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Drug Repositioning Using Sparse Graphs and Subnetwork Identification

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New drug discovery is a long process that requires a large investment of money and time. Drug repositioning focuses on identifying new therapeutic effects for existing drugs. Computational drug repositioning plays an essential role in pharmacology as it can be used to reduce the number of in-vivo and in-vitro experiments. In computational drug repositioning, it is believed that drugs having similar characteristics are more likely to demonstrate similar therapeutic effects. Hence, analysing pairwise drug similarity is crucial. Subnetwork identification (SI) is a network-based approach that identifies a small subnetwork from a large drug similarity network (DSN) focusing on a single disease. Unlike other popular network-based and machine learning approaches, SI can be used to infer repositioning candidates for a single disease at a time. The drugs in the identified subnetwork should share similar characteristics. For the first time, the drugs associated with the nervous system are chosen from Class "N" of Anatomical Therapeutic Chemical (ATC) classification to construct the DSNs. This study aims to demonstrate the generalization of subnetwork identification method for drug repositioning. In the DSNs, drugs are represented by the vertices, and terminals are a predefined set of vertices chosen according to ATC class-N. SI algorithm focuses on identifying subnetworks from the DSN, minimizing the edge-cost of the subnetwork. SI algorithms perform well on sparse graphs. Moreover, employing different DSNs by varying the terminals and varying the sparse graph generation methods (SGGMs) provides an opportunity to assess the drug repositioning candidates based on a consensus solution. This study employs two new SGGMs for identifying subnetworks from large-scaled DSNs. In addition, two existing SGGMs were employed to create four different types of sparse DSNs. The repositioning candidates identified in multiple subnetworks are more likely to reposition for the disease represented by the DSN. Nimodipine, Alclometasone, Lisinopril, Theophylline, Vinblastine, and Naftifine appeared in at least five subnetworks. Hence, they can be inferred as reliable drug repositioning candidates for diseases associated with the nervous system.

Keywords: ATC classification, Drug similarity network, Drug repurposing, Nervous system, Sparse graph