Mining higher-order triadic interactions

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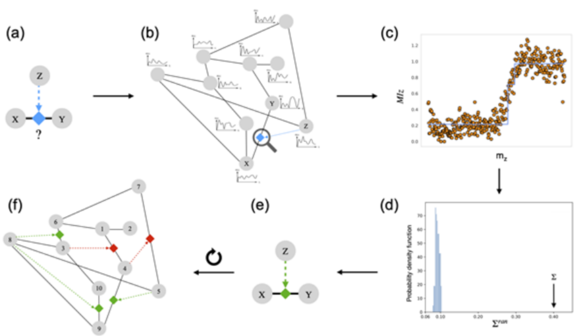
Complex systems often involve higher-order interactions which require us to go beyond their description in terms of pairwise networks. Higher-order networks [1] are attracting large scientific interest in recent years. However, a key challenge is to infer higher-order interactions from data. Triadic interactions [2] are a fundamental type of higher-order interactions that occur when one node regulates the interaction between two other nodes. Triadic interactions are known to be key in ecosystems, in neuronal networks, and in gene regulation networks. However, information theory approaches to mine triadic interactions are still lacking.

In this work we explore the fundamental dynamical properties of networks with triadic interactions between continuous variables. We formulate a general model of networks with triadic interactions. Moreover we propose an information theory framework and an algorithm, visualised in Figure 1, validated on the triadic model that is able to mine triadic interactions from data. To detect dependence and independence of variables we use the mutual information MI and the mutual information conditioned on Z: $\mathrm{MI}_Z(m) = \mathrm{MI}(X, Y \mid Z = z_m)$.



To verify the performance of this approach the described algorithm is applied to a model with strong triadic interactions. It is based on a Gaussian process using a Laplacian to encode the topological structure, which is replaced by a triadic Laplacian in the presence of triadic interactions. Simulations on this network show a strong dependence of $\mathrm{MI}_Z(m)$ on m for the triples of nodes involved in triadic interactions.

This algorithm is not only applied on synthetic data but also on Acute Myeloid Leukemia gene expression data. For instance, understanding the extent to which a modulator promotes or inhibits the interplay between a transcription factor and its target gene is crucial for deciphering gene regulation mechanisms. Here, we aim at finding new candidates for triadic interactions as well as validating already established biological results.

In conclusion, our work proposes a new information theoretic approach to mine triadic interactions and reveals important aspects of higher-order triadic interactions that are often ignored, yet can transform our understanding of complex systems and be applied to a large variety of systems ranging from biology to the climate. In the future, the method could be applied to other types of data including structured missingness.

References:

[1] Bianconi, G.: Higher-order networks: An introduction to simplicial complexes. Cambridge University Press (2021); Battiston, F., et al., 2020. Networks beyond pairwise interactions: Structure and dynamics. Physics Reports, 874, (2020):1-92.

[2] Sun, H., et al.: The dynamic nature of percolation on networks with triadic interactions. Nature Communications, 14(1):1308 (2023).

[3] Niedostatek, M., Baptista , A., Yamamoto, J., MacArthur, B., Kurths, J. Sanchez Garcia, R., Bianconi, G.: Mining higher-order triadic interactions. In: Nature Communications, 14.1 (2023), p. 1308