Communities and Disease Comorbidities from Multiplex Biological Networks

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Functional relationships between genes and proteins are numerous and diverse: protein-protein interaction or gene co-expression, for instance. Biological networks are thus intrinsically multiplex, i.e. they can be represented as a collection of networks sharing the same nodes (the genes/proteins), but encompassing interactions of different nature. One of the leading approaches to extract functional knowledge from biological networks is their clustering into communities – or functional modules – of tightly linked genes/proteins. But what is the best option to identify communities from multiple biological network sources? We assess here classical approaches of network or community aggregations, and compare them to a multiplex-modularity approach that considers the multiplexity of biological network. By simulating random networks, we demonstrate that the multiplex-modularity method outperforms the aggregation approaches when network layers are incomplete or heterogeneous in density. Application to a multiplex biological network containing 4 layers of physical or functional interactions allows recovering communities more accurately annotated than their aggregated counterparts. Overall, the multiplex-modularity framework is better suited to combine different biological networks for community identification[1].

We recently identified overlaps between susceptibility genes[2] and deregulated genes[3] associated to diseases presenting direct or inverse comorbidities. Multiplex networks and communities allow to extend these analyses by considering the genes/proteins functional relationships potentially involved in disease comorbidities. We undertook a systematic study of communities enriched in diabetes and pancreatic/prostate cancer-related genes. This approach provides some molecular hypotheses, including a role for the anti-diabetic drug metformin, to better understand the relationships between these diseases that, at the epidemiological level, show direct and inverse comorbidities.

[1] Didier, Brun and Baudot. Submitted.
[2] Tabarés-Seisdedos et al. Lancet Oncol. 2011 Jun;12(6):604-8.
[3] Ibáñez et al. Plos Genetics 2014 Feb 20;10(2).