Indivumed Therapeutics

A NOVEL APPROACH TO EVALUATE MULTI-OMIC MULTIVARIATE DRUG TARGET IDENTIFICATION ALGORITHMS

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AGENDA

1. Introduction
2. An Input Data-Driven AMI Performance Measure
3. From Single-Omics to Multi-Omics AMI
4. Conclusions and Outlook

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INTRODUCTION

COMPANY PROFILE

Comprehensive biobank with
10 minutes ischemia time

Large colon and
lung cancer cohorts

Multi-Omics and clinical
data with follow-up

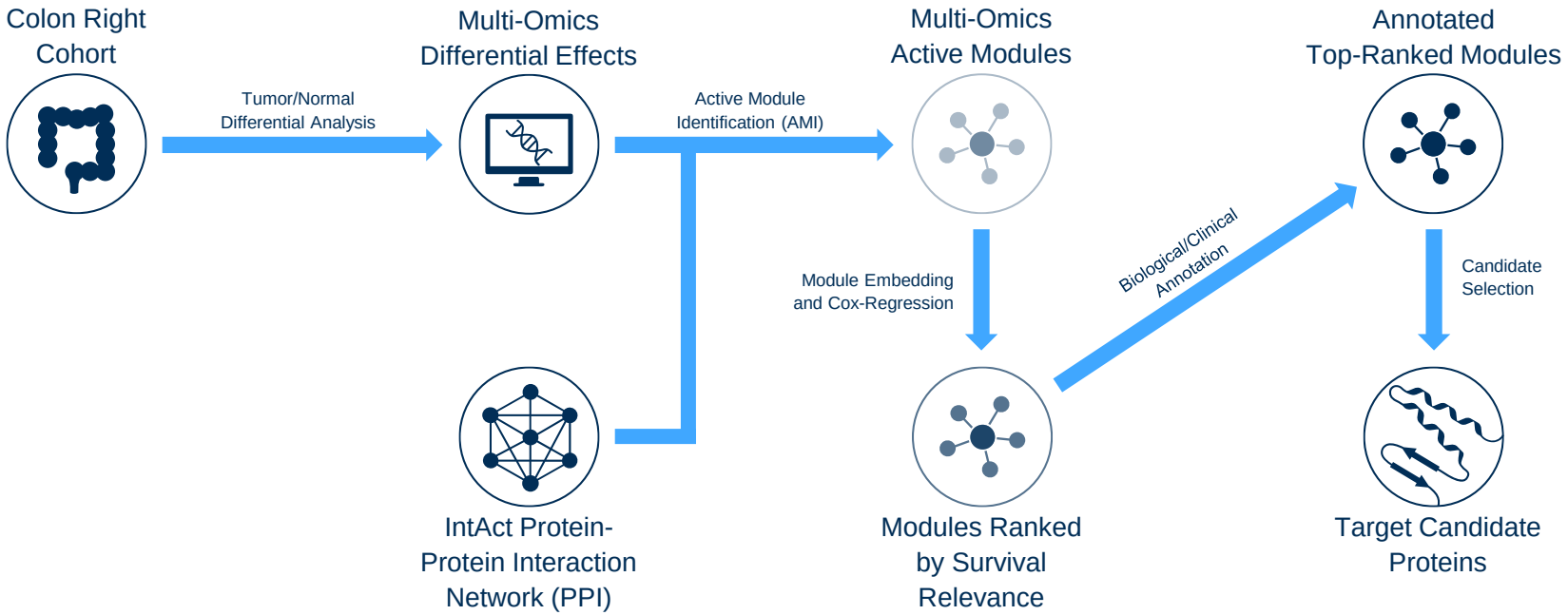
In-silico methods for target
candidate identification

Biomolecular characterization with cell lines and
2D/3D cellular models derived from the original cohort

Indivumed Therapeutics is a Hamburg-based biotech company founded in 2002 with over 80 employees.

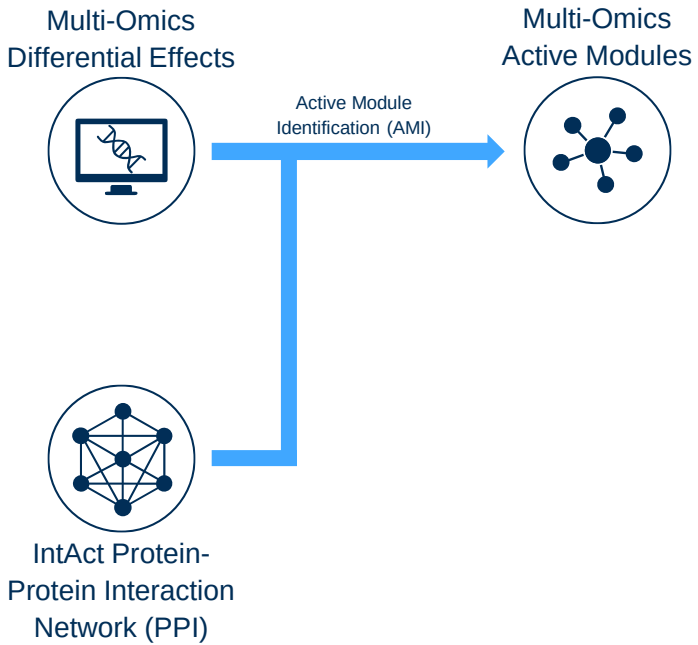
We focus on cancer drug target identification and aim to create target candidate packages, which are screening-ready and have been validated extensively.

OUR APPROACH TO TARGET CANDIDATE IDENTIFICATION



CHALLENGES IN ACTIVE MODULE IDENTIFICATION

- Performance evaluation of AMI methods rely on external biological datasets.
- Single-Omics AMI methods are abundant, but Multi-Omics AMI methods are rare.



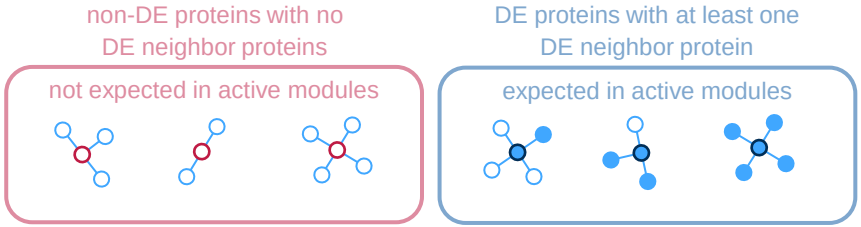
AN INPUT DATA-DRIVEN AMI PERFORMANCE MEASURE

AMI PERFORMANCE WITH ACTIVE MCC

We propose to measure AMI performance based on PPI topology and differential effects

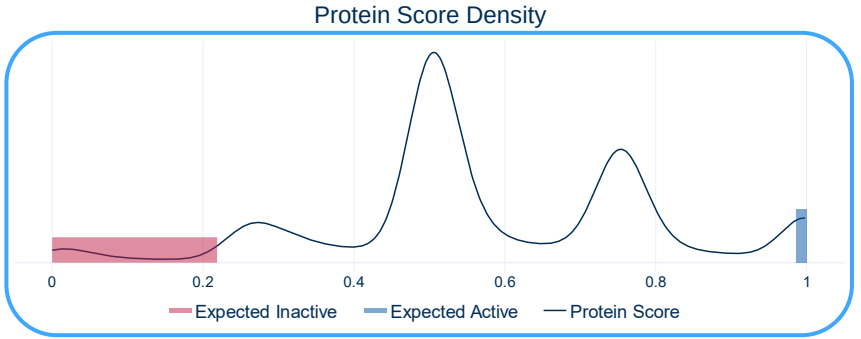
IDEA:

Define two node classes on which AMI can be treated as node classification and measure performance with Matthew Correlation Coefficient (MCC).



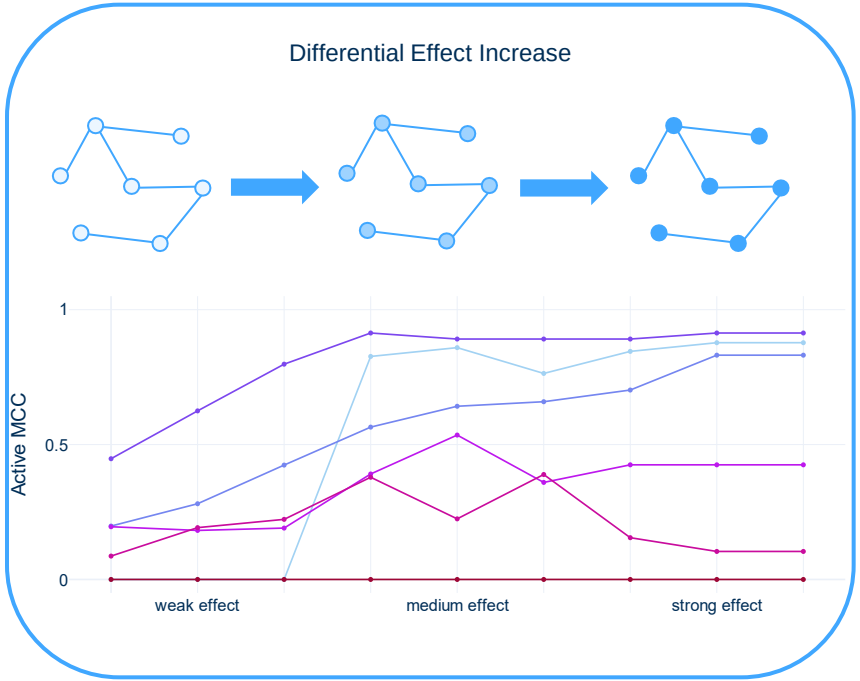
ADVANTAGES:

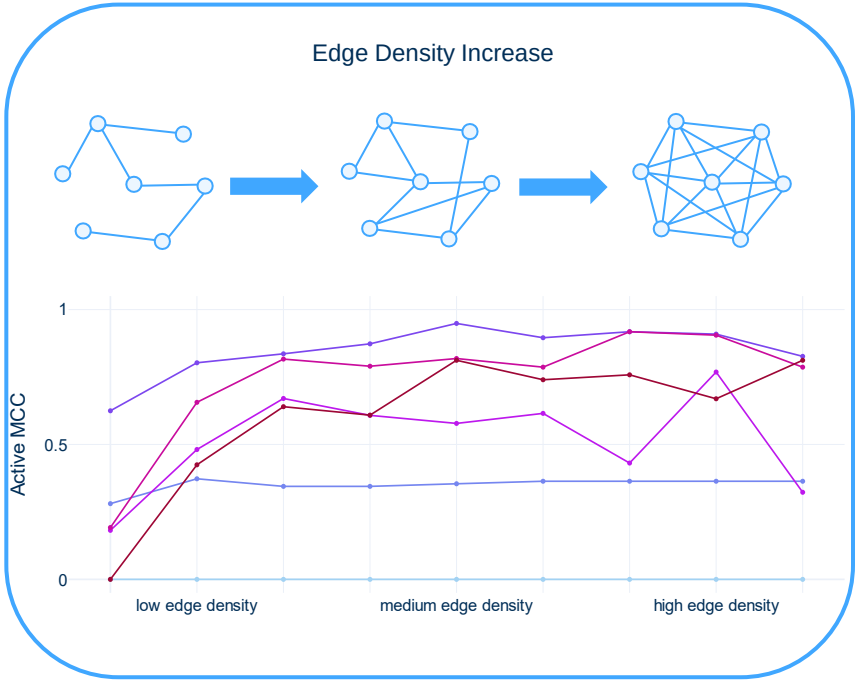
- Makes choice of validation dataset obsolete
- Can be used with artificial input data
- Allows for parameter tuning



PROOF OF CONCEPT ON ARTIFICIAL INPUT DATA

We test validity on a downsampled PPI with artificially generated disjoint active modules with varying sizes





FROM SINGLE-OMICS TO MULTI-OMICS AMI

MULTI-OMICS INTEGRATION STRATEGIES

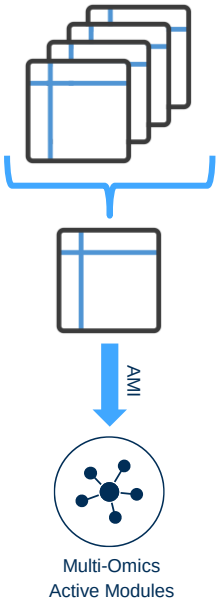
As single-omics methods are abundant, we aim to extend them to a multi-omics setting

Early Integration: Aggregate multi-omics effects to single-omics effect and run single-omics method.

- Easy for any single-omics method
- Detects similar patterns across layers
- Layer specific signals might get lost

Used:

- RFIM (Wang2022)
- DOMINO (Levi2021)
- MONET (Tomasoni2020)

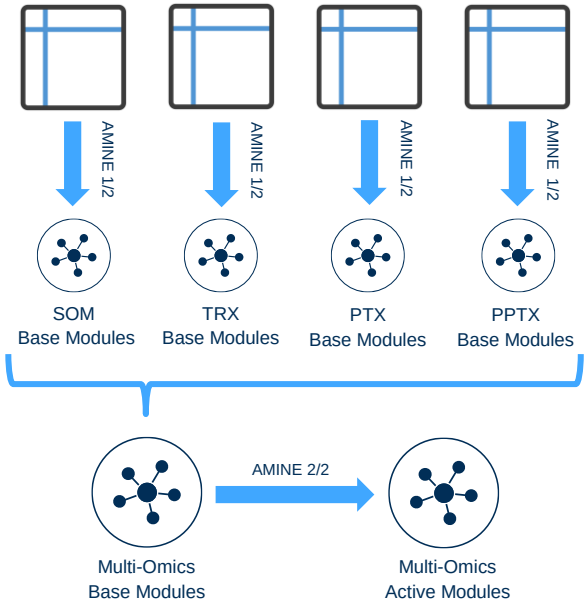


Middle Integration: Extend single-omics method with an intermediate aggregation step.

- Potentially hard, depending on the single-omics method
- Detects weakly connected patterns across layers
- Layer specific signals can get through

Extended:

- AMINE (Pasquier2023)

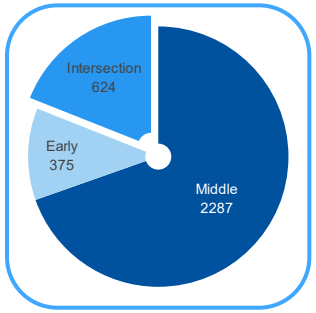


ACTIVE MODULES FOR COLON RIGHT

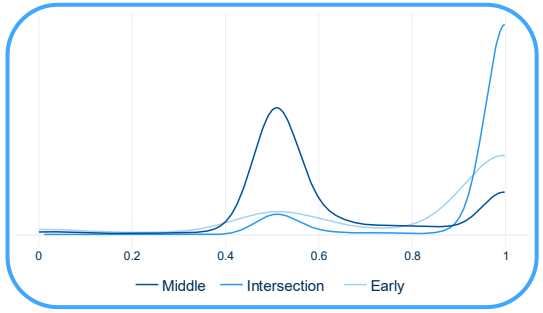
Early vs. Middle Integration AMINE

- PPI: IntAct.246 with physical and functional interactions
- SOM: Somatic mutation overrepresentation
- TRX: Differential expression in RNA-seq layer
- PTX: Differential expression in Proteomics layer
- PPTX: Differential expression in Phosphorylation layer

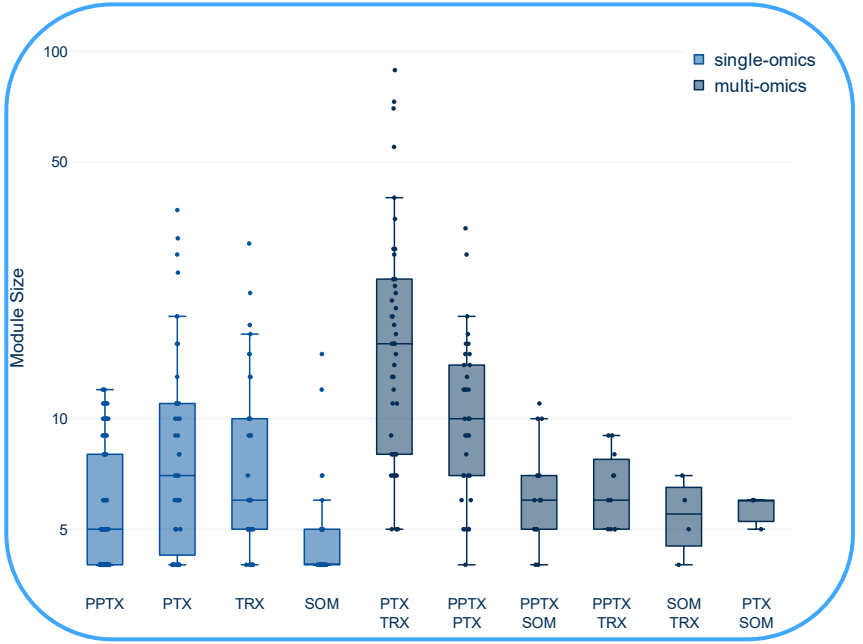
AMINE Active Proteins



Early Integration Effect Density



Module Type Statistics for Middle Integration AMINE



CONCLUSIONS AND OUTLOOK

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- We developed an AMI performance measure derived only by input data
- We created a Multi-Omics extension of AMINE with middle integration
- We currently analyze our colon right cohort with the described multi-omic multivariate workflow
- In the future we are going to study other cancer cohorts

REFERENCES

- **Ischemia time analysis:** Von der Heyde et al., 2024, *Tumour specimen cold ischemia time impacts molecular cancer drug target discovery*, https://doi.org/10.1038/s41419-024-07090-x
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- **RFIM:** Wang et al., 2022, *A statistical physics approach for disease module detection*, https://doi.org/10.1101%2Fgr.276690.122
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THANK YOU!

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