

# Decoding multi-omic regulatory networks: a regression-based approach.

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Multi-omic experiments offer an unprecedented opportunity to explore gene expression regulation, providing deep insights into the intricate regulatory mechanisms of biological systems. However, the high dimensionality, heterogeneity, and multicollinearity of multi-omic datasets present significant challenges for statistical modeling and variable selection when inferring regulatory networks. Additionally, most existing tools for multi-omic regulatory network inference either fail to accommodate diverse omic modalities or lack the ability to generate and compare phenotype-specific networks.

To address these limitations, we developed MORE (Multi-Omics Regulation), a novel methodology that leverages regression-based frameworks and advanced variable selection strategies to construct phenotype-specific regulatory networks across any number or type of omic data. MORE integrates prior regulatory knowledge and offers functionalities for systematic comparison of the resulting networks.

We benchmarked MORE against other state-of-the-art tools using simulated datasets and applied it to an ovarian cancer case study. Our results demonstrate the robustness and versatility of MORE in unraveling regulatory mechanisms in complex biological systems, underscoring its potential as a valuable resource for multi-omic data analysis.

**Keywords:** multi-omics, regression models, variable selection, regulatory networks.