Persistent Homology tested: functional & effective networks, fMRI & EEG, schizophrenia & seizures

Jaroslav Hlinka[1,2], Luigi Caputi[1,3], Anna Pidnebesna[1,2]

[1] Institute of Computer Science, Czech Academy of Sciences, Prague, Czech Republic
[2] National Institute of Mental Health, Klecany, Czech Republic
[3] University of Aberdeen, United Kingdom

Study supported by Czech Health Research Council Project NV17-28427A and Czech Science Foundation project 21-17211S.

Introduction

Distinguishing normal and abnormal brain states is a key neuroscientific challenge. Topological Data Analysis (TDA [1]), despite its relative novelty, already attracted attention of neuroscientists. We conjecture that its prominent tool of persistent homology (PH) may benefit from going beyond analysing structural and functional connectivity (FC) to effective connectivity (EC) graphs. We assess the potential of PH by testing its discriminatory power in two enigmatic examples of disease-related brain connectivity alterations: epilepsy seizures and schizophrenia. We estimate connectivity from functional magnetic resonance imaging (fMRI) and electrophysiology (EEG) data, employ a range of PH-based features and quantify ability to distinguish healthy from diseased brain states by applying a support vector machine (SVM). We compare this novel approach to using standard undirected PH and raw EC/FC [2].

Data

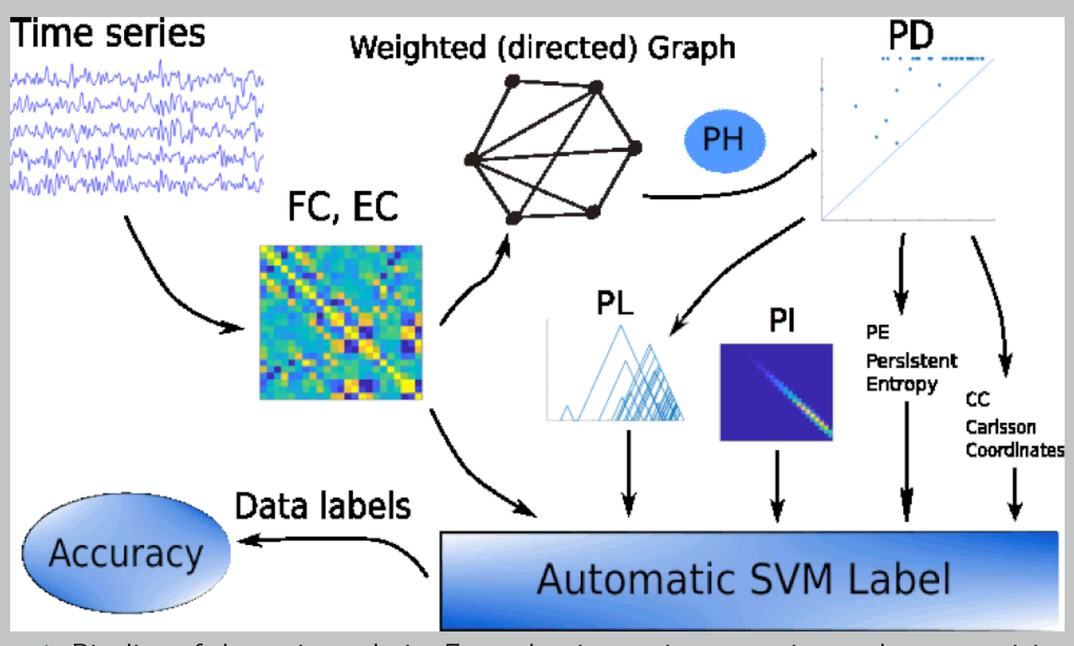

Figure 1: Pipeline of the main analysis. From the time series, we estimate the connectivity matrix, based on which build a weighted graph. After estimating Persistent Homology (PH) of the graph, we get Persistent Diagram (PD), that is represented by different features (Persistent Landscape PL, Persistent Image PI, Persistent Entropy PE, Carlsson Coordinates CC) for classification. Finally, classification based on PH features is compared with classification using matrices itself.

1) fMRI: 10 minute resting state from 90 schizophrenia patients and 90 healthy controls. GRE-EPI data (3T MR Siemens Magnetom Trio): voxel 3x3x3mm, TR/TE 2000/30ms; T1w image (TR/TE/TI = 2300/4.6/900 ms, voxel 1x1x1mm for anatomical reference. Realignment and unwarping, slice-timing correction, segmentation (white matter and cerebrospinal fluid), normalization to MNI space (CONN defaultMNI), outlier detection, smoothing 8mm kernel. Six head-motion parameters with first order derivatives and five PC of WM and CSF signal regressed out; detrending, band-pass [0.009-0.08Hz], average BOLD signal for 90 regions (AAL).
2) Scalp EEG: (23 electrodes, fs=256Hz, band-pass filter [1-70Hz], notch filter at 50Hz, global signal removal) from 18 pediatric subjects with intractable seizures were used [3], providing 102 epileptic events of length 20 to 120 seconds. Non-epileptic segments of the same length chosen randomly from each record. For each subject we average all the connectivity matrices for ictal (interictal) periods, leaving two connectivity matrices per subject.
(3) Intracranial EEG: from 16 patients with pharmacoresistant epilepsies [4]. We consider the recordings of the first 30 seconds of the first seizure ('ictal' data), and the 30 seconds segment starting 1 min before the first seizure ('preictal' data). The first minute of interictal data provides baseline connectivity to be subtracted.

Methods

Pearson correlation/Granger Causality for FC/EC; selection of common PH features extracted and fed to linear SVM classification (healthy/patient from fMRI, ictal/interictal from (i)EEG); see Figure 1 for pipeline visualization.

Results

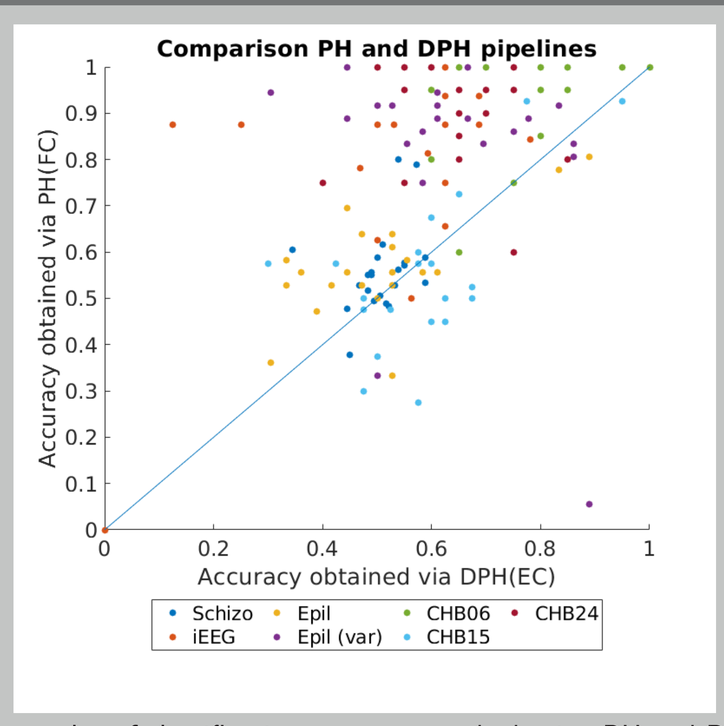

Figure 2: Scatter plot of classification accuracy reached using PH and DPH pipelines.

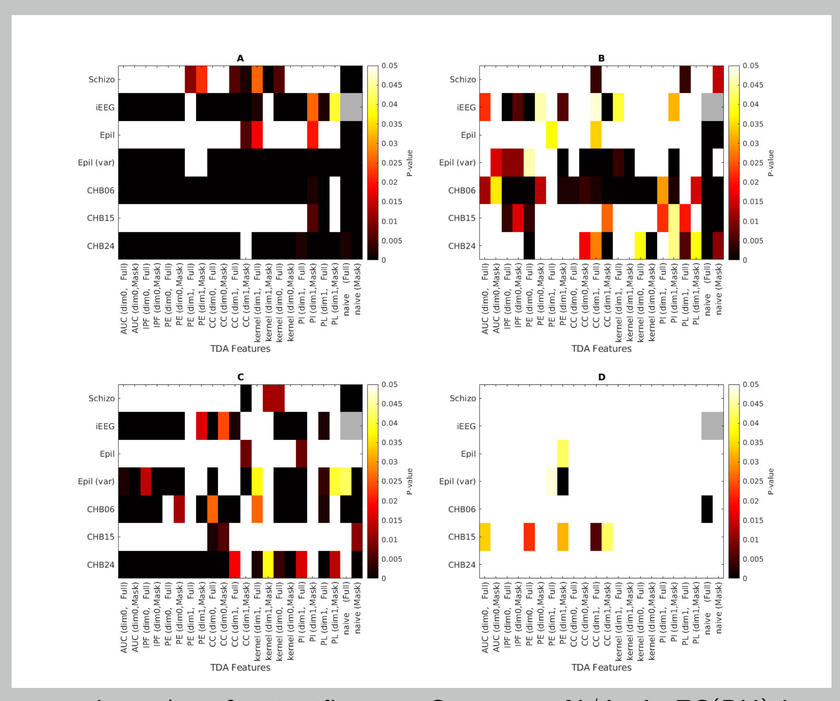

Figure 3: Uncorrected p-values for significance. Grey area: N/A. A. FC(PH)-based accuracy is higher than random. B. EC(DPH)-based accuracy is higher than random. C. FC(PH)-based accuracy is higher than EC(DPH)-based. D. EC(DPH)-based accuracy is higher FC(PH)-based.

In the schizophrenia classification, TDA performs close to random, while classifications from raw connectivity perform substantially better; potentially due to topographical (rather than topological) specificity of the differences. In seizure discrimination from scalp EEG, PH features reached comparable performance to raw connectivity, albeit with typically smaller accuracies obtained for the EC compared to the FC. Specific niche for PH opens when direct comparison of connectivity matrices is unsuitable - such as for intracranial EEG with individual number and location of measurements. While standard PH performed overall better than directed PH, this could be due to imperfect estimation of EC by GC.

Discussion and conclusions

We showed directed PH can also detect altered brain connectivity. However, comparison to standard PH and the use of the raw FC/EC matrices reveals challenges to be overcome to fully utilize the theoretical promise of TDA and establish it as a pragmatic tool in neuroimaging. These include topographical versus topological specificity of the brain alterations, inter-individual biases and homogeneous/heterogeneous sampling.

References

[1] Carlsson G. Topology and data. Bull. Amer. Math. Soc. 2009; 46:255-308. doi.org/10.1090/ S0273-0979-09-01249-X.
[2] Caputi L, Pidnebesna A, Hlinka J. Promises and pitfalls of Topological Data Analysis for brain connectivity analysis. NeuroImage. 2021; doi.org/10.1016/j.neuroimage.2021.118245
[3] https://physionet.org/content/chbmit/1.0.0/
[4] http://ieeg-swez.ethz.ch/

hlinka@cs.cas.cz