ModuleDiscoverer: Identification of regulatory modules in protein-protein interaction networks.

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Abstract

The identification of disease-associated modules based on protein-protein interaction networks (PPINs) and gene expression data has provided new insights into the mechanistic nature of diverse diseases. However, their identification is hampered by the detection of protein communities within large-scale, whole-genome PPINs. A presented successful strategy detects a PPIN's community structure based on the maximal clique enumeration problem (MCE), which is a non-deterministic polynomial time-hard problem. This renders the approach computationally challenging for large PPINs implying the need for new strategies. We present ModuleDiscoverer, a novel approach for the identification of regulatory modules from PPINs and gene expression data. Following the MCE-based approach, ModuleDiscoverer uses a randomization heuristic-based approximation of the community structure. Given a PPIN of Rattus norvegicus and public gene

expression data, we identify the regulatory module underlying a rodent model of non-alcoholic steatohepatitis (NASH), a severe form of non-alcoholic fatty liver disease (NAFLD). The module is validated using single-nucleotide polymorphism (SNP) data from independent genome-wide association studies and gene enrichment tests. Based on gene enrichment tests, we find that ModuleDiscoverer performs comparably to three existing module-detecting algorithms. However, only our NASH-module is significantly enriched with genes linked to NAFLD-associated SNPs. ModuleDiscoverer is available at http://www.hki-jena.de/index.php/0/2/490 (Others/ModuleDiscoverer).

Involved units

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Topics

Databases, Web-servers and Prediction Tools

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