Comparing Brain Connectivity Fingerprints of Singular-Node Motifs

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Abstract

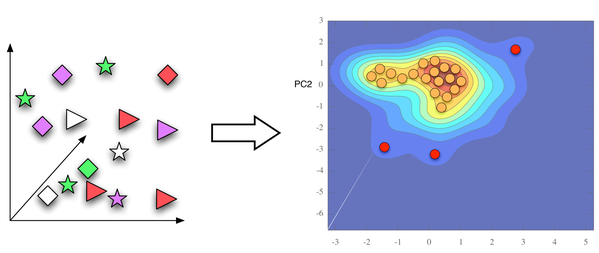
Network analyses of subjects suffering from brain diseases (e.g. epilepsy) revealed underlying changes in network topology; Identifying such disease-specific deviations can benefit both diagnosis and treatment. We have recently presented a new methodology that can potentially yield such knowledge [3] by determining global singular nodes from local network features. This technique involves a multi-step workflow that requires few but crucial parameters, which had to be chosen by hand. We now automated parameter determination, such that the technique can be applied to a large number of networks without user interaction. We use this to provide a case study of brain connectivity networks in patients and control subjects identifying differences in the number and classes of singular-node motifs. In conclusion, we developed an automatic fingerprinting tool for brain connectivity comparisons in clinical and experimental studies.

1. Introduction

COMMONLY, networks are characterised by measurements that allow a precise quantification of their structure [1, 2], which facilitates their classification and comparison. Indeed, situations exist where many networks must be compared to each other in order to gain insights. Corresponding examples are families of protein interaction networks, brain connectivity networks in patient- and control-populations, or time-dependent (developing or declining) networks [5]. Comparing such sets of networks requires consistent approaches, which are often non-trivial, because networks differ in size or they comprise a disjoint sets of nodes. We have recently proposed a new methodology for such comparative studies [3], which we further refined lately. We applied the resulting tools to brain networks (Section 3) and identified a singular node motif that might be specific to late life depression.

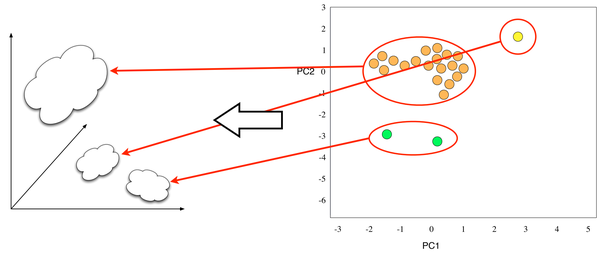
2. Methodology

Step 1:



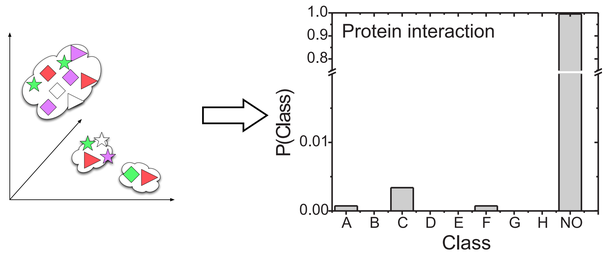
A set of *local measurements* is chosen to characterise the network. These measures are computed for all nodes (*feature vectors*) and mapped to 2D-space using PCA. Probabilities are estimated for all nodes (Parzen window approach) in order to identify the least probable ones (*singular nodes*).

Step 2:



Singular nodes are clustered to *motif groups*, which are mapped back to the full feature space. Corresponding Voronoi cells are determined (using a modified Mahalanobis distance) and joined if they are too close to each other (*motif regions*).

Step 3:



Relative frequencies of nodes falling into motif regions yield a characteristic *fingerprint* of the network, which can be also be computed for other networks for comparison.

APPLYING this work-flow to networks from different domains (air transportation, protein-protein interaction, Roget's thesaurus) showed that each of them involves specific singular motifs (Fig. 1). Similarly, brain networks are likely to exhibit characteristic motifs, but which might be altered in subjects suffering from brain diseases. We thus work on identifying disease-specific deviations relevant to diagnosis and treatment.

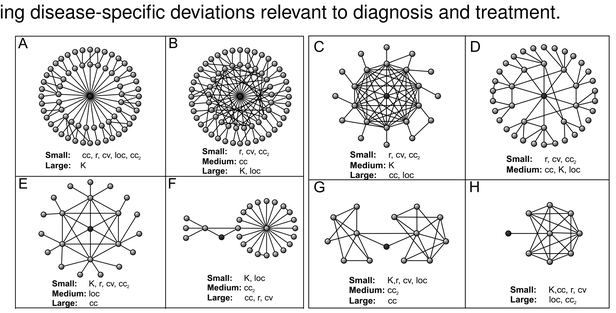


Figure 1: *Singular network motifs identified in three considered real-world networks [3] (singular node black): (A) global relay hub, (B) local relay hub, (C) local integrator, (D) integrator, (E) community center, (F) cluster-tail, (G) cluster-cluster, and (H) tail.*

3. Early Results

DEFAULT mode networks were extracted from fMRI resting state recordings in 15 late-life depression (LLD) patients and 16 healthy control subjects. Networks (à 1105 nodes) from both groups differ in variety of expressed network motifs (Fig. 2). Other than in healthy subjects, we could identify a singular node motif (similar to Fig. 1H) that occurs predominantly and frequently in LLD patients.

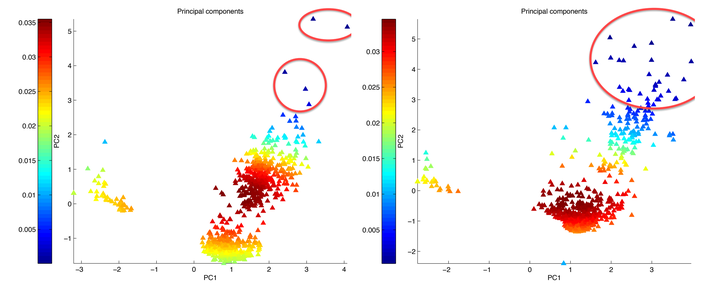


Figure 2: *Dissimilarity of reduced feature vectors for a control- (left) and LLD-subject (right): Both individuals differ widely in number of singular nodes (5 vs. 35, highlighted with circles) as well in variability of local measures. Patient-networks generally show a broader variety of outliers, but few motifs are found consistently across different patients.*

4. Conclusions

OUR improved analysis-workflow (Section 2) now allows to process networks automatically, which makes it possible to fingerprint large numbers of networks. Preliminary results indicate that such studies may reveal important insights into disease-specific brain network characteristics. Our ongoing modelling work aims at combining identified features in a probabilistic framework for network classification.
We will make the implementation of the automated workflow available on our website (`http://www.biological-networks.org/`). Two versions of the code are in preparation: The first one requires Matlab (Mathworks Inc, Natick, USA) and allows the user to apply the workflow using a graphical user interface. The other one is a command line utility that either requires Matlab or the free equivalent Octave [4] and it can be easily used to batch process many networks without user interaction.

References

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