

Interpretable Lipid Structure and Network Analysis

Nikolai Köhler^{1,*}, Tim D. Rose^{1,2,*}, Lisa Falk¹, Lucie Klischat¹, Olga E. Lazareva^{2,3,4}, and Josch K. Pauling¹

¹LipiTUM, Chair of Experimental Bioinformatics, TUM School of Life Sciences, Technical University of Munich

²European Molecular Biology Laboratory, Heidelberg

³German Cancer Research Center (DKFZ), Heidelberg

⁴Chair of Experimental Bioinformatics, TUM School of Life Sciences, Technical University of Munich

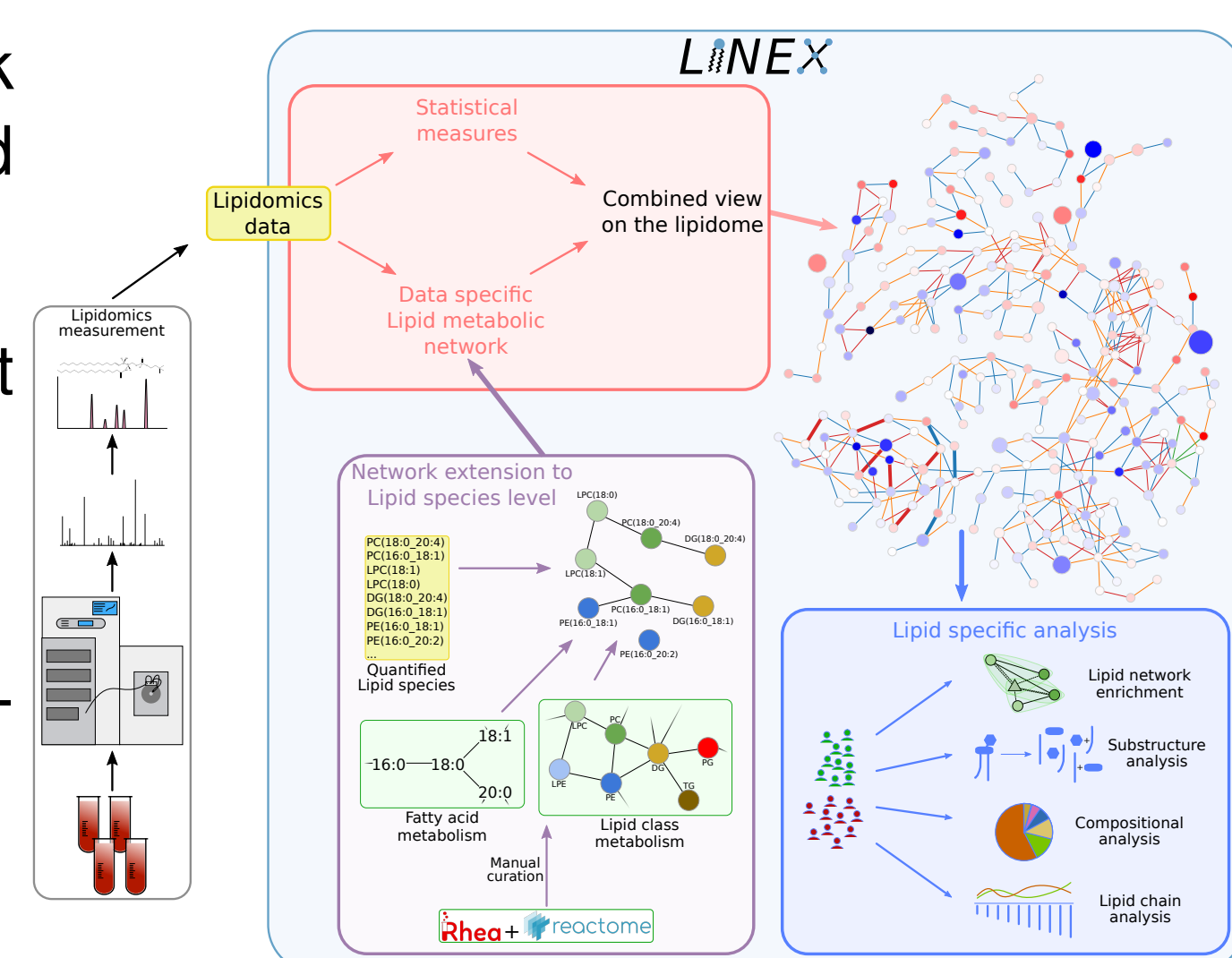
*These authors contributed equally

Method Overview

Input: abundances of identified lipids

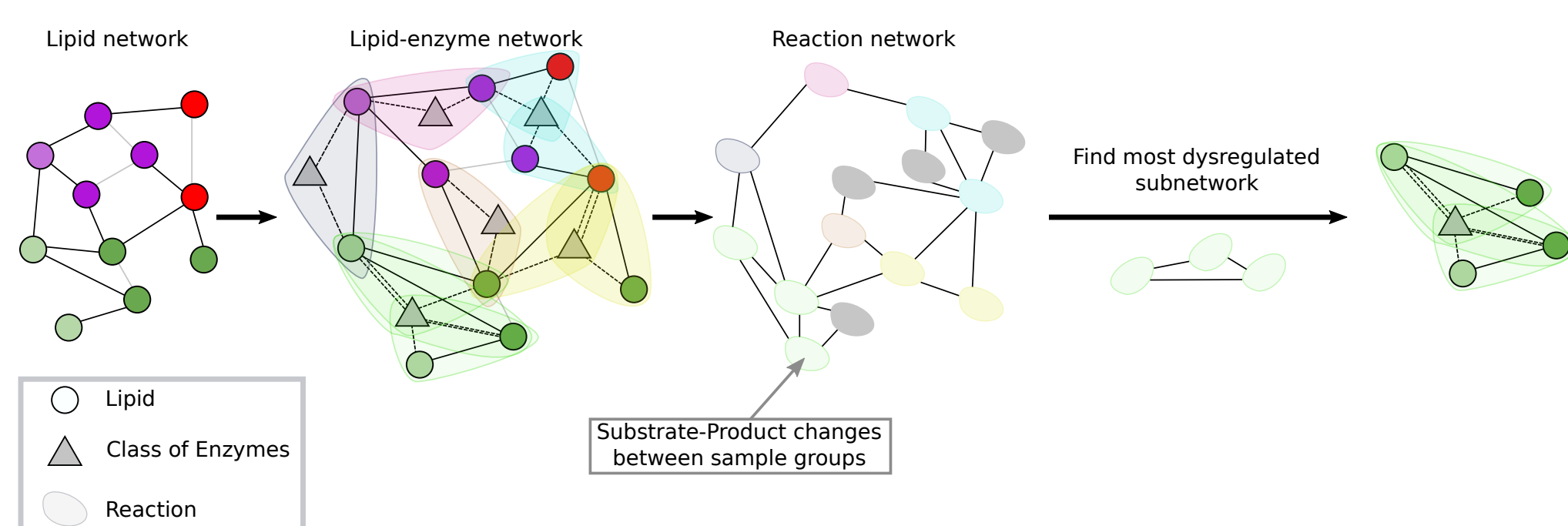
Analysis steps

1. Generate data-specific lipid network combining lipid class and fatty acid metabolism
2. Compute lipid statistics and project data onto the network
3. *Lipid-specific analysis*
 - Network enrichment to find dysregulated “*de-novo* pathways”
 - Lipid substructure analysis
 - Compositional and lipid chain analysis for coarse grained summaries



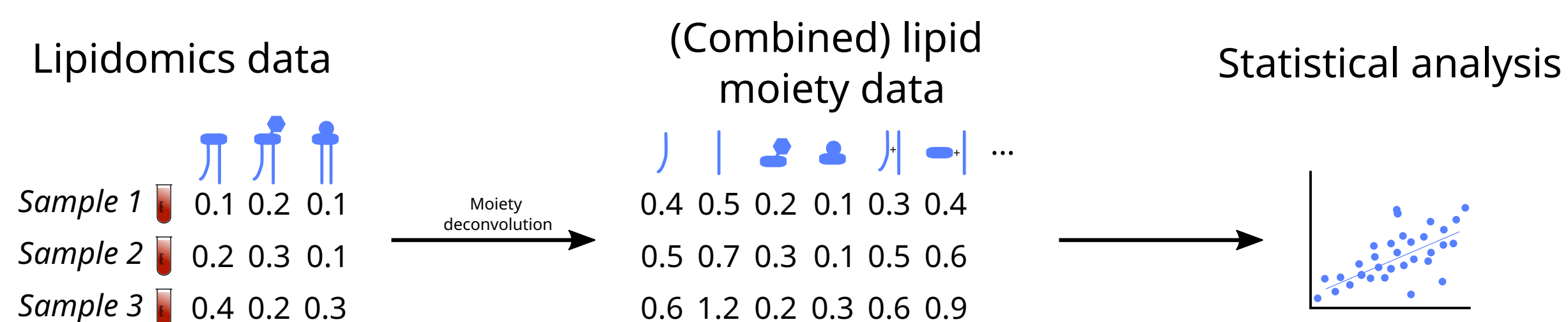
Finding Dysregulated Subnetworks

1. Expand to lipid-enzyme network
2. Collapse lipid-enzyme multipliers to hypernodes
3. Compute substrate-product changes on reaction network
4. Identify most dysregulated part of the network



Substructure Analysis

1. Find all existing substructure combinations
2. Sum abundances for each combination
3. Compute statistics and perform feature selection



Results

MBOAT7 Knock-Out Experiment

Proof-of-Principle: Identifying a knocked-out lipid metabolic reaction

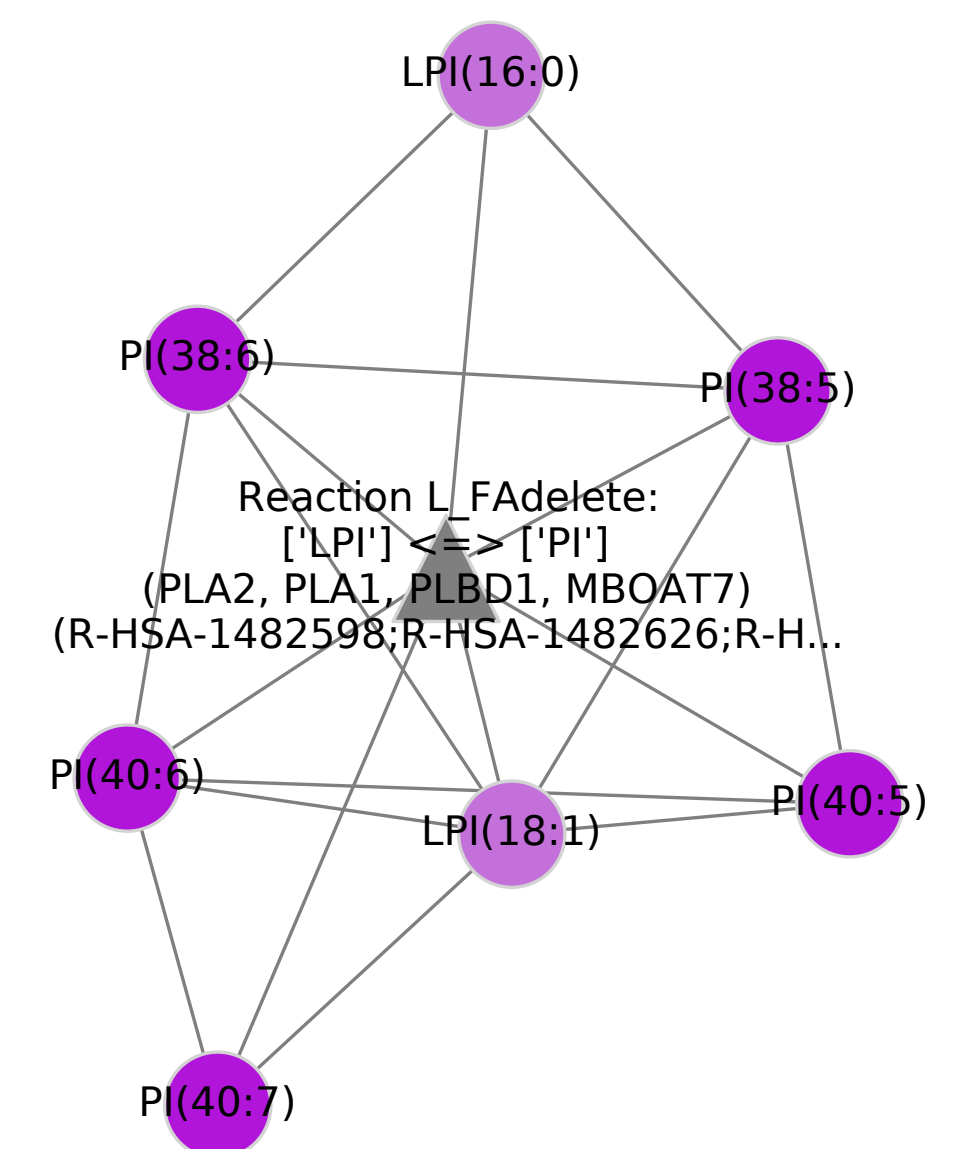
Data from Thangapandi et al.¹ with two mouse genotypes

- wild-type (WT)
- MBOAT7 deletion

MBOAT7 catalyzes distinct lipid reactions

- Lyso-Phosphatidylinositol (LPI) → Phosphatidylinositol (PI)
- Preference for Arachidonic Acid (20:4)

⇒ our proposed method accurately identifies the target reaction including MBOAT7-specific fatty acid preference



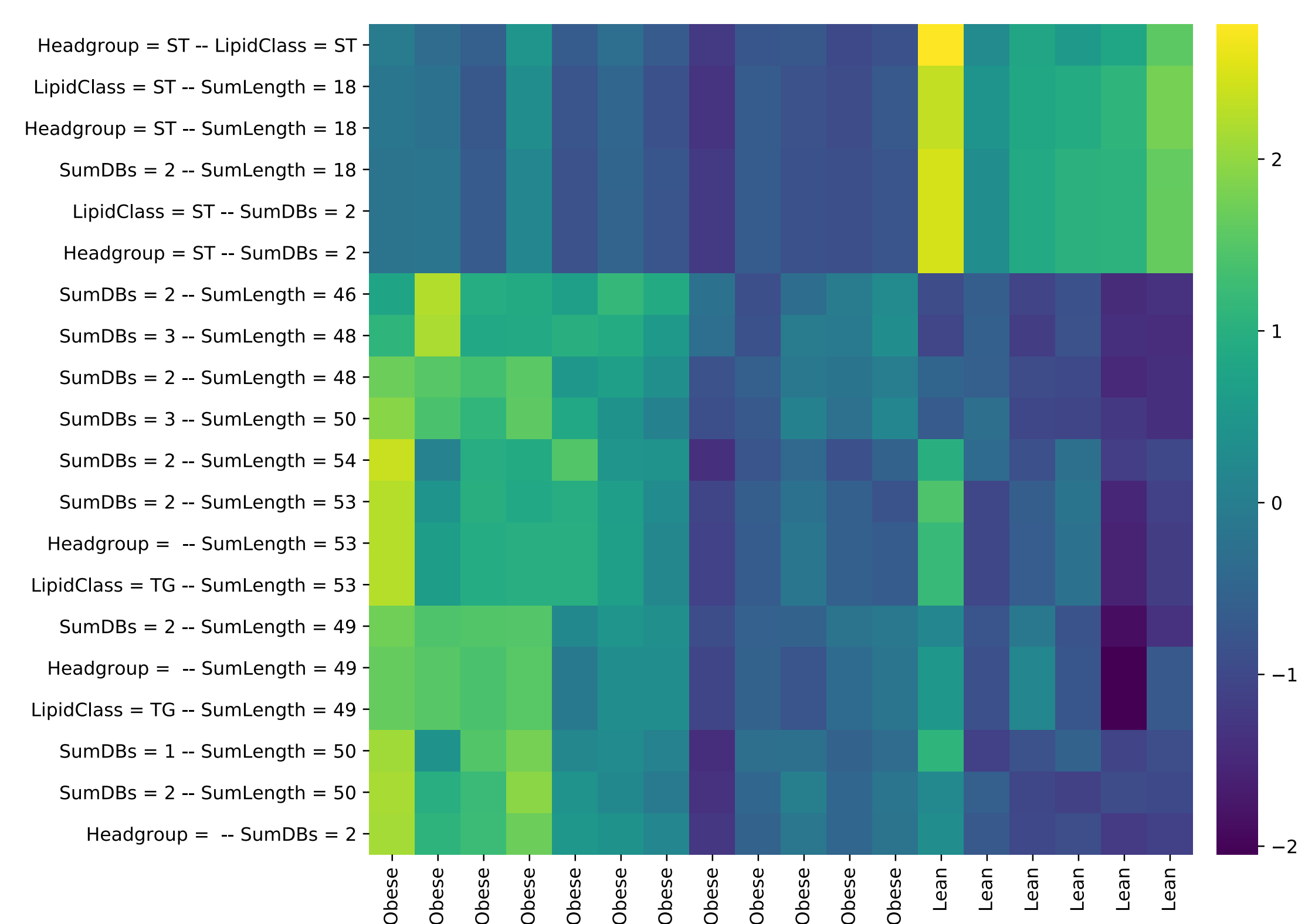
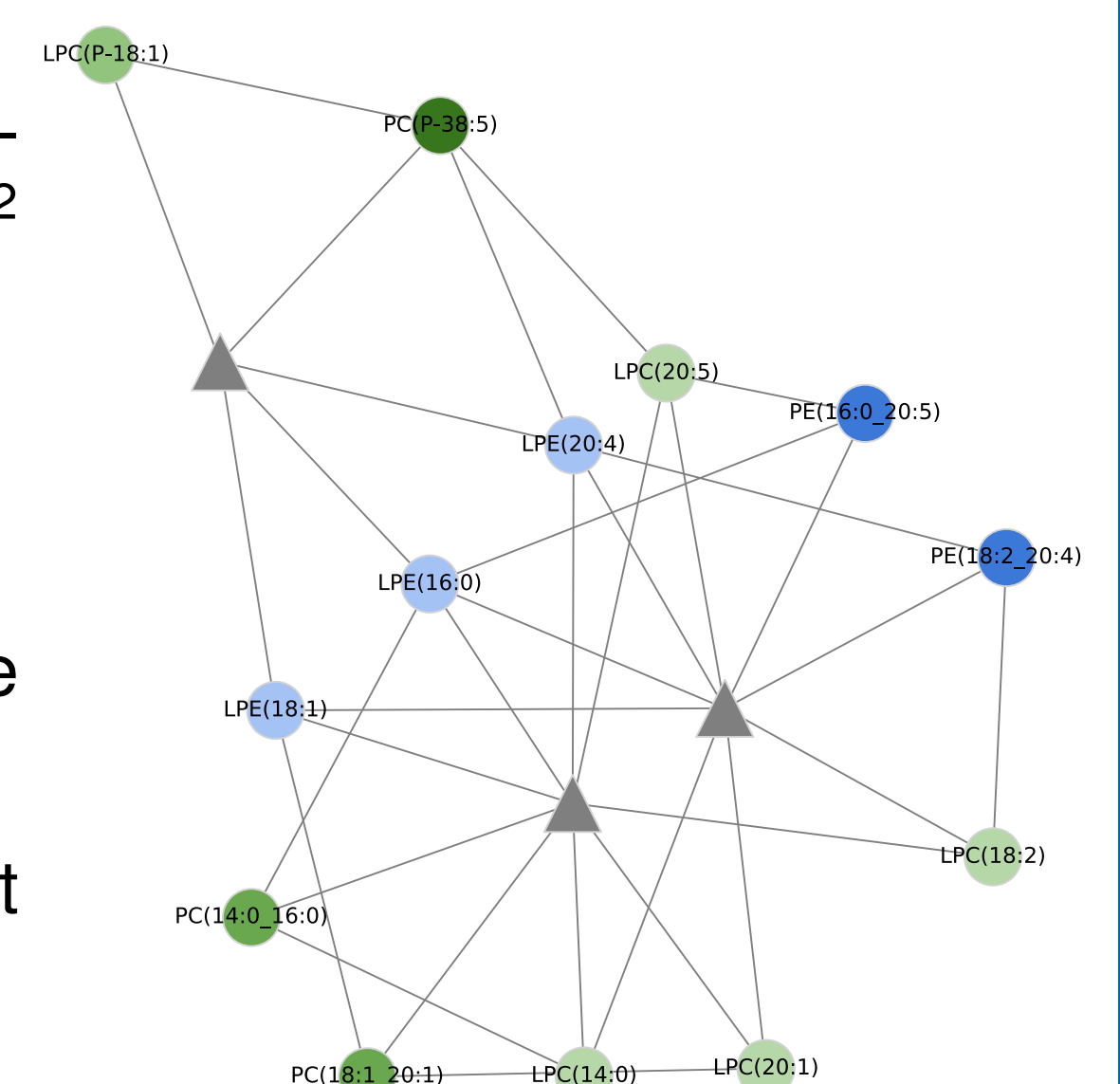
Human Adipocyte Lipidomics

Lipidome measurements of adipose tissue from obese and non-obese patients²

Network enrichment (left): Phospholipid subnetwork

Substructure analysis approach (right): fatty acid-related features (chain length-double bond combinations) of neutral lipids

⇒ complementary approaches for different metabolic effects



Find Out More

Rose and Köhler et al. “Lipid network and moiety analysis for revealing enzymatic dysregulation and mechanistic alterations from lipidomics data”, Briefings in Bioinformatics, 2023



Paper



GitLab



Web Interface



Lab Homepage

Web Interface

Interactive visualization and exploration

