A106 · Enhancing causal network-based perturbation inference through literature-derived knowledge

Presenter: Zheng Liu — Northeastern University

Authors: Zheng Liu, Benjamin M. Gyori

Session: Day 2 · Fri Oct 2, 2026 · 2:15–4:15 PM

Inferring active regulators from perturbation readouts is a central problem in systems biology. Network propagation methods such as MOON (Meta-fOOtprint aNalysis) propagate activity signals through a directed prior knowledge network (PKN) to score candidate upstream regulators, but performance is constrained by network coverage and quality. Most PKNs aggregate manually curated databases, which are high confidence but incomplete. We benchmarked PKN expansion using INDRA (Integrated Network and Dynamical Reasoning Assembler), an automated system that extracts mechanistically resolved molecular interaction statements from biomedical literature with associated confidence scores. Candidate edges were ranked by confidence and evaluated at thresholds spanning the top 0.1% to 10% of INDRA's 11 million edges. We evaluated perturbation inference across four independent benchmarks: CytoSig and CellSig (cytokine and growth factor stimulation), the NicheNet ligand treatment validation compendium (51 ligands, 101 experiments), and CREED (single drug perturbation profiles with drug target ground truth). Integrating the top 0.3–0.4% highest confidence INDRA edges consistently improved performance across all datasets. AUCs increased from 0.554 to 0.707 (+27.7%) on CytoSig, 0.609 to 0.715 (+17.4%) on CellSig, 0.573 to 0.737 (+28.6%) on NicheNet, and 0.502 to 0.55 (+9.5%) on CREED. Performance declined monotonically beyond 0.5%, as lower confidence edges introduced contradictory signals. A belief score ablation confirmed that randomly selected edges of equivalent size yielded no consistent gain, demonstrating that confidence ranked selection drives the improvement. These results show that selective integration of high confidence literature derived knowledge enhances network based perturbation inference across diverse contexts, and that edge confidence matters more than coverage.