Explainable AI for Understanding Associations Between Disease-Related Genes

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In recent years, we have witnessed the impressive successes of "black-box" models such as deep neural networks, and these have contributed to unravel new Artificial Intelligence (AI) and Machine Learning (ML) applications with the purpose of growing scientific knowledge. However, in areas such as genomics, drug-discovery, and pathology analysis, these applications are limited in the sense they fail to provide human-understandable logical decisions and often lack some degree of explainability[1].

One well-known strategy for understanding molecular and pathological mechanisms is discovering disease-associated genes (DGs), which may provide new candidate genes for targeted therapy and research tracks for developing new drugs. However, in prioritizing genes for further investigation, the need for AI and ML models to provide human understandable explanations becomes ever more apparent[2].

This is the case for a Network-Based approach called S2B[3] (Specific-Double Betweenness), which uses protein-protein interaction (PPI) networks to predict DGs simultaneously associated with two diseases. S2B has shown promising results but it only focuses on PPI networks to provide DGs, and even though we might generate interesting candidates with S2B, not only is the interactome itself limited, but we are still lacking contextual information about the generated candidate genes.

We believe that Ontologies may be the solution for providing more scientific knowledge to this method, as well as the explainability it requires. We developed a novel approach to enrich PPI networks with information from ontologies and assessed the impact of using different methods of filtering the content provided to the network to obtain the best possible results with S2B.

S2B's performance in predicting genes associated with Amyotrophic Lateral Sclerosis (ALS) and Spinal Muscular Atrophy (SMA) was evaluated with different PPI networks as an input, some of them containing information from the Gene Ontology[4]. Preliminary results show an increase in S2B performance with the use of a network containing only physical PPIs and the Gene Ontology, and these results motivate further work in refining a method to retain important information and enriching PPI networks with ontologies.

References

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