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Interpretable Predictions of Genetic Perturbation Transcriptional Outcomes with Multi-View Graph Learning

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Genetic perturbation techniques such as gene activation, knockdowns or knockouts, are vital for understanding gene functions, disease mechanisms, and the nature of various biological topics. The evolution of these methods, particularly with single-cell RNA sequencing and combinatorial perturbation screens, has significantly broadened our ability to explore genetic interactions. However, a significant challenge remains in the limited interpretability of the mechanisms by which genetic perturbations impact other genes. In this study, we propose a multi-view graph learning model that integrates various biological networks, including gene regulatory networks, protein-protein interactions, gene ontology, and coexpression networks, to predict perturbation outcomes. Proposed model demonstrates superior performance in handling out-of-distribution scenarios, particularly in unseen gene perturbations, and offers biologically meaningful interpretations through attention and graph flow, thus advancing the understanding of genetic interactions and aiding in the design of future experiments.