Novel-DTI: A Machine Learning Pipeline To Predict Drug-Target Interactions for Large-Scale Drug Repurposing and Drug Discovery Using Multiplex, Heterogeneous Networks

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Antibiotic-resistant diseases, orphan diseases, and disease outbreaks are the cause of millions of deaths annually. Inefficient treatment of these diseases, alongside other diseases, contributes to the need for a quick and cost-efficient alternative to current drug discovery methods. Drug development is significantly time-consuming and expensive, taking up to 14 years and $2 billion; therefore, drug repurposing (finding new uses for drugs) is the best way to identify new treatment options for these diseases. Novel-DTI can accurately predict new treatment options for a multitude of diseases and rank drug candidates by predicting new drug-target interactions (DTIs) using a multiplex, heterogeneous network. This network was generated using 11 different types of data describing the relationships among all approved drugs and known protein targets. Node embeddings using graph-convolution, graph-attention, and linear factorization methods were created using this network. An ensemble of these embeddings was generated to develop the most comprehensive graph representations. These embeddings were inputted into a deep neural network, which outputted binary class labels for DTI prediction and ranking scores indicating potential interaction strengths, which were further validated through molecular docking studies. Novel-DTI was then run on all possible drug-target combinations, identifying 60,083 new drug-target interactions, which span across 2,013 approved drugs and more than 7,000 different diseases, including orphan, antibiotic-resistant, and viral diseases. Novel-DTI was able to predict literature-supported and previously unknown DTIs, therefore, validating it as a tool that can be used for large-scale drug repurposing and drug discovery.

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