

Title:

Network Medicine GPT – A foundation model for disease mechanism mining and drug repurposing

Abstract:

Network medicine leverages large biomedical knowledge graphs (KGs) to model disease mechanisms and identify therapeutic opportunities. However, most deep learning approaches that use KGs in biomedicine remain task-specific, limiting their ability to generalize across diverse applications within a unified framework. Here, we introduce NetMedGPT, a transformer-based foundation model trained on a large-scale biomedical KG using masked token prediction. By learning contextualized representations of biomedical nodes, NetMedGPT enables unified, zero-shot inference across different drug discovery tasks.

Specifically, in five tasks, i.e., predicting the association of drugs with indications, targets, adverse drug reactions, contraindications, and off-label uses, NetMedGPT consistently outperforms all specialized baselines, achieving area under the precision-recall curve gains of between 2.2% and 26%. When evaluated on independent external datasets, NetMedGPT outperformed baseline on an expert-curated clinical indications set and also preferentially prioritized clinically relevant drug-disease pairs in ClinicalTrials.gov. NetMedGPT's generative capability further supports the construction of mechanistically plausible subnetworks offering biological insights. NetMedGPT provides a unified foundation model for network medicine that supports scalable hypothesis generation and provides potential to accelerate drug repurposing. We further provided an interactive interface (<https://apps.cosy.bio/netmedgpt/>) that allows users to obtain model inferences through natural-language queries.