

Modular organization of brain connectivity networks beyond the resolution limit

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Introduction

Neuroimaging methods, like functional MRI, have shown that the brain consists of functionally specialized modules hierarchically organized to form highly integrated networks. Graph theory provides a valuable framework for the analysis of the modular structure of this complex architecture. Indeed the brain can be represented as a graph comprising N nodes connected by M edges. The nodes correspond to brain regions and the edges to measures of inter-regional interaction.

The most widely used metric to investigate modular structure of FC networks is **Newman's Modularity** [3], which identifies modules within which links are more abundant than expected on the basis of a random network. However, this approach is **limited in its ability to detect relatively small communities, a problem known as resolution limit**. We have recently demonstrated [4] that a quality function grounded in probability theory dubbed **Surprise** [1, 5] is resolution-limit free and may be applied to detect tightly knit clusters regardless of their size.

Here we demonstrate that **Surprise** and its weighted counterpart **Asymptotical Surprise** can be applied to detect functional modules in brain connectivity datasets **beyond the resolution limit**. We benchmark them in a set of tests where we manually control the noise level as well as the number of subjects involved in a typical resting state fMRI experiment. Finally we apply them to a real-world rs-fMRI dataset, to show the heterogeneity of size of its functional modules.

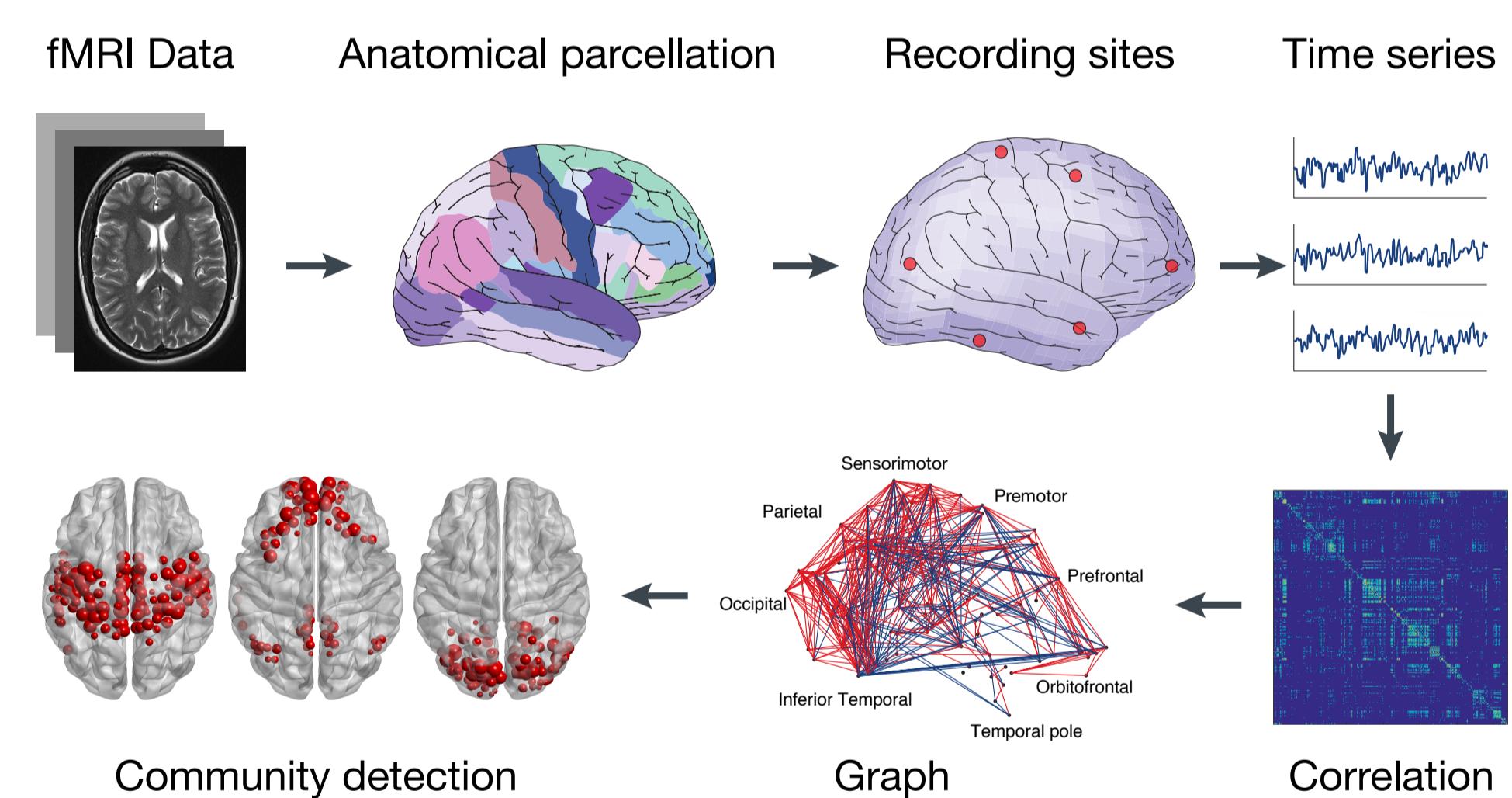


Figure 1: Workflow in graph-theoretical analysis of brain functional connectivity.

Methods

Surprise S and **Asymptotical Surprise** S_a are defined as:

$$S = \sum_{i=m_\zeta}^m \frac{\binom{p_\zeta}{i} \binom{p-p_\zeta}{m-i}}{\binom{p}{m}}, \quad S_a = m D_{KL} \left(\frac{m_\zeta}{m} \parallel \frac{p_\zeta}{p} \right) \quad (1)$$

where m_ζ is the total weight of intracluster weights, p_ζ is the total intracluster number of pairs, m is the total sum of link weights, p is the total number of pairs in the graph. We studied the properties of **Surprise** with respect to Newman's Modularity in terms of degeneracy and resolution limit. We specifically designed an optimization algorithm, named **FAGSO**, for community detection based on Surprise maximization.

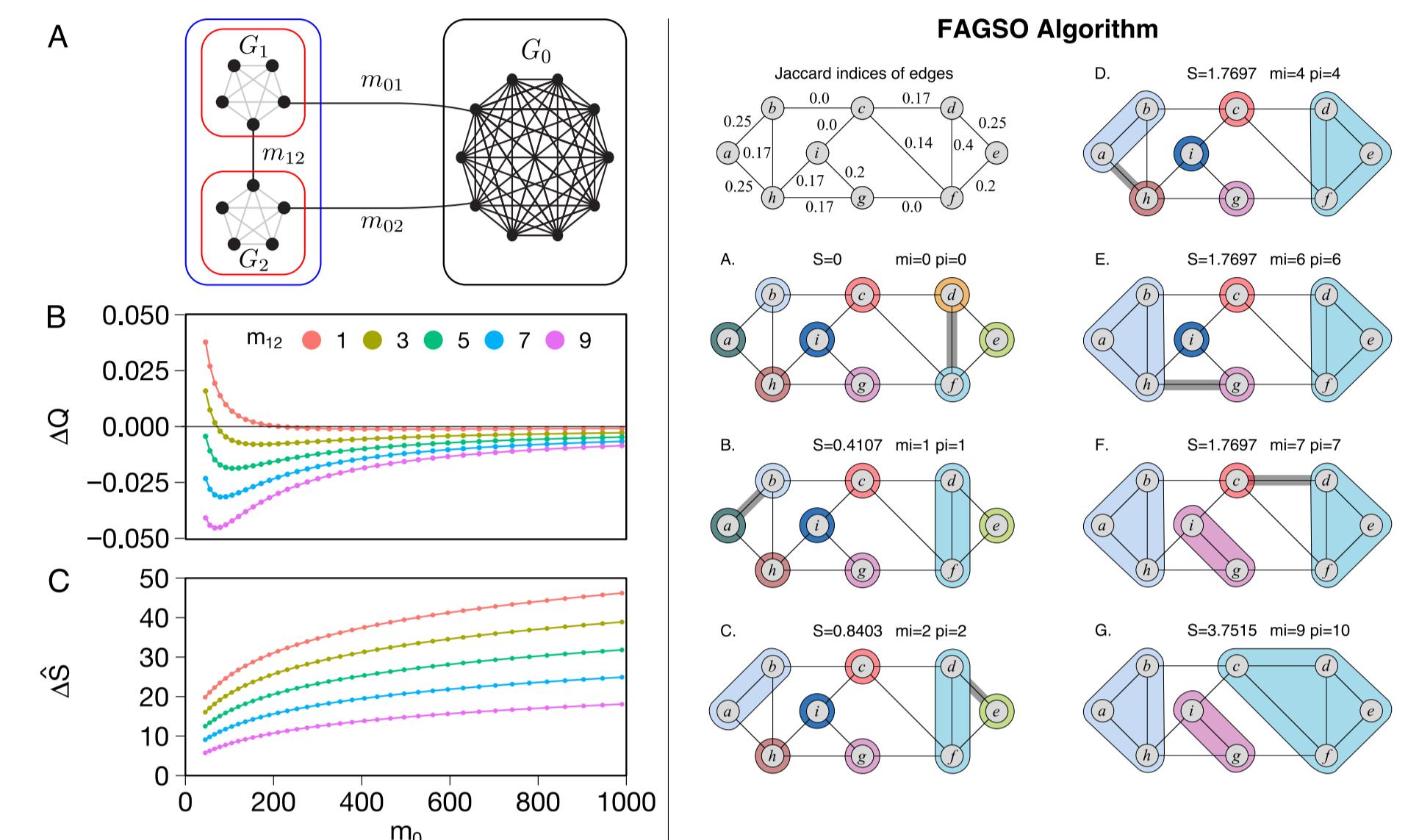


Figure 2: (LEFT) The onset of the resolution limit in optimal partition of a pathological network (A). With larger size of G_0 module, the two cliques G_1 and G_2 are merged by Modularity optimization (B), but never merged by Surprise optimization (C). (RIGHT) FAGSO works by iterative aggregation of endpoint of edges that lead to maximum Surprise increment. It first computes the Jaccard indices of every edges, sort them in decreasing order and then start the aggregation.

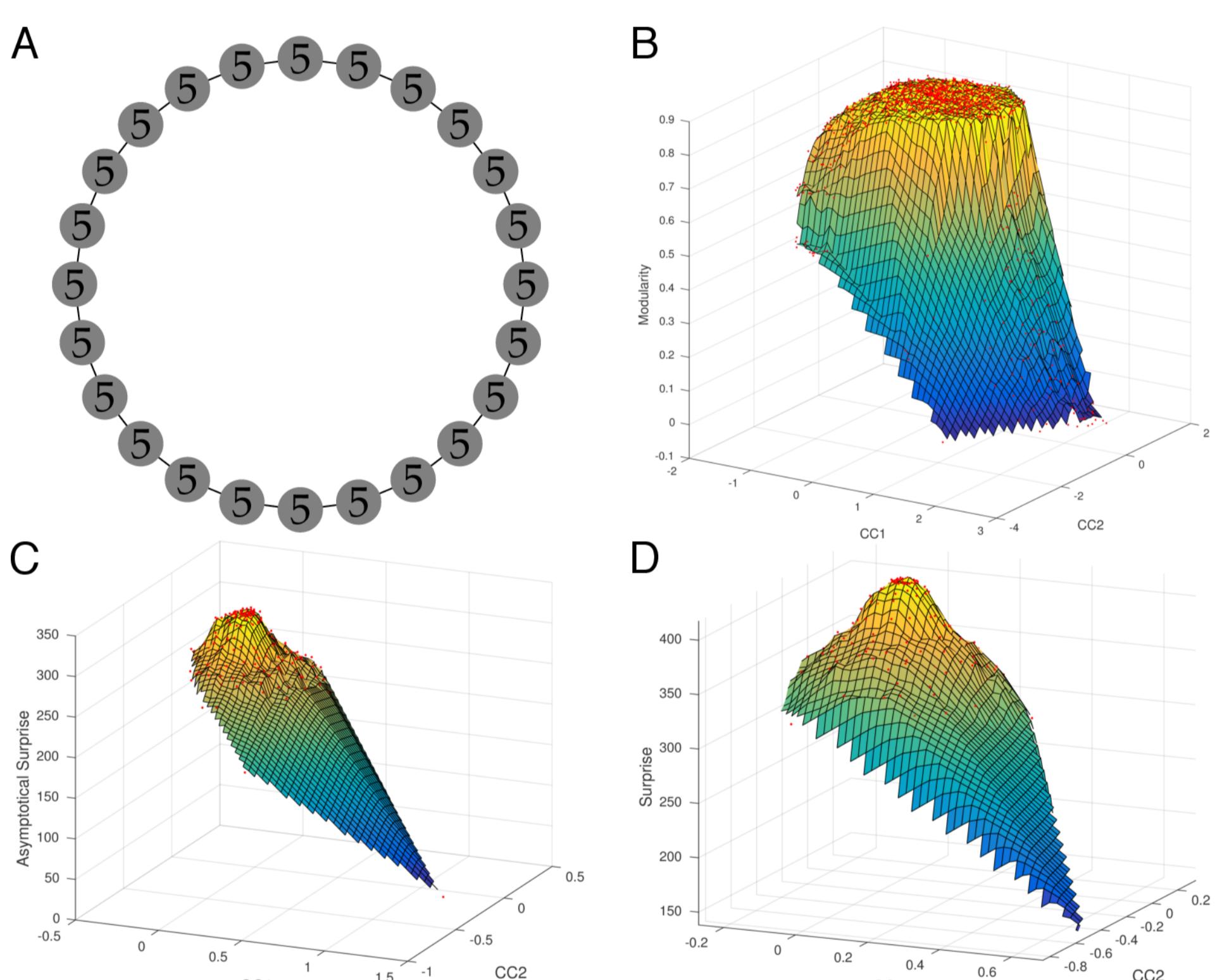


Figure 3: Degeneracy landscape after dimension reduction of optimal partitions for Modularity (B), Surprise (C) and Asymptotical Surprise (D) on a benchmark ring of cliques structure consisting of 30 K_5 graphs (A). The landscape B has a broad and flat top, meaning that individual optimal partitions are different but with similar values of Modularity.

We benchmarked the performance of Surprise and Asymptotical against widely applied algorithms (**Newman's Modularity** and **Infomap**), and quantitatively assess their performance in synthetic correlation networks with different levels of noise, and in human resting state functional connectivity data. We used **Normalized Mutual Information (NMI)** and classical contingency table based measures like **Sensitivity** and **Specificity** to compare the performances of the three methods.

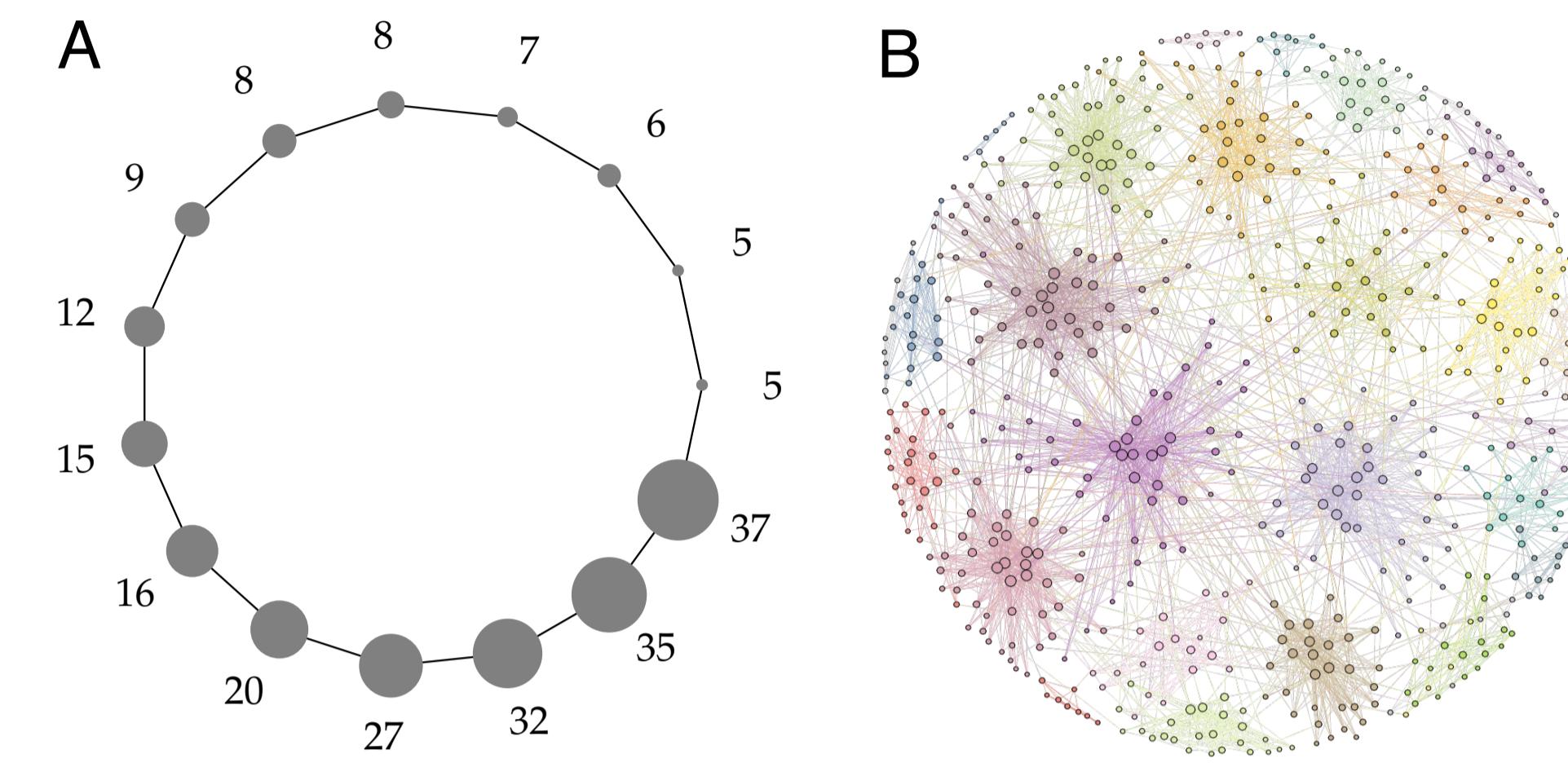


Figure 4: Benchmark networks used to study the performance of Surprise/Asymptotical Surprise optimization. (A) is a ring of cliques connected by one edge whose sizes are sampled from a power-law, (B) is an LFR [2] benchmark network, whose community structure defined a-priori.

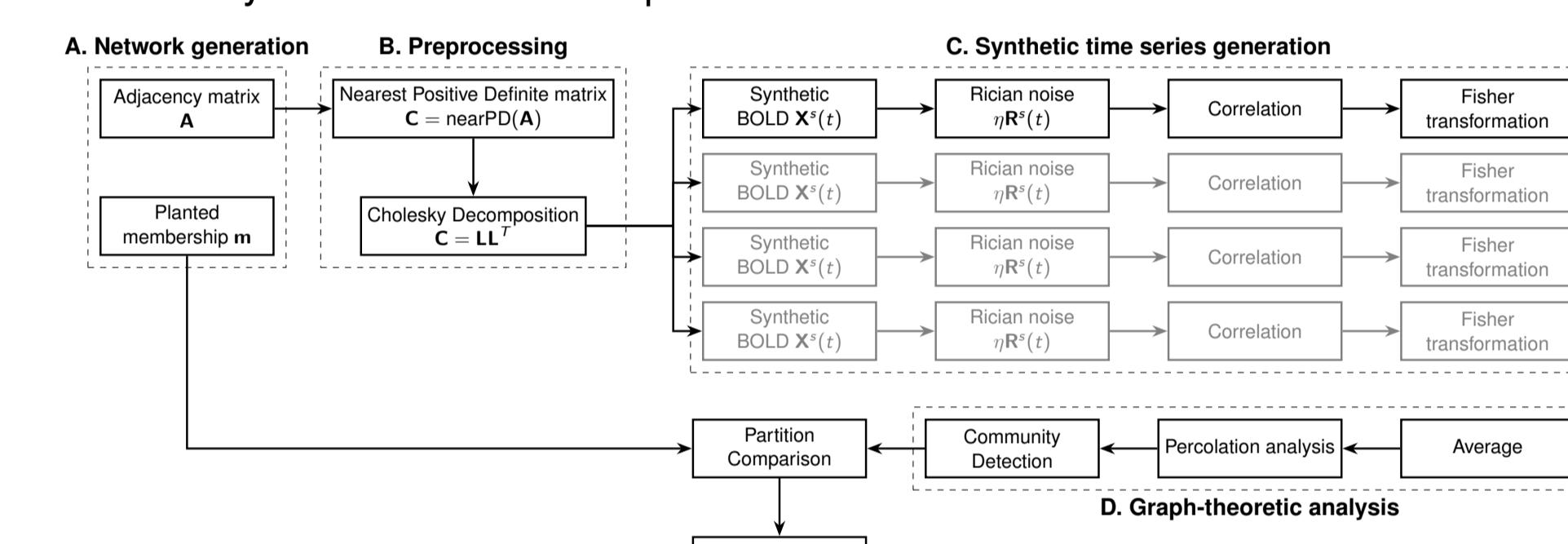


Figure 5: Workflow of synthetic benchmarks. Starting from a network with known community structure (A), after computing the Cholesky decomposition of its adjacency matrix (B), we generate a number of synthetic time series remnant of the BOLD signal but with controllable noise parameters (C) and use the structure of the original network to set their community structure. After average of all subjects and thresholding of the group-level network (D), we apply a community detection algorithm (Modularity, Infomap or FAGSO) and compare the resulting community structure with the planted one. The result is the Normalized Mutual Information (NMI) that tells how much two clusterings are similar, the higher the better.

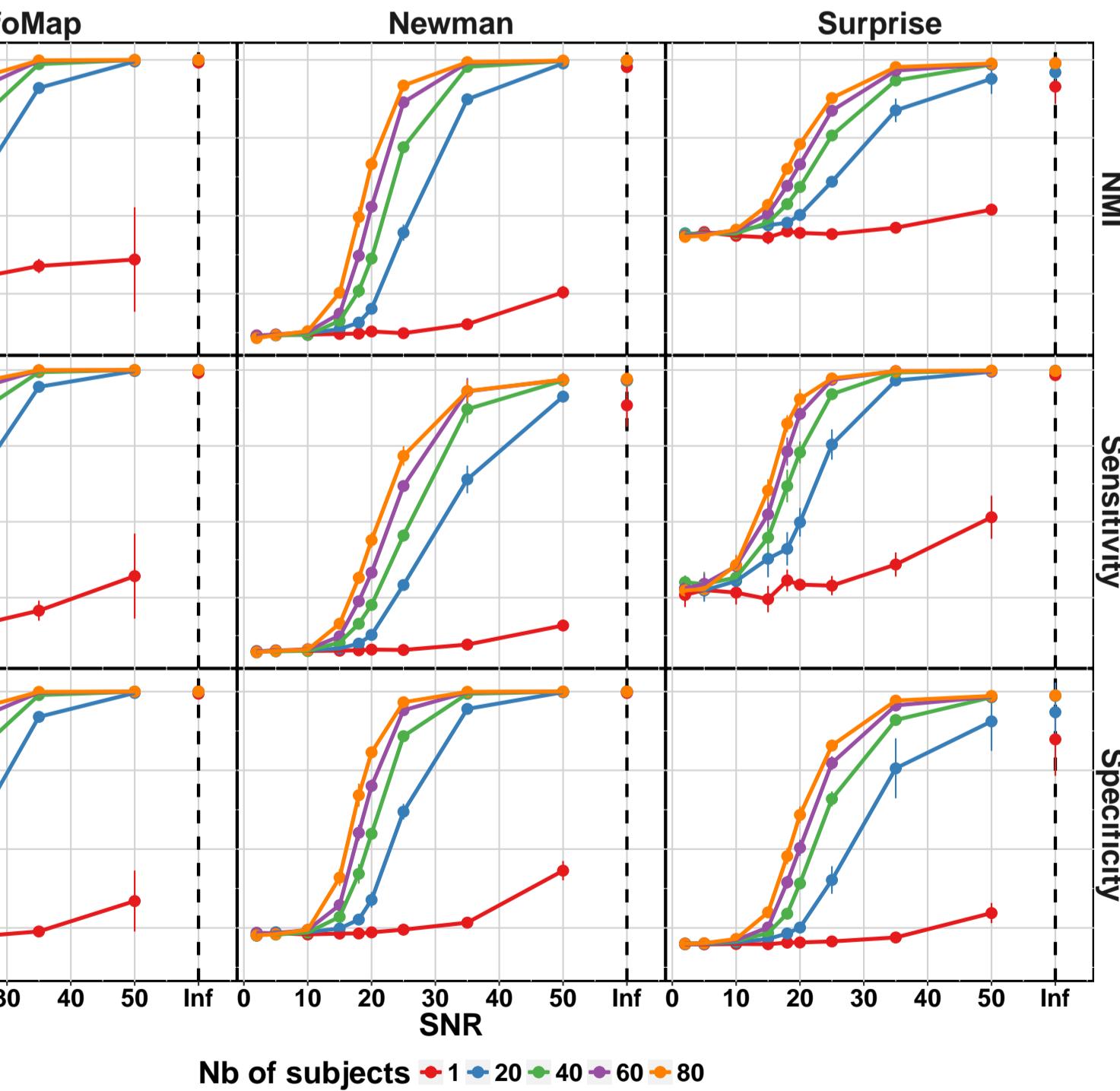
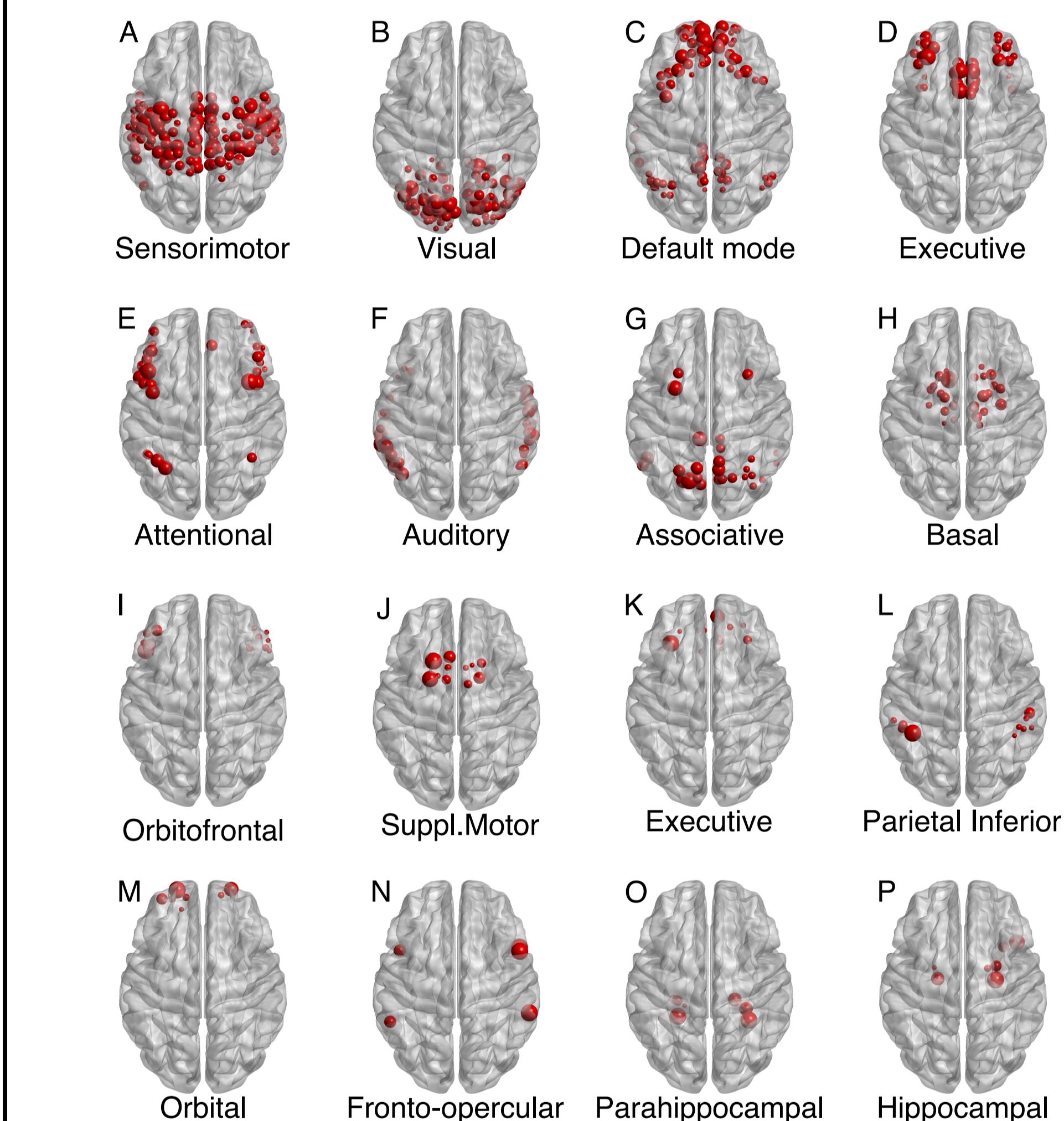


Figure 6: Profiles of NMI, Sensitivity and Specificity for the community detection of LFR benchmark at different levels of noise (Signal-To-Noise-Ratio) and virtual number of subjects. Surprise performs well compared to state-of-art algorithms such Infomap and Newman's Modularity, in particular the Sensitivity to small modules is increased as it does not suffer the resolution limit.

Results

In synthetic networks, Surprise shows better sensitivity and non-inferior specificity in the detection of ground-truth structures, particularly in the presence of noise and variability such as those observed in experimental functional MRI data. Surprise maximization in human resting state networks reveals the presence of a rich structure of modules with heterogeneous size distribution undetectable by current methods.



Conclusions

Our results indicate that the resolution limit may have affected previous analyses of brain connectivity networks. Surprise is a promising alternative to current methods, and demonstrates the presence of functional modules of very different sizes in resting state networks. This calls for a revisit of some of the current models of brain modular organization.

References

- [1] R. Aldecoa and I. Marin. Deciphering network community structure by surprise. *PLoS ONE*, 6(9):e24195, 2011.
- [2] A. Lancichinetti, S. Fortunato, and F. Radicchi. Benchmark graphs for testing community detection algorithms. *Phys. Rev. E*, 78:046110, 2008.
- [3] M. E. J. Newman. Modularity and community structure in networks. *Proc. Natl. Acad. Sci. U.S.A.*, 103(23):8577–8582, 2006.
- [4] C. Nicolini and A. Bifone. Modular structure of brain functional networks: breaking the resolution limit by surprise. *Sci. Rep.*, 6:19250, 2016.
- [5] V. Traag, R. Aldecoa, and J.-C. Delvenne. Detecting communities using asymptotical surprise. *Phys. Rev. E*, 92(2):022816, aug 2015.

