



UNIVERSITÀ
DI TRENTO

Dipartimento di
Matematica

DOTTORATO



CYCLE 35th
ORAL DEFENCE OF THE PHD THESIS

Monday 17th June 2024 – at 3.00 pm
Polo Ferrari 1
Room A203

The event will take place in presence and online through the ZOOM platform.
To get the access codes, please contact the secretary office.

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PhD Student in Mathematics

Inference of Gene Regulatory Networks with integration of prior knowledge

Abstract:

Gene regulatory networks (GRNs) are crucial for understanding complex biological processes and disease mechanisms, particularly in cancer. However, GRN inference remains challenging due to the intricate nature of gene interactions and limitations of existing methods. Traditionally, prior knowledge in GRN inference simplifies the problem by reducing the search space, but its full potential is unrealized. This research aims to develop a method that uses prior knowledge to guide the GRN inference process, enhancing accuracy and biological plausibility of the resulting networks.

We extended the Fused Sparse Structural Equation Models (FSSEM) framework to create the Fused Lasso Adaptive Prior (FLAP) method. FSSEM incorporates gene expression data and genetic variants in the form of expression quantitative trait loci (eQTLs) perturbations. FLAP enhances FSSEM by integrating prior knowledge of gene-gene interactions into the initial network estimate, guiding the selection of relevant gene interactions in the final inferred network.

We evaluated FLAP using synthetic data to assess the impact of incorrect prior knowledge and real lung cancer data, using prior knowledge from various gene network databases (GIANT, TissueNexus, STRING, ENCODE, hTFtarget). Our findings demonstrate that integrating prior knowledge improves the accuracy of inferred networks, with FLAP showing tolerance for incorrect prior knowledge. Using real lung cancer data, functional enrichment analysis and literature validation confirmed the biological plausibility of the networks inferred by FLAP. Different sources of prior knowledge impacted the results, with GIANT providing the most biologically relevant networks, while other sources showed less consistent performance.

FLAP improves GRN inference by effectively integrating prior knowledge, demonstrating robustness against incorrect prior knowledge. The method's application to lung cancer data indicates that high-quality prior knowledge sources enhance the biological relevance of inferred networks. Future research should focus on improving the quality and integration of prior knowledge, possibly by developing consensus methods that combine multiple sources. This approach has potential applications in cancer research and drug sensitivity studies, offering a more accurate understanding of gene regulatory mechanisms and potential therapeutic targets.

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CONTATTI

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