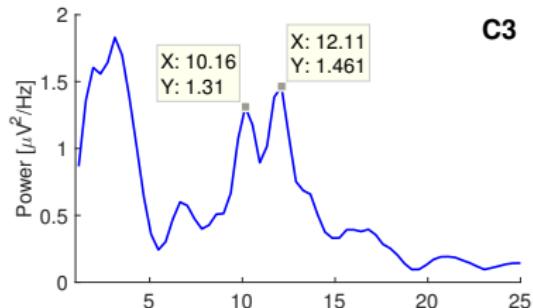


O1

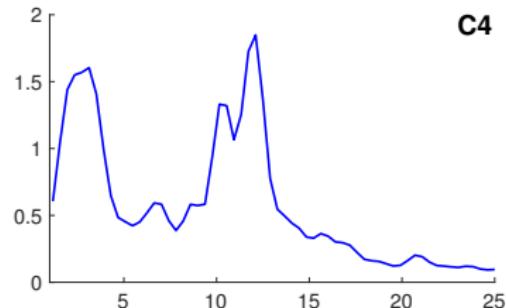


O2

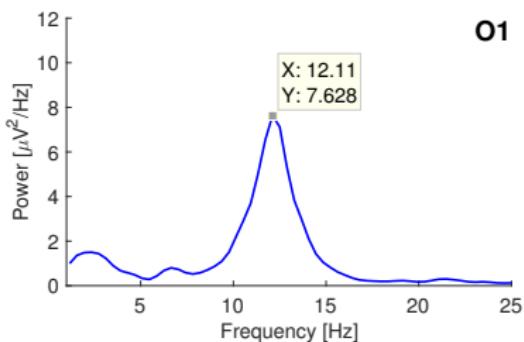
Motivational Examples (frequency)



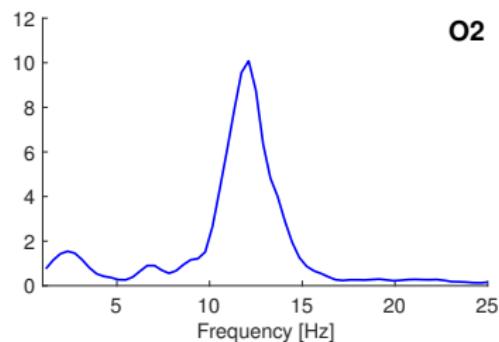
C3



C4

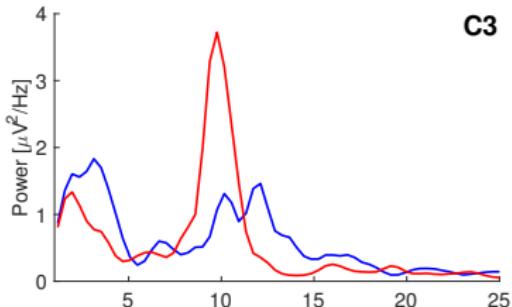


O1

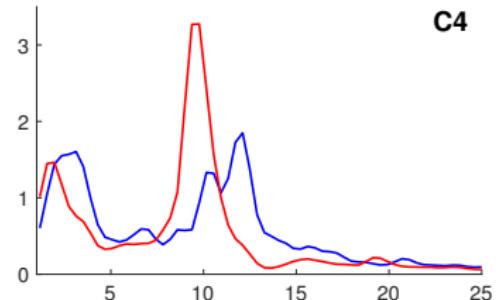


O2

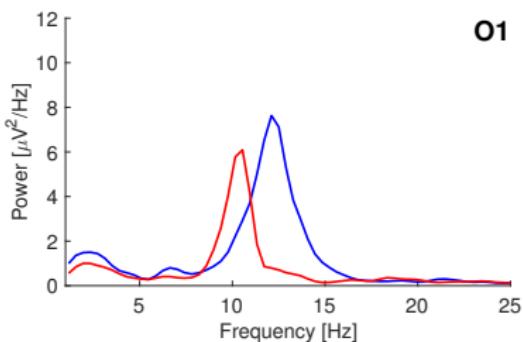
Motivational Examples (frequency)



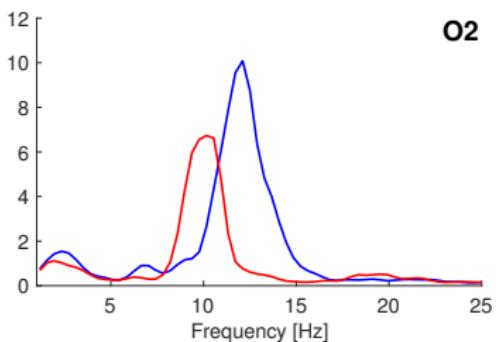
C3



C4

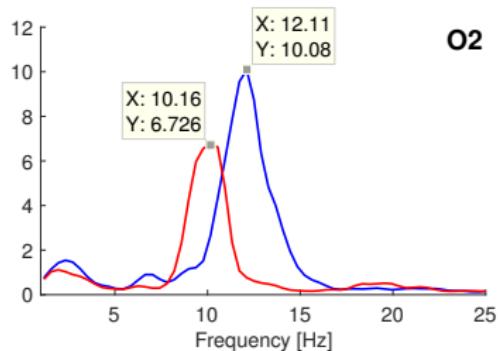
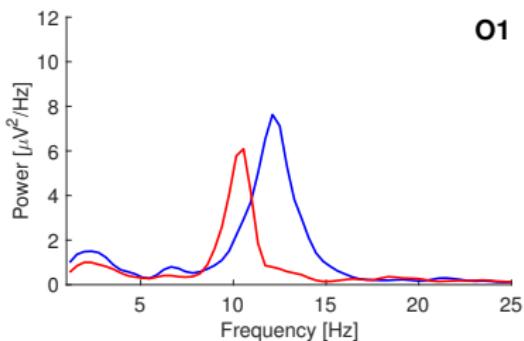
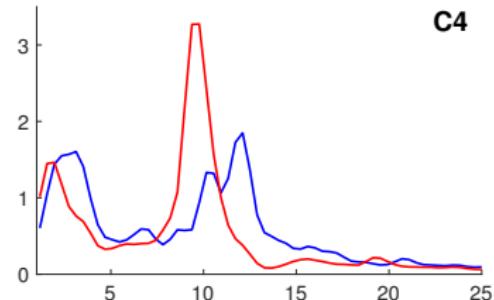
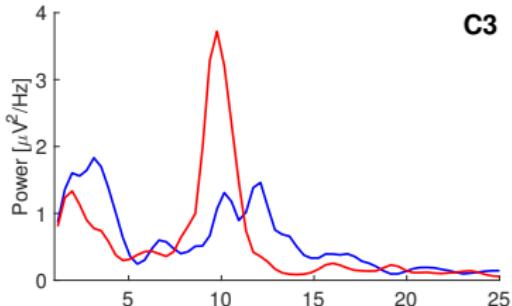


O1

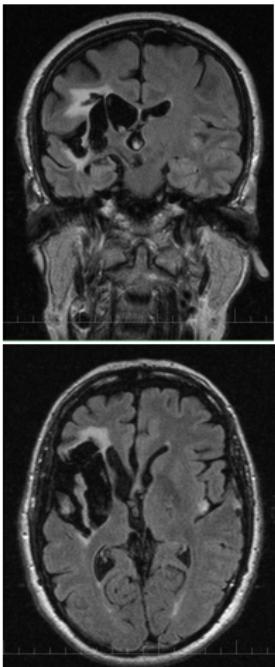
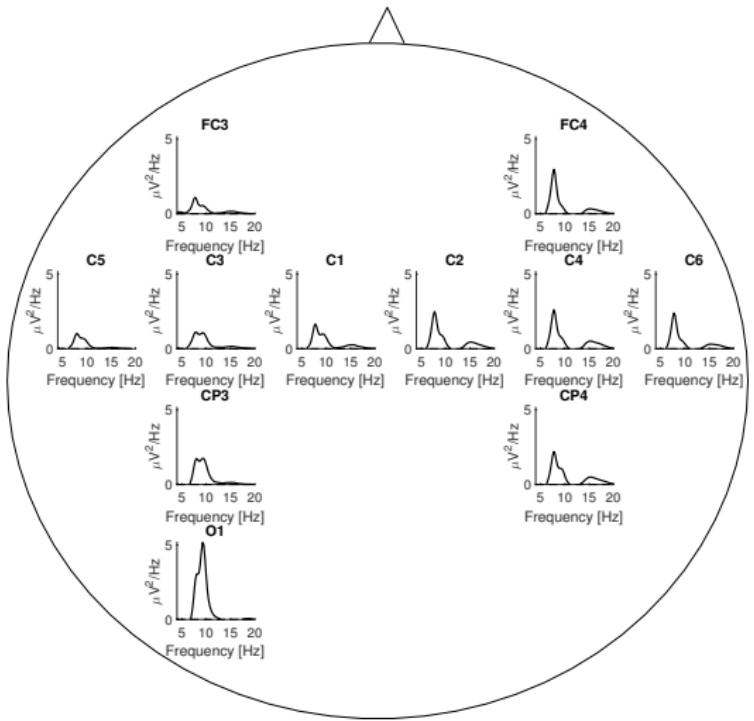


O2

Motivational Examples (frequency)



Motivational Examples (space)



Averaged oscillatory part of the EEG power spectrum recorded during resting eyes-closed. A chronic stroke patient with ischemia in the fronto-temporo-parietal area on the left side

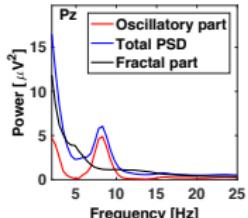
Applied Procedure

Clinical Study (EEG, PK, etc.)

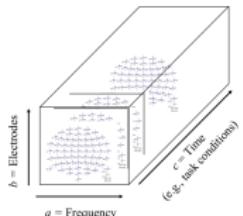
EEG recording & preprocessing



IRASA Spectrum Decomposition



Multi-way Data Structure

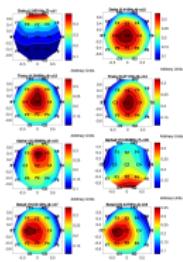


PARAFAC

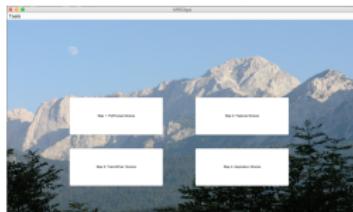
Formal Statistical Testing
ANCOVA, ER, etc.

```
PROJ_IDEE: DATAfile_name (PROJ_IDEE)
(LAB) Subject_Treatment_Time;
(RBL) Pre_Proj_IDEE + PreTreatmentTime / SOLUTION_CLI;
(RBL) Post_Proj_IDEE + PostTreatmentTime / SOLUTION_CLI;
(URBL) Treatment_Time / CLI;
(RBL) 
```

Endpoints (e.g. time-scores)



Clustering (e.g. DBSCAN)



Brain Oscillations vs. Scale-free Brain Activity

Trends Cogn Sci. 2014 September ; 18(9): 480–487. doi:10.1016/j.tics.2014.04.003.

Neuron. 2010 May 13; 66(3): 353–369. doi:10.1016/j.neuron.2010.04.020.

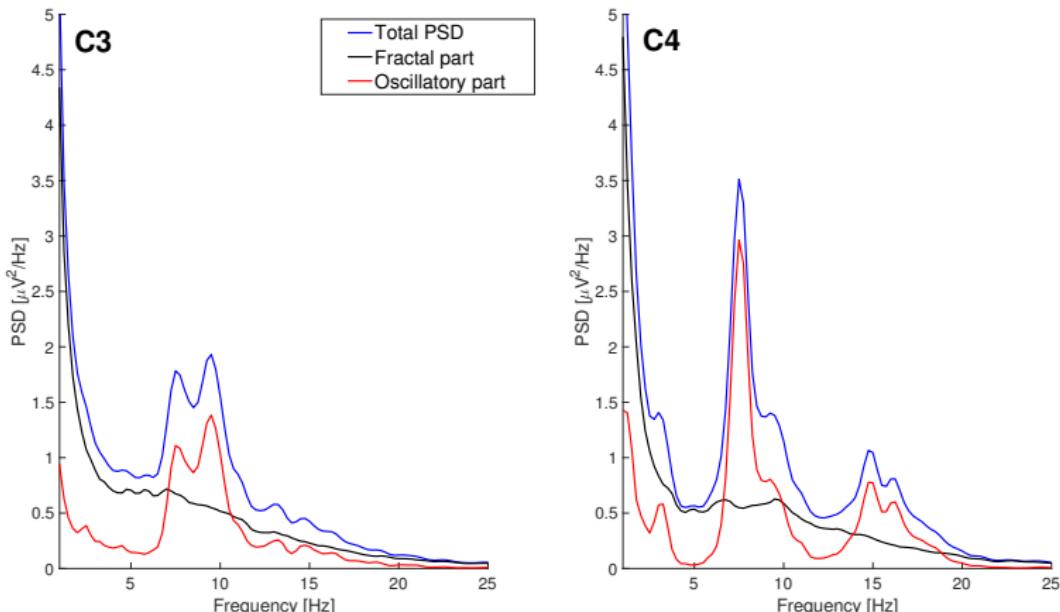
Scale-free brain activity: past, present and future

Biyu J. He

The temporal structures and functional significance of scale-free brain activity

Biyu J. He^{1,*}, John M. Zempel², Abraham Z. Snyder^{1,2}, and Marcus E. Raichle^{1,2,3,4}

- “..... *there are two types of brain activity that coexist: the broadband, arrhythmic activity and the narrow-band, rhythmic oscillations*”. [He, 2014]
- EEG recorded from the scalp originates from electrical currents generated by a mixture of a large number of quasi-random neural sources across the entire cortex (broadband background EEG) and a small number of more localized cortical sources whose power spectra are narrow-band (oscillatory).
[Nunez, 2006; He, 2014]



Decomposition of the power spectrum density (PSD) into the fractal (scale-free) and oscillatory components underlying the eyes-closed awake state recorded after mirror-box training. Plots represent means of the IRASA decomposition computed separately for 4-s-long overlapping segments of approximately two minutes long resting block at two central EEG electrodes C3 and C4. Frequencies were restricted to the range 1-25 Hz for the visualization purposes..

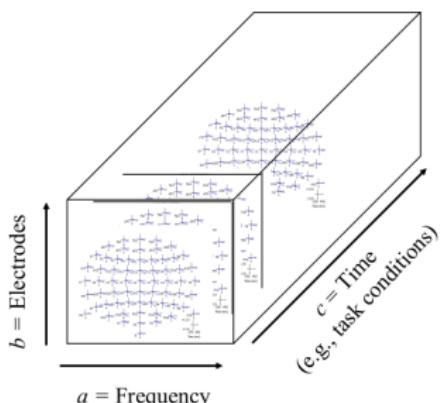
- Data matrix construction:

$$\mathbf{X}_{(I \times J \times K)}$$

I - time segments

J - electrodes

K - power or amplitude (or log+)



$$\begin{array}{c} \text{[Stack of } F \text{ matrices]} \\ = \sum_{f=1}^F \end{array}$$

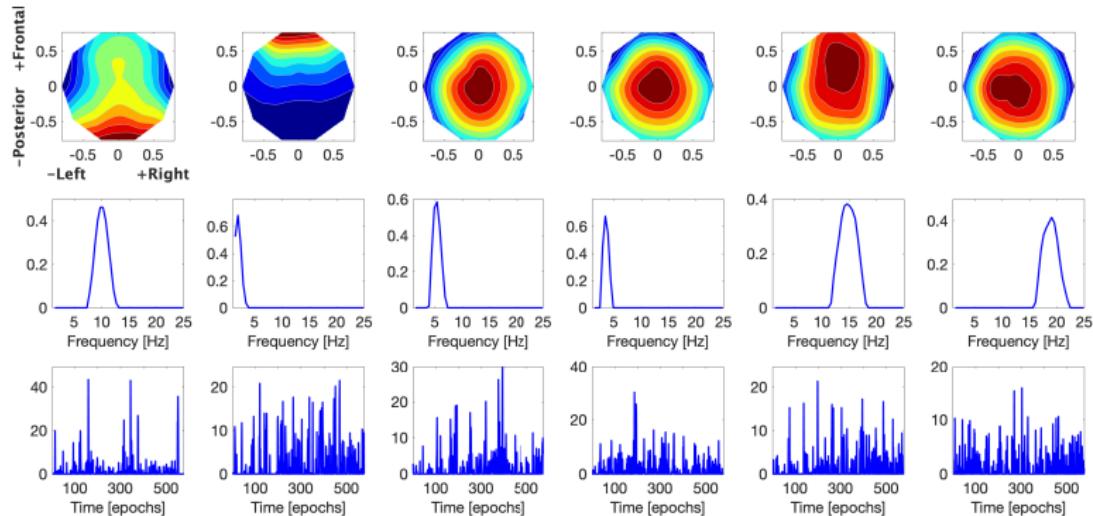
- The PARAFAC model with *F* factors:

$$x_{ijk} = \sum_{f=1}^F a_{if} b_{jf} c_{kf} + \epsilon_{ijk}$$

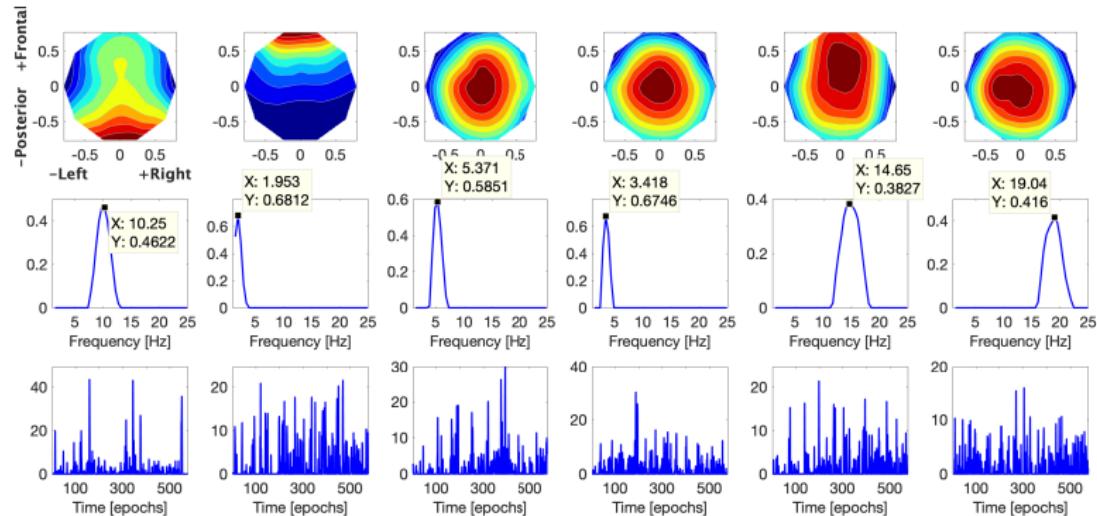
- The criterion:

$$\min_{a_{if}, b_{jf}, c_{kf}} \| x_{ijk} - \sum_{f=1}^F a_{if} b_{jf} c_{kf} \|^2$$

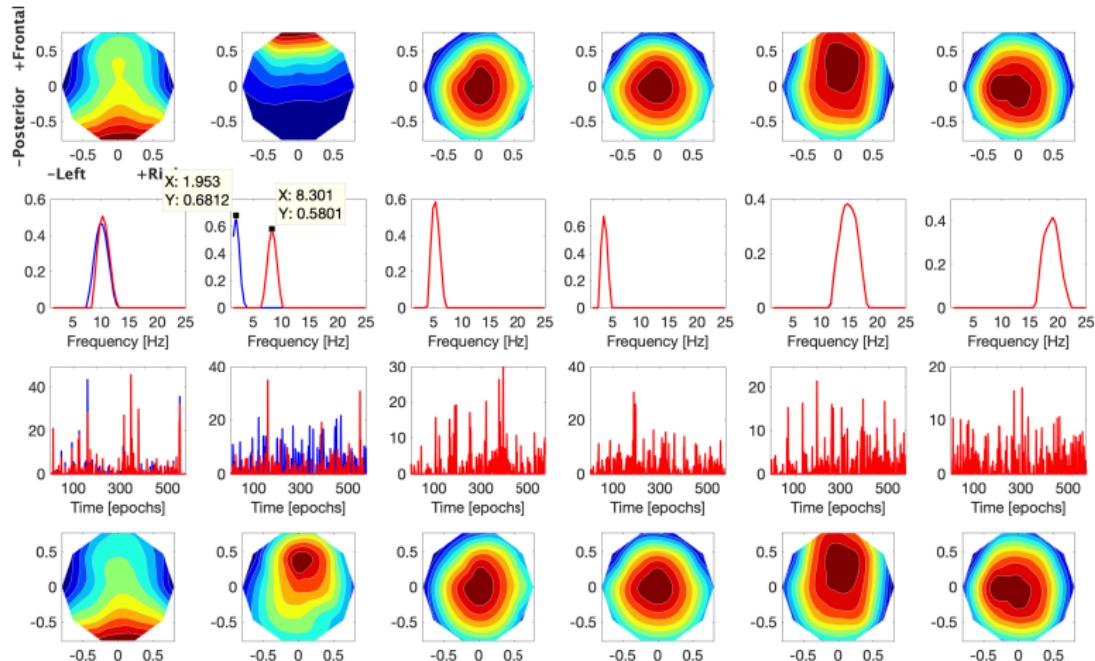
PARAFAC - single subject



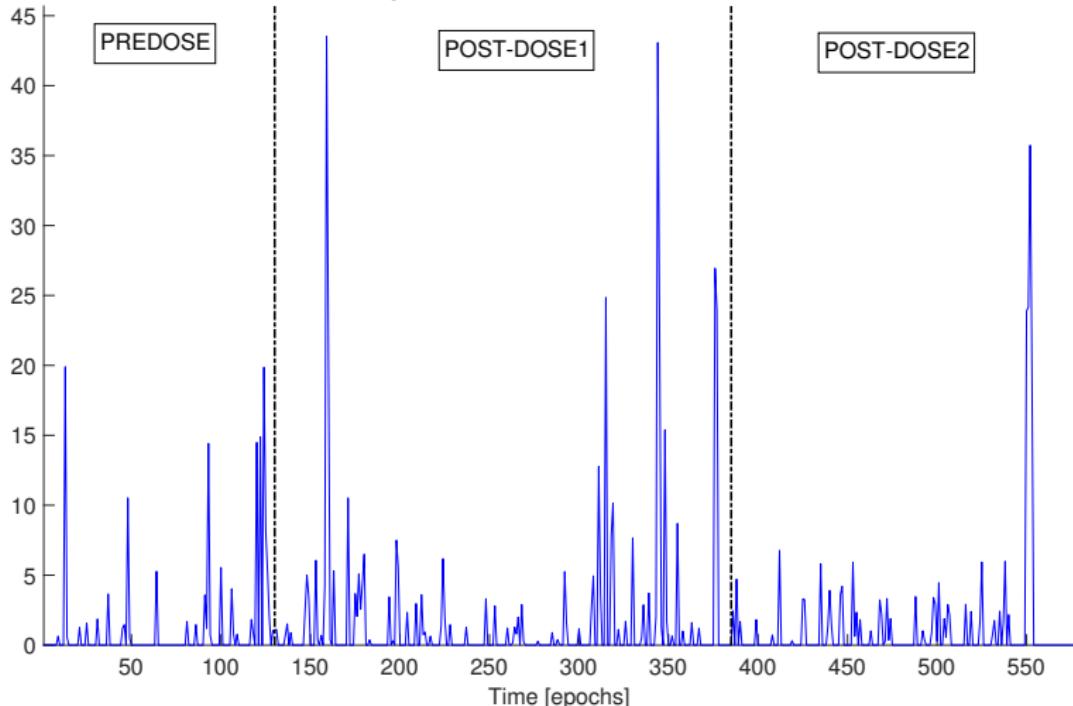
PARAFAC - single subject



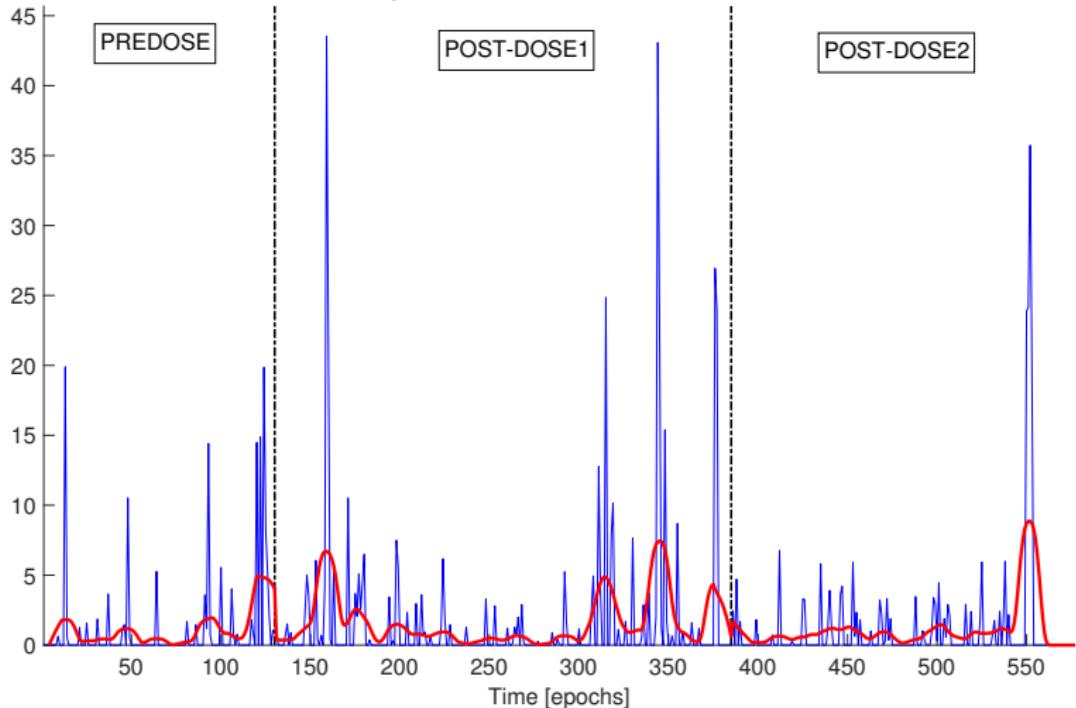
PARAFAC - single subject (remove eye-blink atom and re-run)



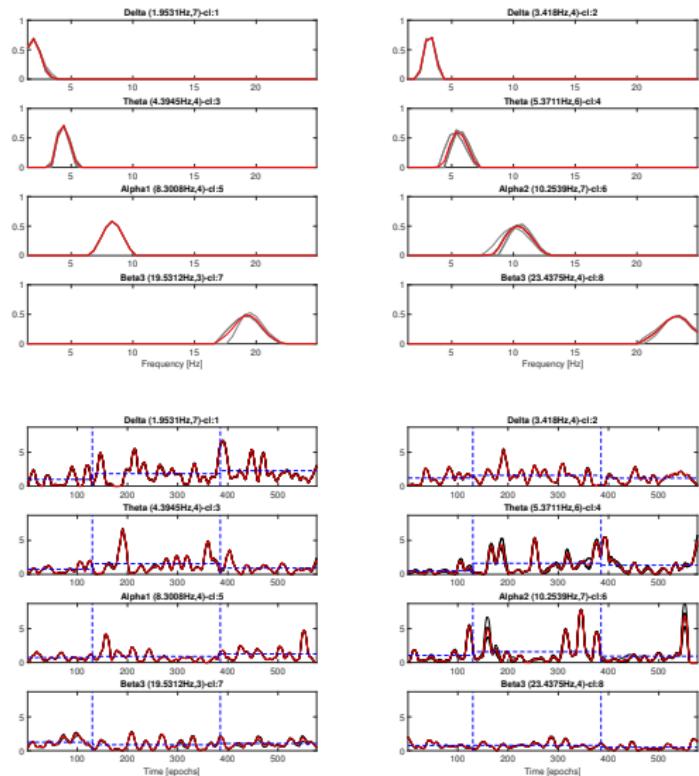
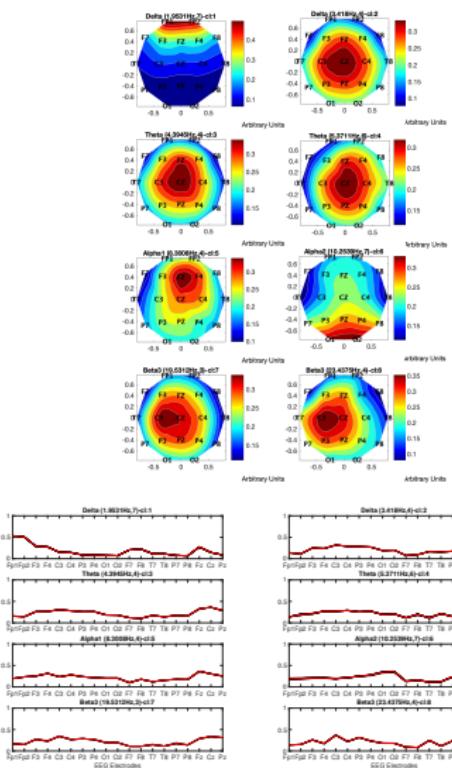
Alpha PARAFAC Atom Time-scores



Alpha PARAFAC Atom Time-scores



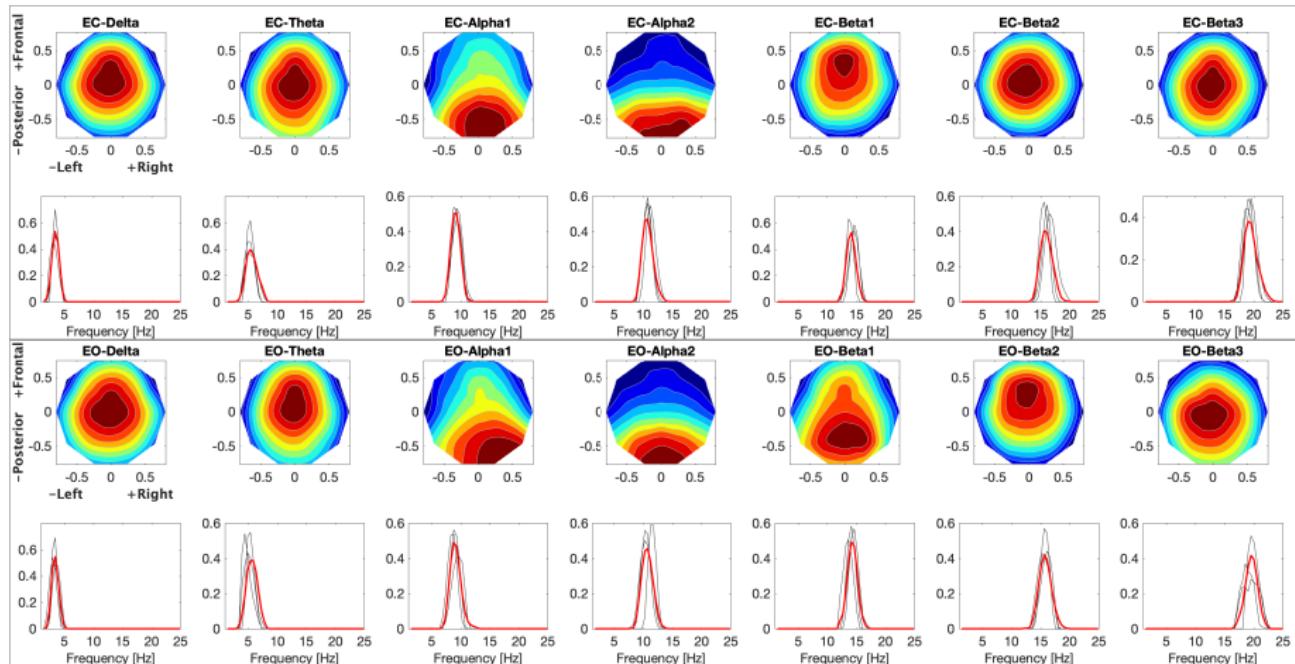
Clustering PARAFAC runs - DBSCAN (by space, frequency and time-scores)



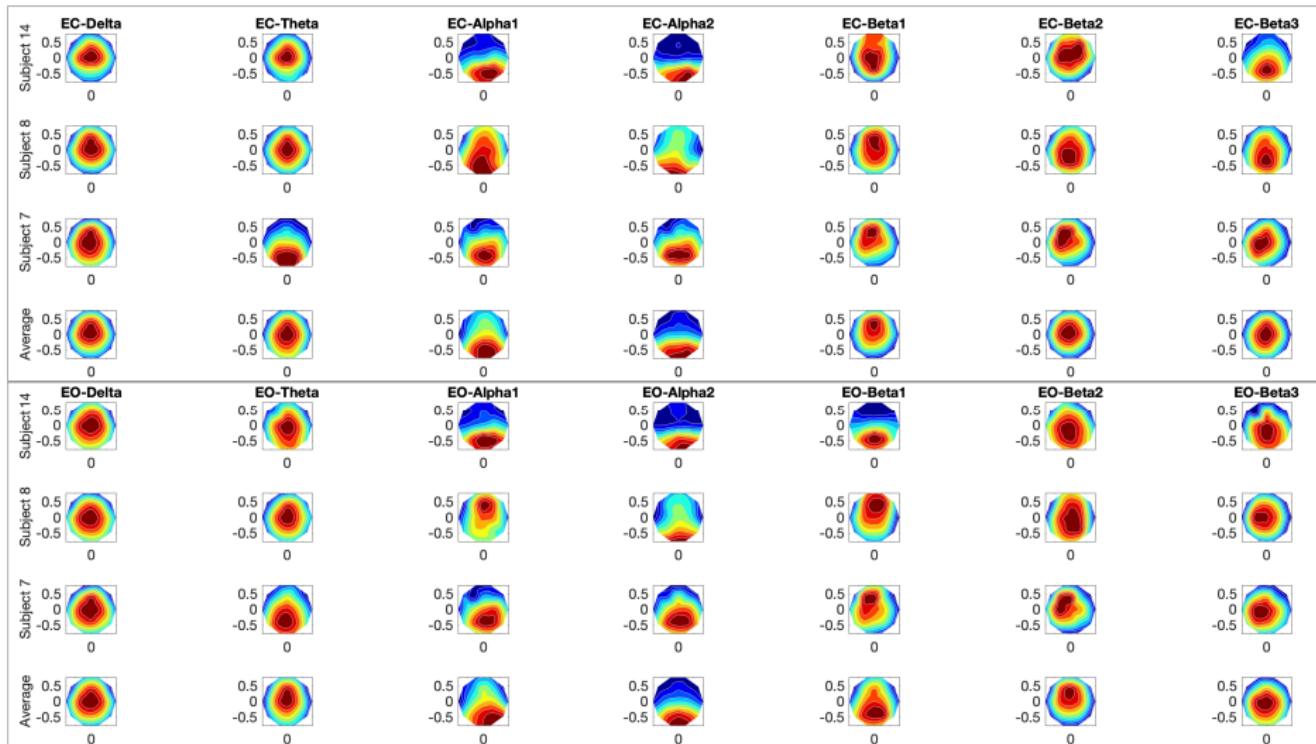
Space PARAFAC weights

Frequency PARAFAC weights (top) and time scores

Averaged space and frequency PARAFAC weights (8 subjects)



Variability of the PARAFAC spatial weights: individual subjects

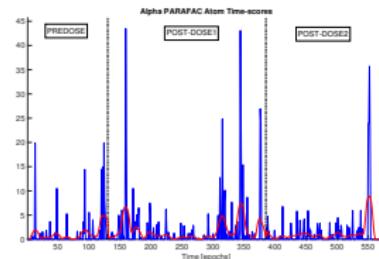


A statistic(s) of time-scores can be computed

- mean over time-points
- frequency, duration of activation
- etc.

and used for formal testing

- ANOVA or ANCOVA,
- exposure response
- etc.



```
PROC MIXED DATA=Data_modelB EMPIRICAL;
  CLASS Subject Treatment Time;
  BY Band;
  MODEL Pz_Pre_Diff = PreDose Treatment Time Treatment*Time / SOLUTION CL;
  REPEATED Time / SUBJECT = subject TYPE = AR(1);
  LSMEANS Treatment Time / CL;
RUN;
```

- Using the approach we analyzed a collection of data from:
 - two pharmaco-clinical studies
 - longitudinal study focused on motor neurorehabilitation
 - neurobiofeedback studies
- We found that:

- Using the approach we analyzed a collection of data from:
 - two pharmaco-clinical studies
 - longitudinal study focused on motor neurorehabilitation
 - neurobiofeedback studies
- We found that:
 - A discrete set of common PARAFAC atoms can be identified across different task conditions and subjects
 - The atoms show a high day-to-day stability
 - Time-scores allow to built parsimonious EEG representation suitable for formal drug effects testing
 - Pharmaco-clinical studies indicate that effects not observed with standard QEEG testing can be found

Thank you !

The screenshot shows the homepage of the Pacific Development and Technology website. At the top, there is a navigation bar with the company logo 'PACDEL' and the text 'PACIFIC DEVELOPMENT & TECHNOLOGY'. The navigation menu includes links for HOME, ABOUT US, TEAM, SERVICES, OUR PUBLICATIONS, REFERENCES, and CONTACT. Below the navigation bar is a large banner featuring a hand holding a glowing brain-like structure against a dark background with a network of glowing points. A yellow callout box in the upper left corner of the banner contains the text 'PACIFIC DEVELOPMENT AND TECHNOLOGY'. Below this, a paragraph of text reads: 'provides designs and solutions for data analysis and intelligent computation. We serve the scientific, engineering, and hi-tech communities in:'. To the right of this text are two columns of services, each preceded by a blue arrow:

EEG and ERP Analytics	Machine Learning Applications
Custom Programming	System Development and Testing
Statistical Analysis of Experiments	Scientific Management, Writing and Reporting

At the bottom of the banner, there is a copyright notice: '© 2017 Pacific Development and Technology, LLC. All rights reserved.' and a credit line: 'Responsive Web Design by Artweby.cz'.

www.pacdel.com

Acknowledgments

The work was also supported by the Slovak Research and Development Agency (projects APVV-16-0202 and APVV-0668-12) and by the Slovak Grant Agency for Science (projects VEGA-2/0011/16 and VEGA 2/0151/18).