

Multi-Omics Microsampling for The Profiling of Lifestyle-Associated Changes in Health

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Outline

- </> **Background**
- </> **Multi-Omics Microsampling Workflow**
- </> **Metabolic Phenotyping Response to Ensure Shake Consumption**
- </> **24/7 Personalized Whole Physiome Profiling**
- </> **Summary**

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*“**Blood** is one of the most important biological samples for biomarker study and disease diagnosis.”*

Traditional Blood Collection: Intravenous Blood Sampling

- × Invasive
- × Need clinic help
- × High sample volume needed

Traditional Blood Collection: Intravenous Blood Sampling

- *Intravenous blood sampling can't be used for high-frequency sampling for personalized health monitoring.*

- 
- ✓ **Less painful**
 - ✓ **Easy and flexible**
 - ✓ **Small sample volume needed**

What Information Can We Get From Microsamples?



Information in Microsamples

Proteins

SWATH proteomics
> 500 proteins

Metabolites

Untargeted mass spec
> 700 identified metabolites

Lipids

Targeted mass spec
> 800 quantified lipids

Targeted assay

Cytokines
Hormones
Cortisol



Outline

</> Background

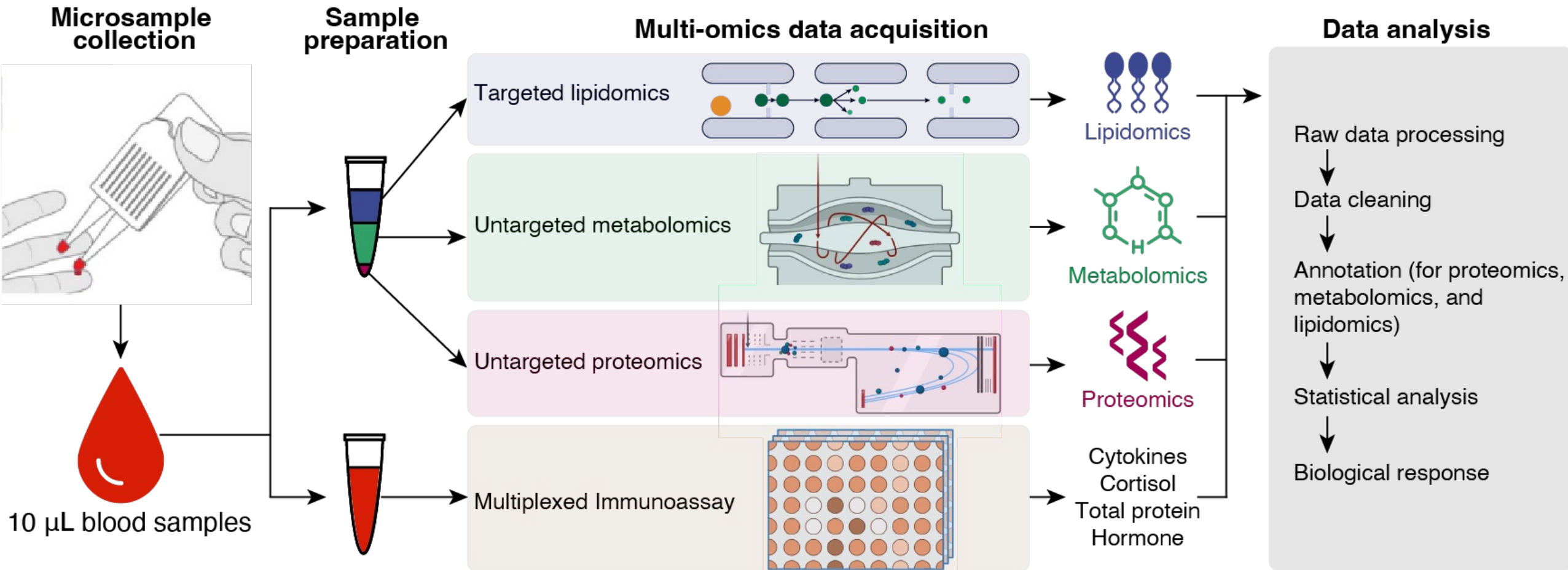
</> Multi-Omics Microsampling Workflow

</> Metabolic Phenotyping Response to Ensure Shake Consumption

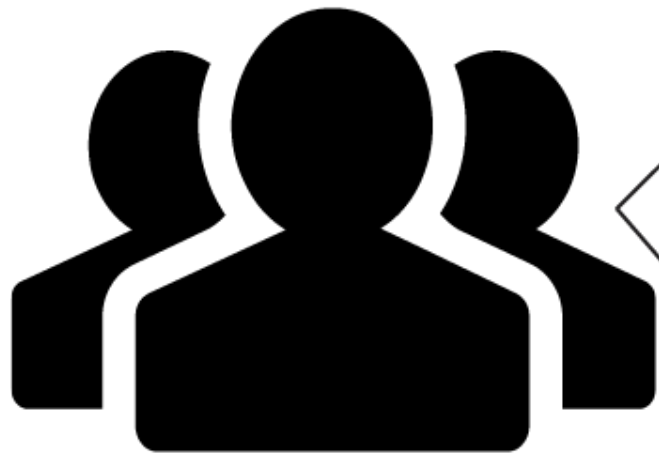
</> 24/7 Personalized Whole Physiome Profiling

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The Workflow of Microsampling Multi-Omics Platform



Comparison Between Microsample and Intravenous Plasma Sample



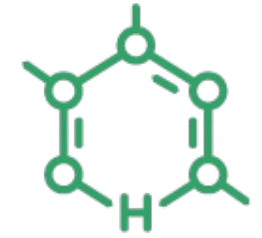
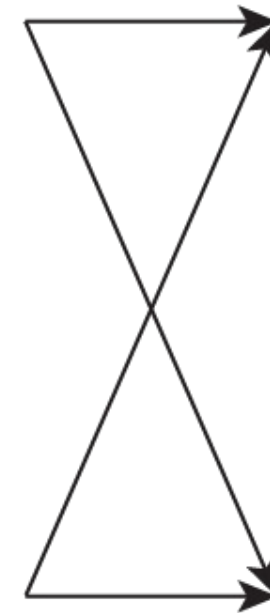
34 participants



Microsampling



Intravenous blood sampling

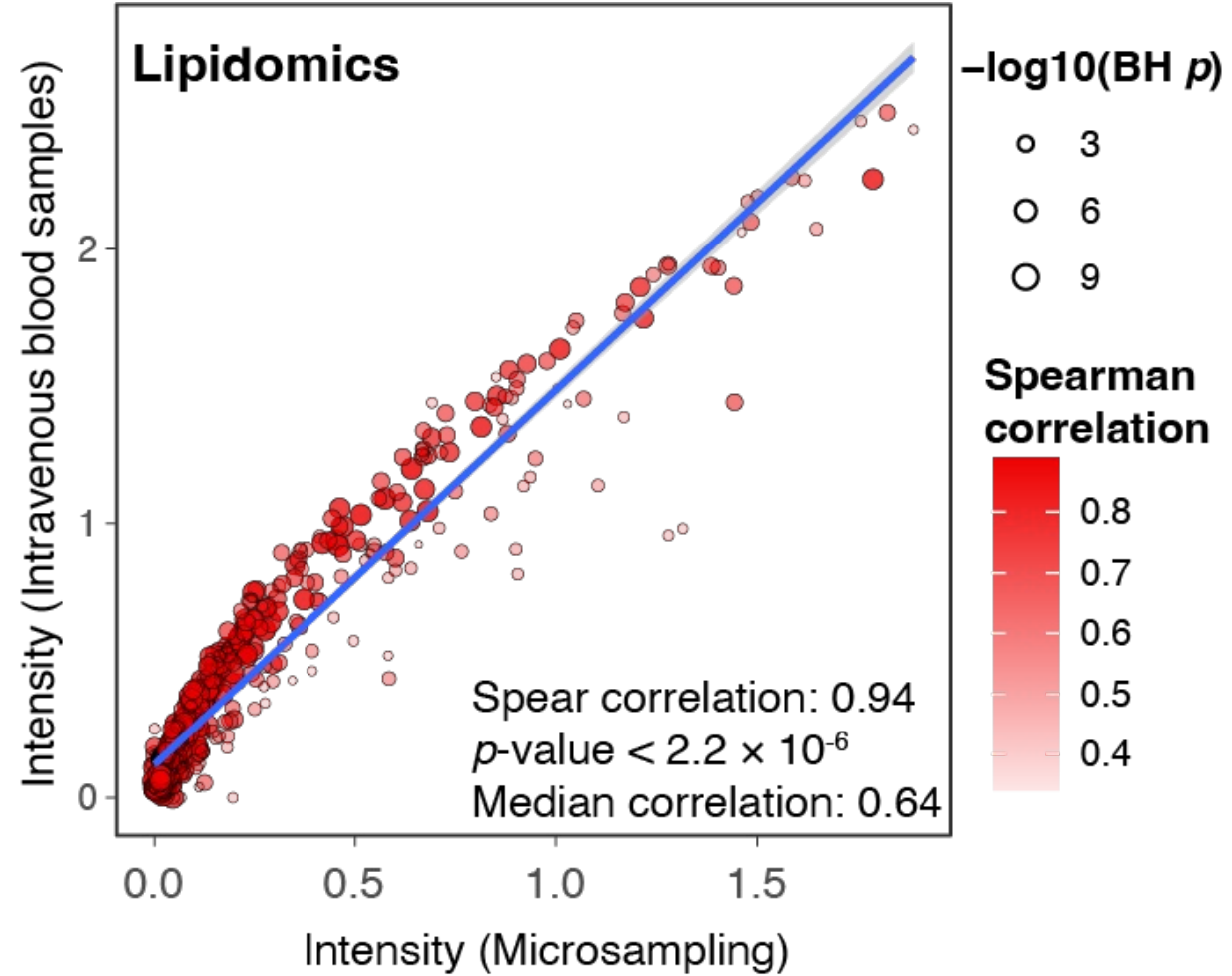
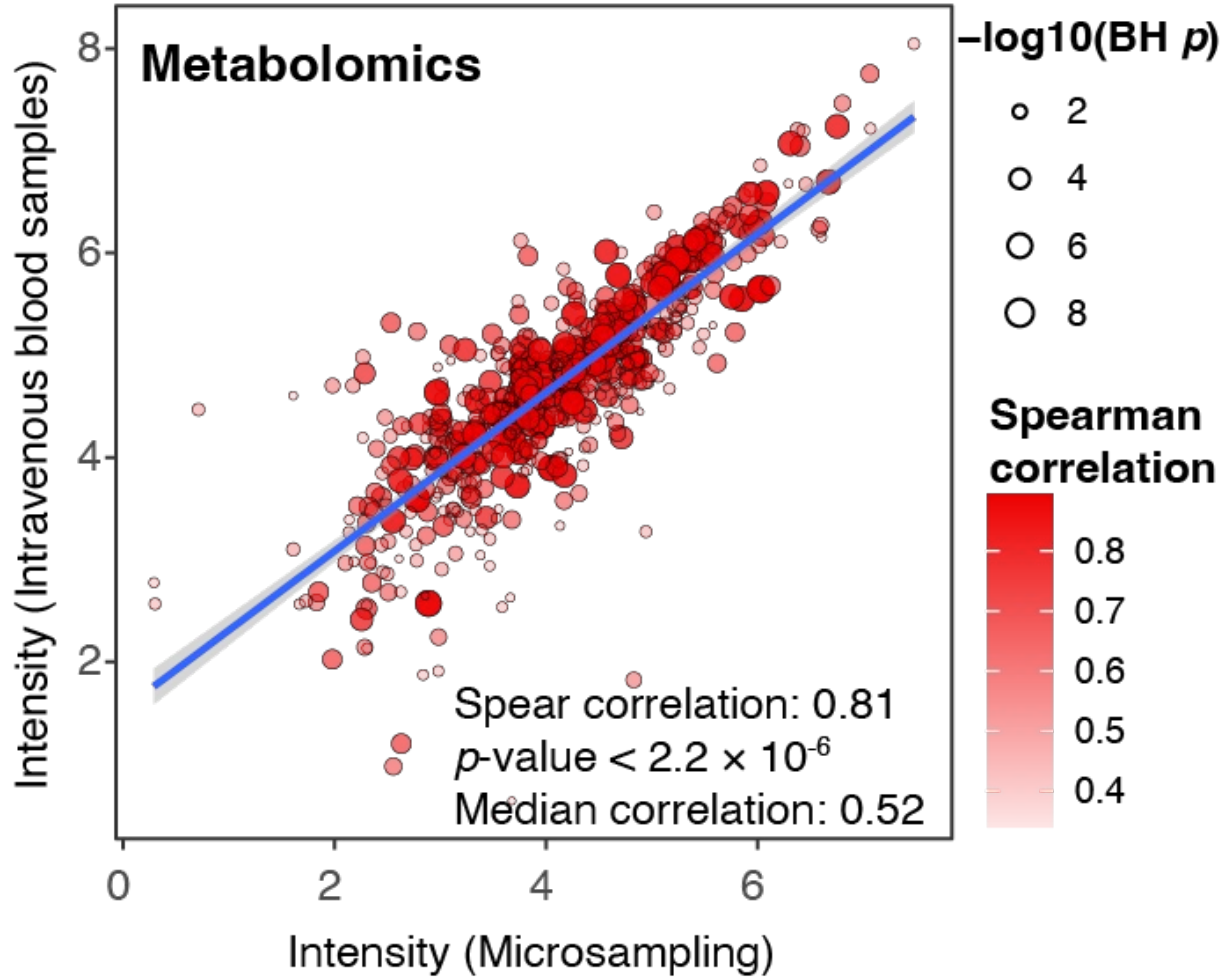


Metabolomics



Lipidomics

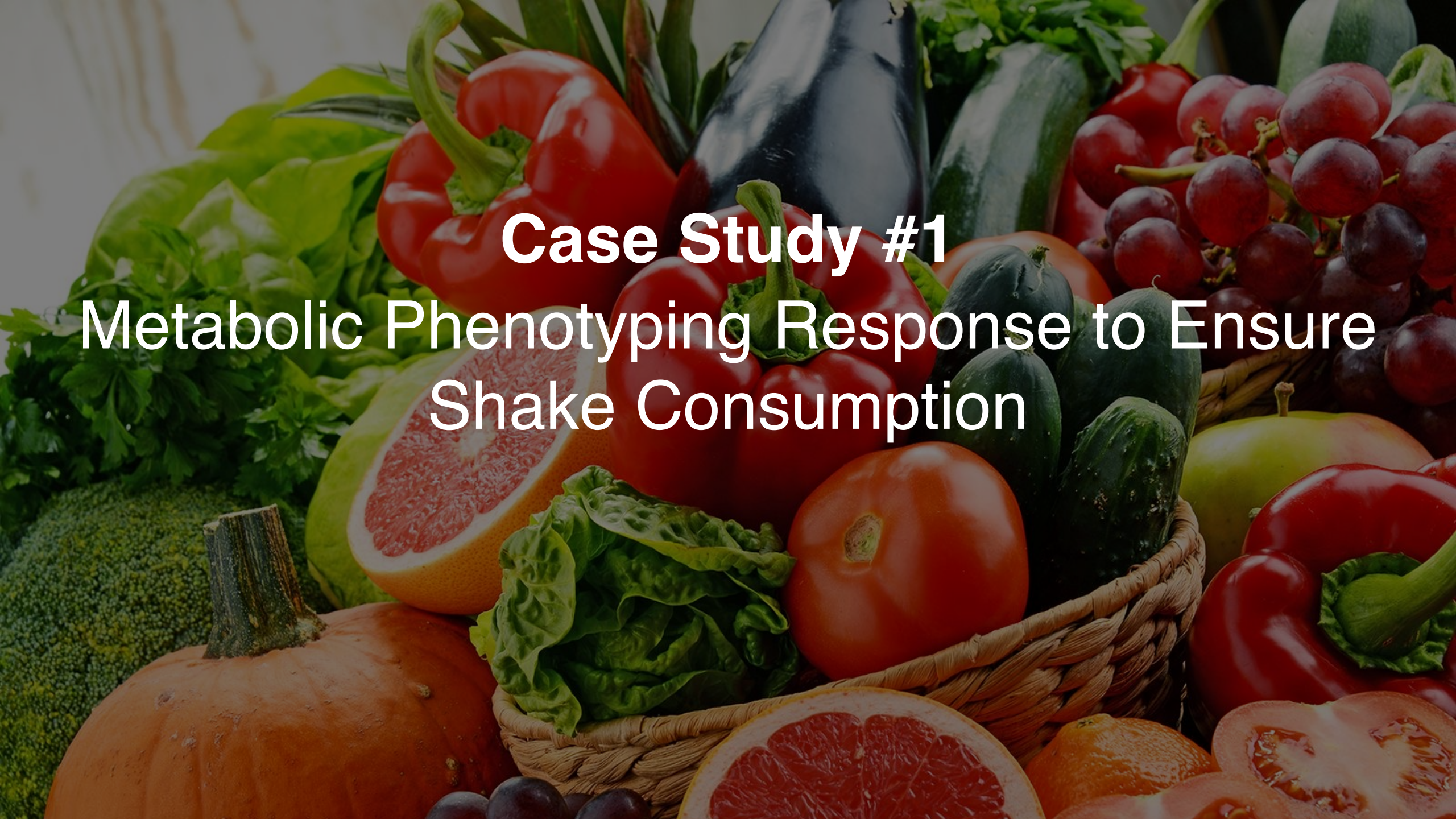
Comparison Between Microsample and Intravenous Plasma Sample



Can Microsampling Multi-Omics Used For Precision Medicine?

Outline

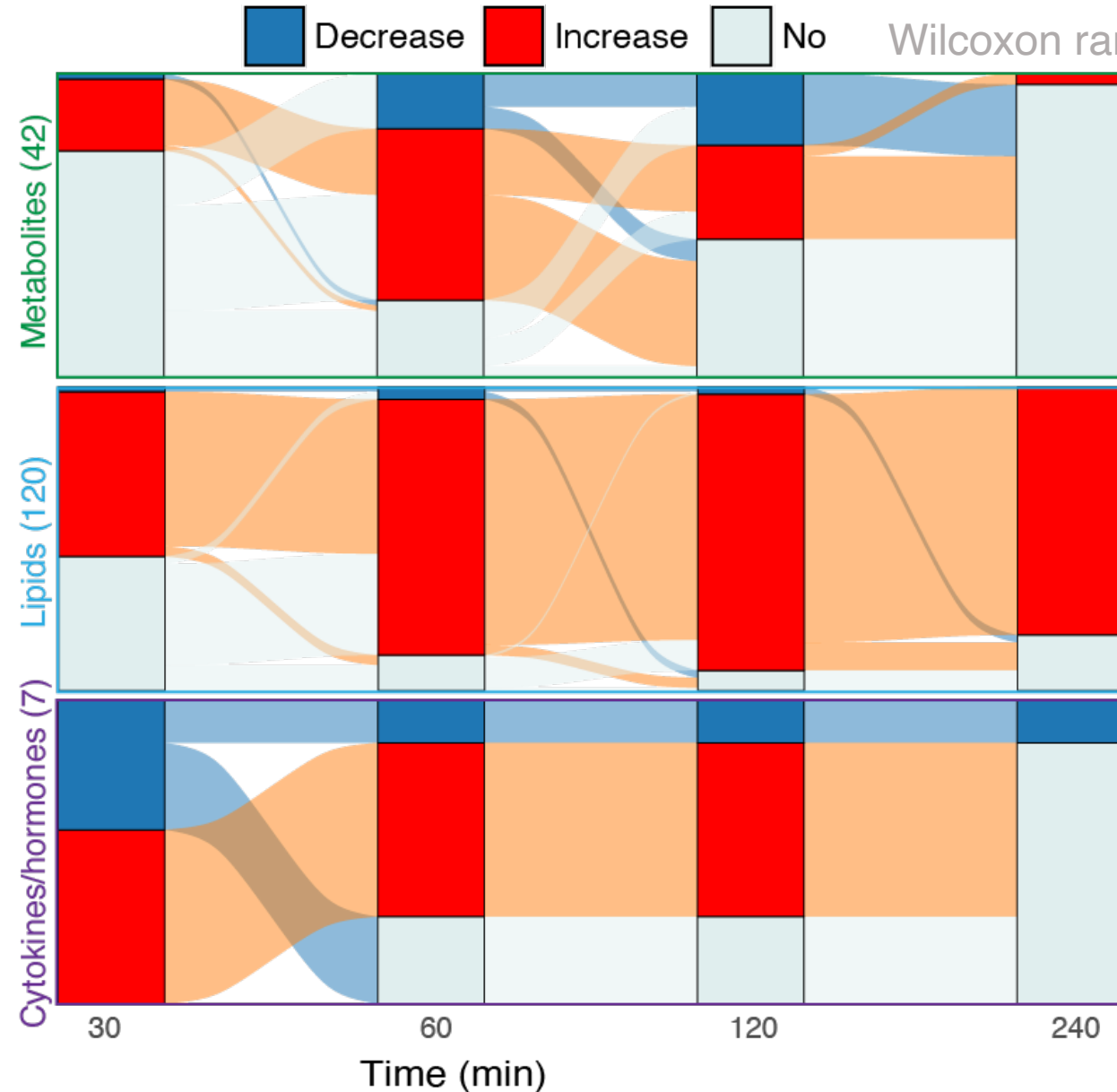
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Case Study #1

Metabolic Phenotyping Response to Ensure
Shake Consumption

Multi-Omics Data Significantly Reflect the Consumption of Ensure Shake



99 out of 560 (17.7%) metabolites

115 out of 155 (74.2%) lipids

7 out of 54 (13.0%) cytokines/hormones

Study Design and Overview

Study Design and Overview

Nutrition Facts			
Serving Size 1 bottle (8 fl oz)			
Amount Per Serving			
Calories 220		Calories from Fat 50	
	% DV*		% DV*
Total Fat 6g	9%	Sodium 190mg	8%
Saturated Fat 1g	5%	Potassium 390mg	11%
Trans Fat 0g		Total Carb. 33g	11%
Polyunsaturated Fat 3g		Dietary Fiber 1g	4%
Monounsaturated Fat 2g		Sugars 15g	
Cholesterol 5mg	2%	Protein 9g	18%
Vitamin A 25%	Vitamin C 50%	Calcium 30%	
Iron 25%	Vitamin D 50%	Vitamin E 25%	
Vitamin K 25%	Thiamin 25%	Riboflavin 25%	
Niacin 25%	Vitamin B ₆ 25%	Folate 25%	
Vitamin B ₁₂ 25%	Biotin 25%	Pantothenic Acid 25%	
Phosphorus 25%	Iodine 25%	Magnesium 25%	
Zinc 25%	Selenium 25%	Copper 25%	
Manganese 60%	Chromium 25%	Molybdenum 50%	
Chloride 8%			

*Percent Daily Values (DV) are based on a 2,000 calorie diet.

INGREDIENTS: WATER, CORN MALTODEXTRIN, SUGAR, MILK PROTEIN CONCENTRATE, SOY OIL, SOY PROTEIN ISOLATE, SUCROMALT, COCOA POWDER (PROCESSED WITH ALKALI), CANOLA OIL; LESS THAN 0.5% OF: CORN OIL, MAGNESIUM PHOSPHATE, POTASSIUM CITRATE, CELLULOSE GEL, NATURAL AND ARTIFICIAL FLAVOR, POTASSIUM CHLORIDE, SODIUM CITRATE, CALCIUM PHOSPHATE, CALCIUM CARBONATE, SALT, CHOLINE CHLORIDE, ASCORBIC ACID, CELLULOSE GUM, MONOGLYCERIDES, SOY LECITHIN, CARRAGEENAN, POTASSIUM HYDROXIDE, LIQUID SUCRALOSE, FERRIC ORTHOPHOSPHATE, DI-ALPHA-TOCOPHERYL ACETATE, ACESULFAME POTASSIUM, ZINC SULFATE, NIACINAMIDE, MANGANESE SULFATE, CALCIUM PANTOTHENATE, COPPER SULFATE, VITAMIN A PALMITATE, THIAMINE CHLORIDE HYDROCHLORIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, FOLIC ACID, CHROMIUM CHLORIDE, BIOTIN, SODIUM MOLYBDATE, SODIUM SELENATE, POTASSIUM IODIDE, CYANOCOBALAMIN, PHYLLQUINONE AND VITAMIN D₃.

CONTAINS MILK AND SOY INGREDIENTS.

Abbott Nutrition, Abbott Laboratories, Columbus, Ohio 43219-3034 USA



**Nutrient Shake
(2x 8 fl oz)**

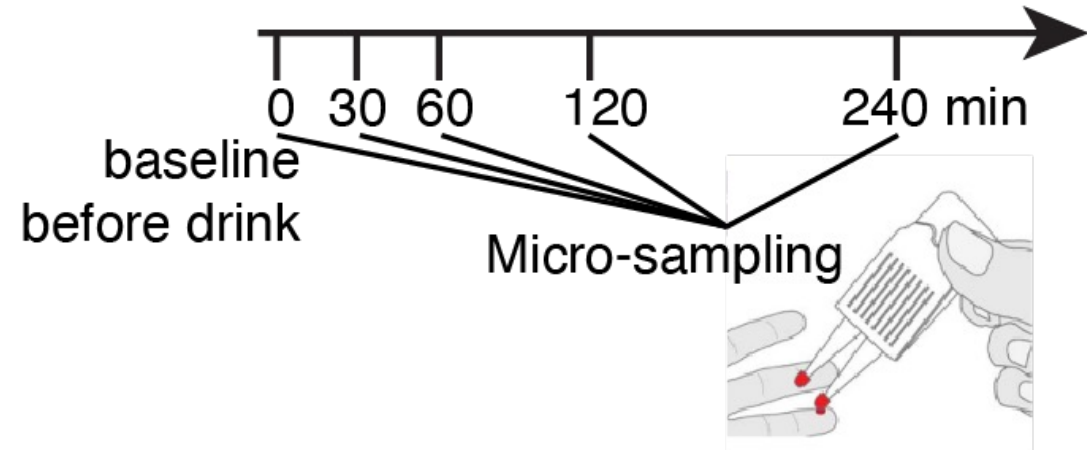
440 kcal
66g carbohydrate
18g protein
12g fat

Ensure shake

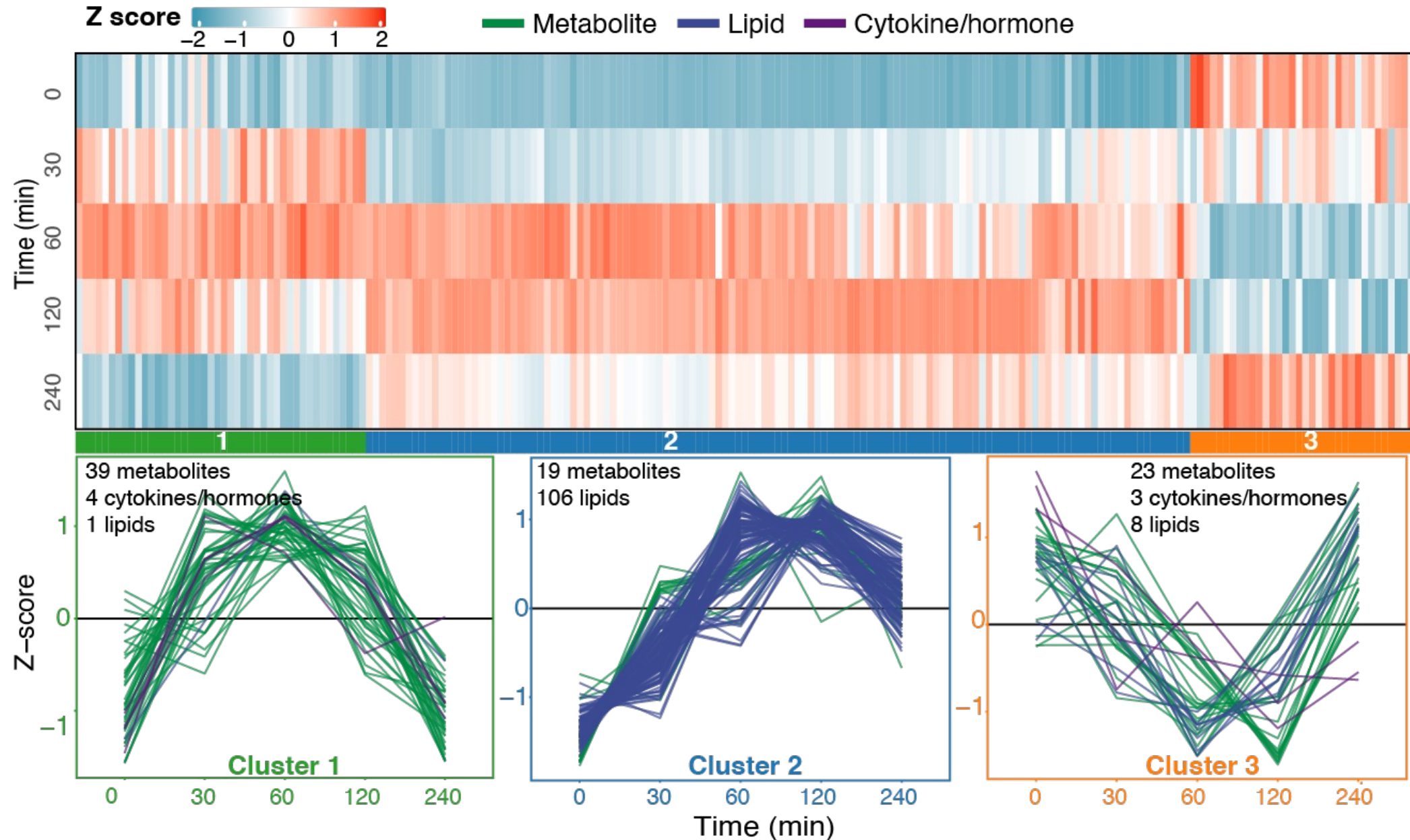
32 Participants



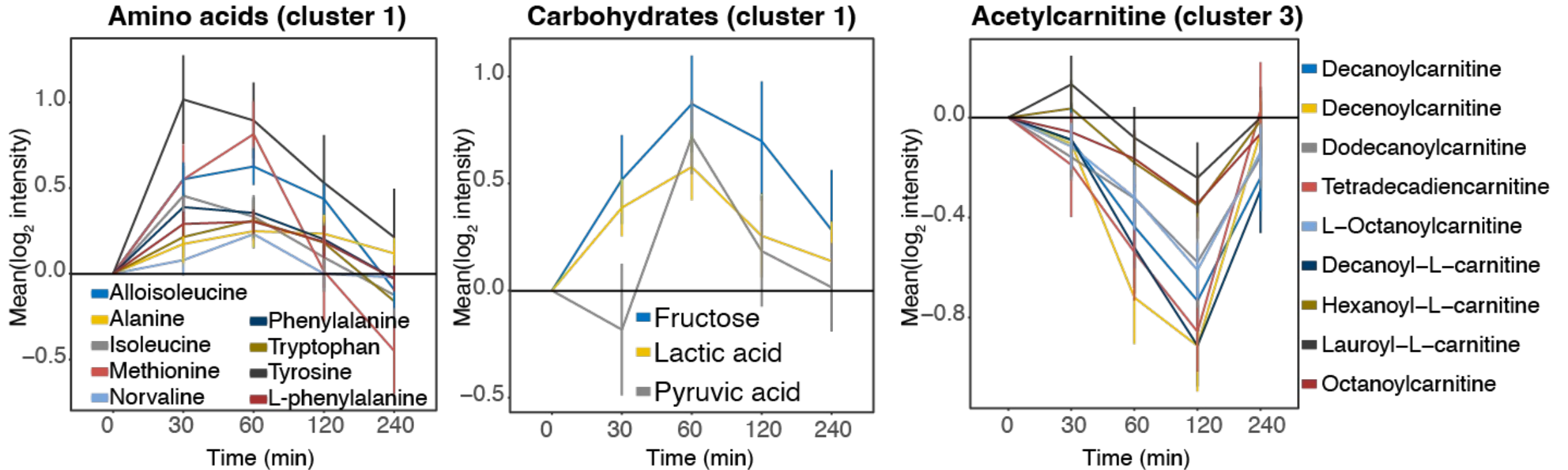
Morning, fasted



Molecules Have Different Kinetics of Biochemical Responses to Ensure Shake

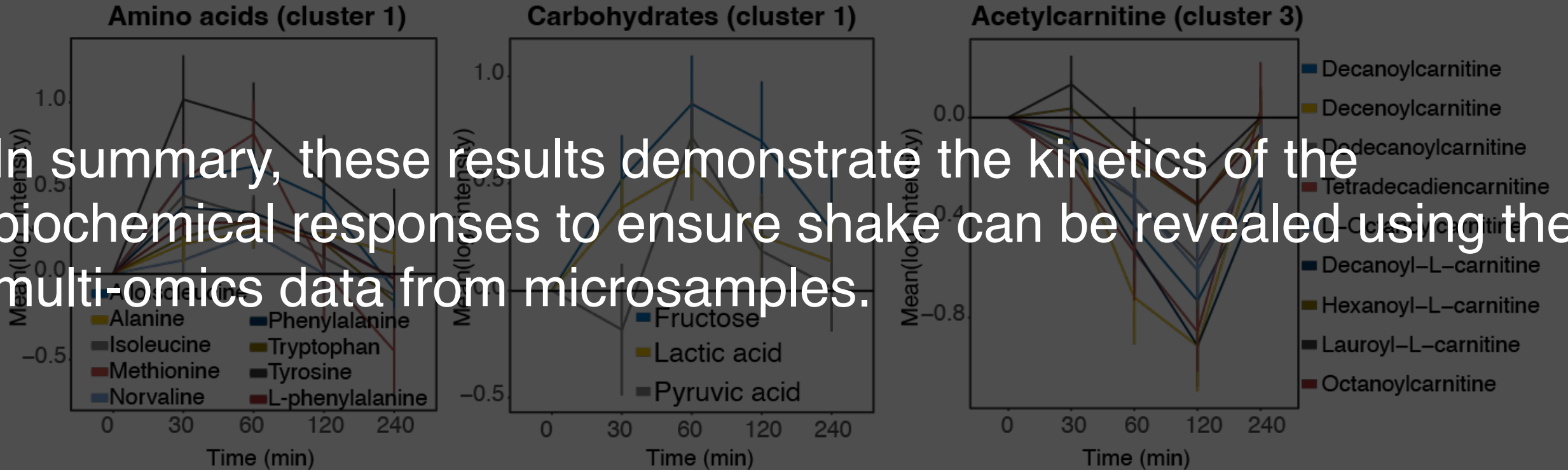


Metabolite Responding to Ensure Shake



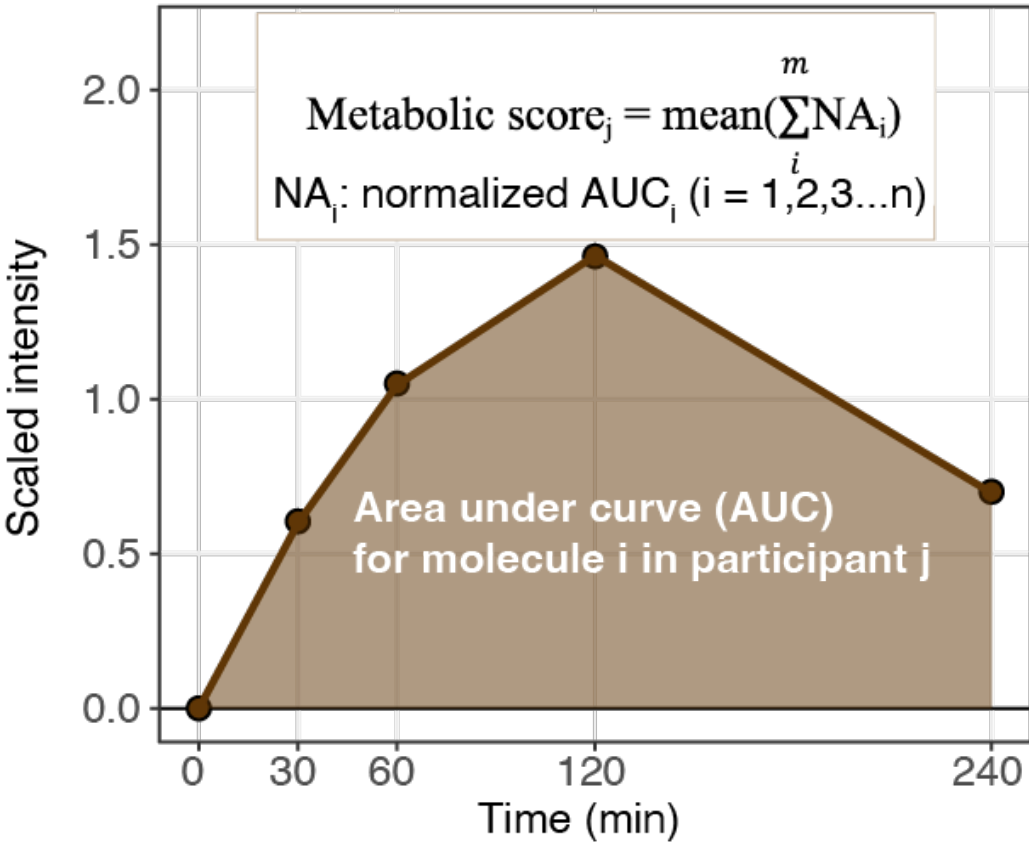
Metabolite Responding to Ensure Shake

In summary, these results demonstrate the kinetics of the biochemical responses to ensure shake can be revealed using the multi-omics data from microsamples.



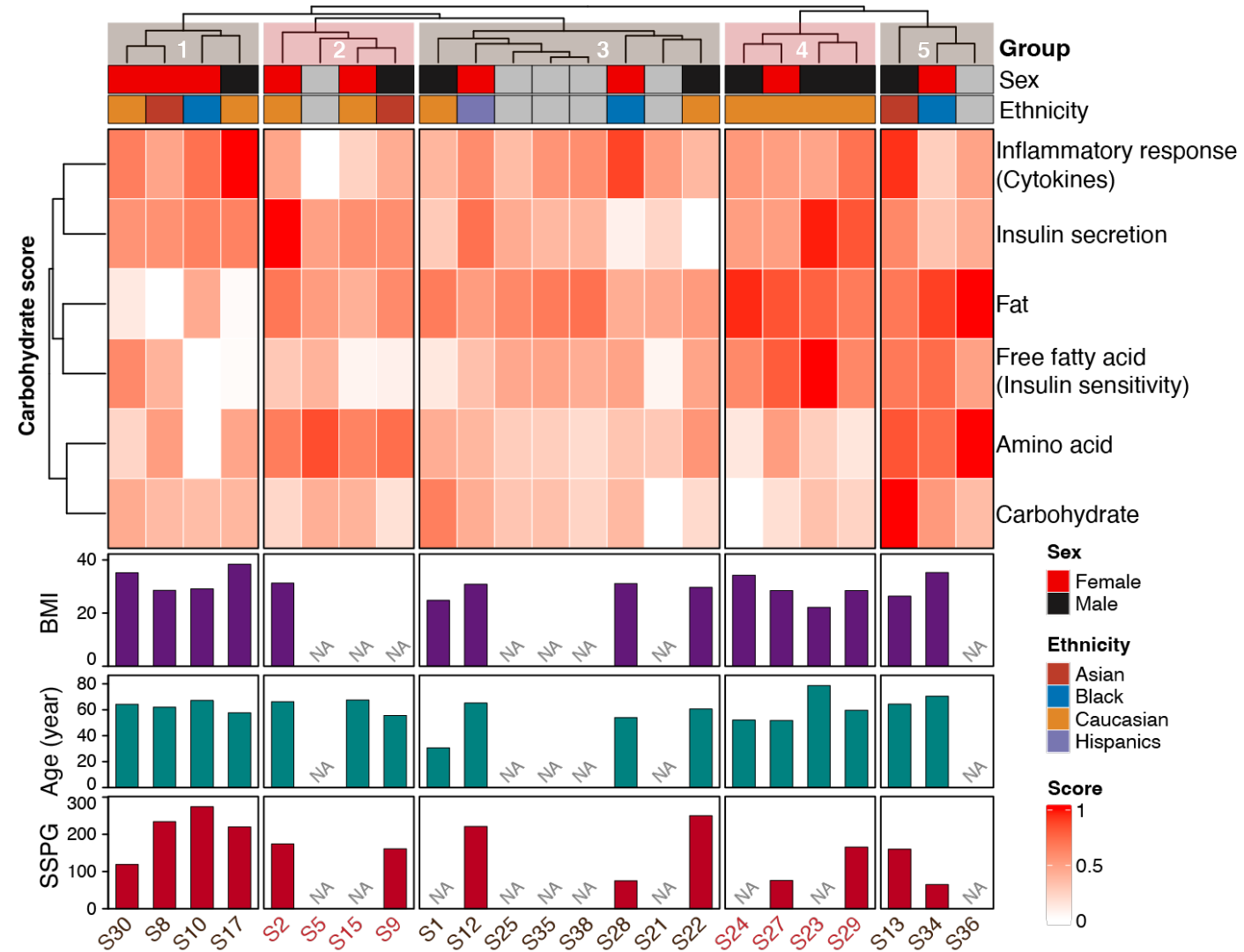
Quantify People's Responses to Different Nutrition

Metabolic Scores

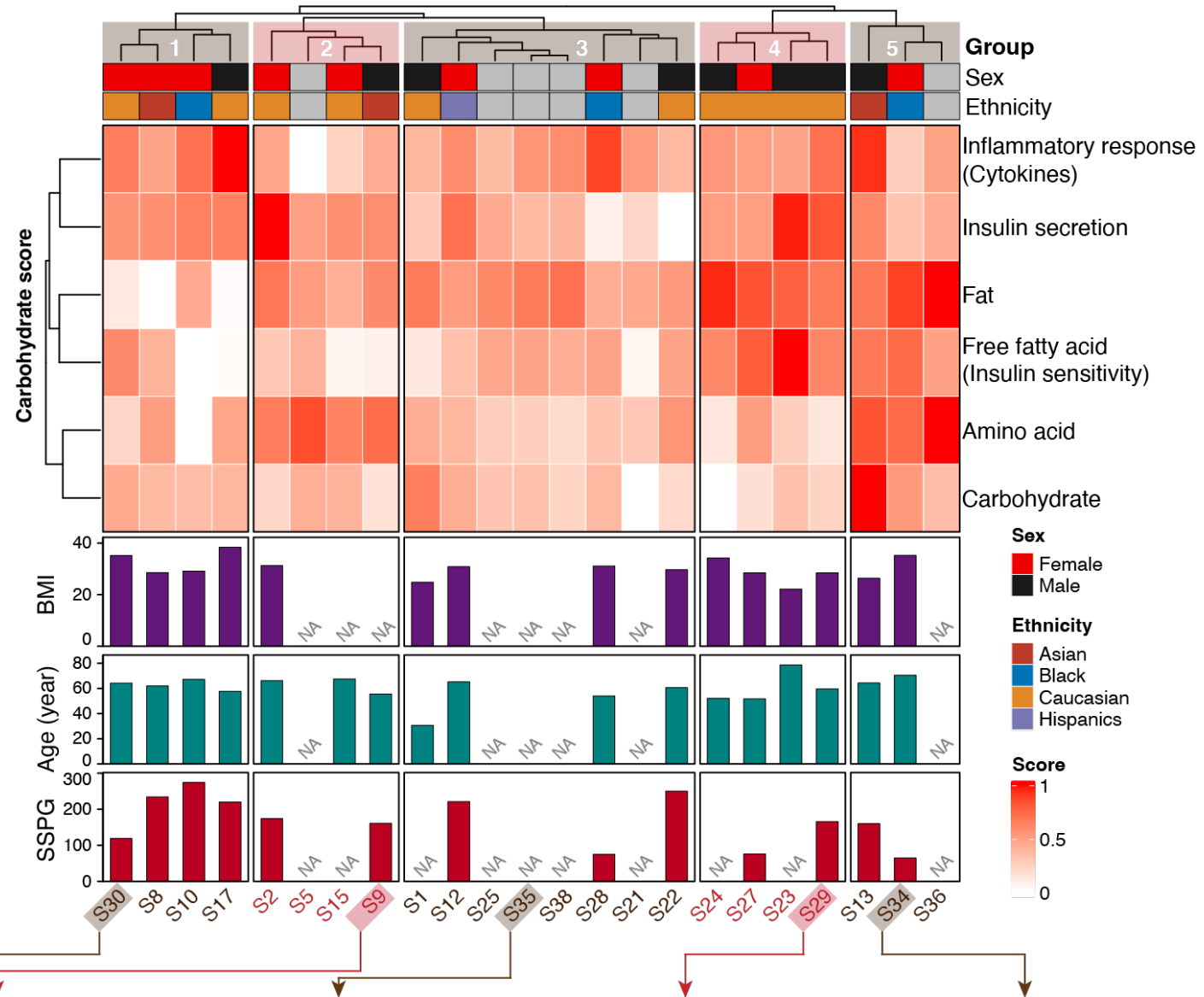


Metabolic score	Molecules
1 Carbohydrate score	Fructose, lactic acid, pyruvic acid
2 Fat score	All TAGs (triacylglycerols)
3 Amino acid score	Alloisoleucine, alanine, isoleucine, methionine, norvaline, phenylalanine, tryptophan, tyrosine, L-Phenylalanine
4 Insulin secretion score	C-peptide, insulin
5 Free fatty acid score	All FFAs (free fatty acid)
6 Inflammatory response	All cytokines

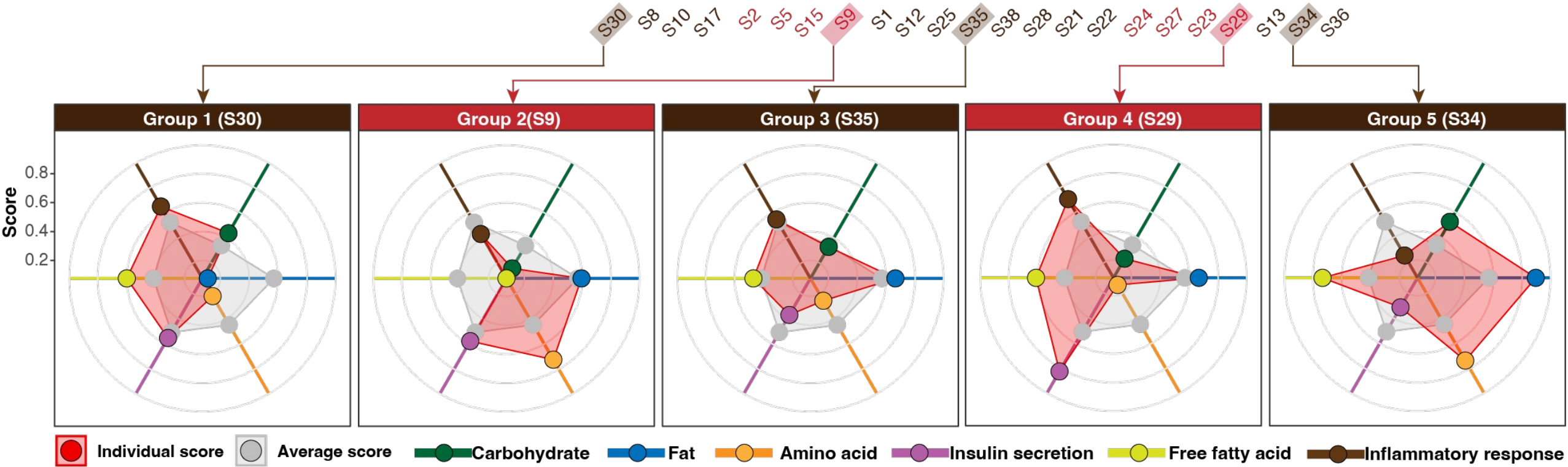
Quantify People's Responses to Different Nutrition



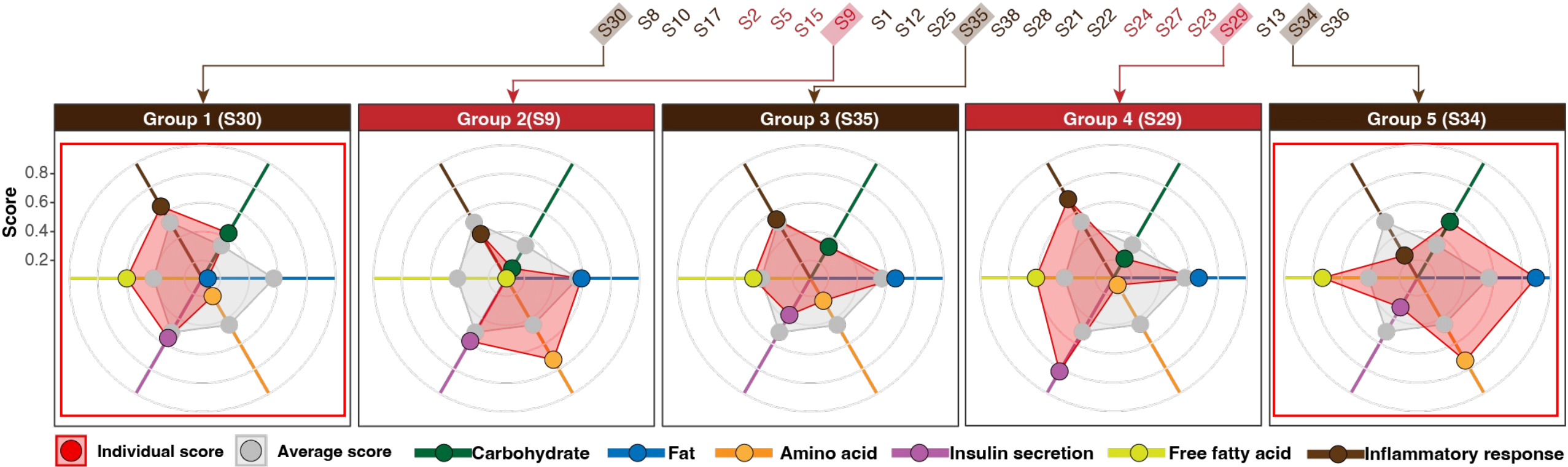
Quantify People's Responses to Different Nutrition



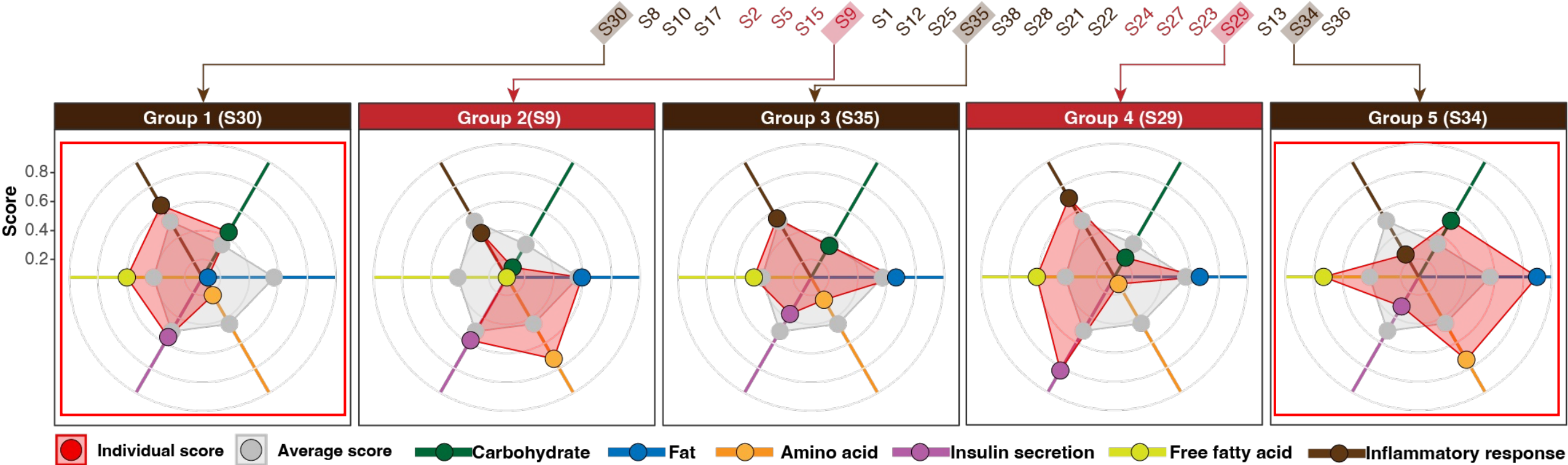
Quantify People's Responses to Different Nutrition



Quantify People's Responses to Different Nutrition

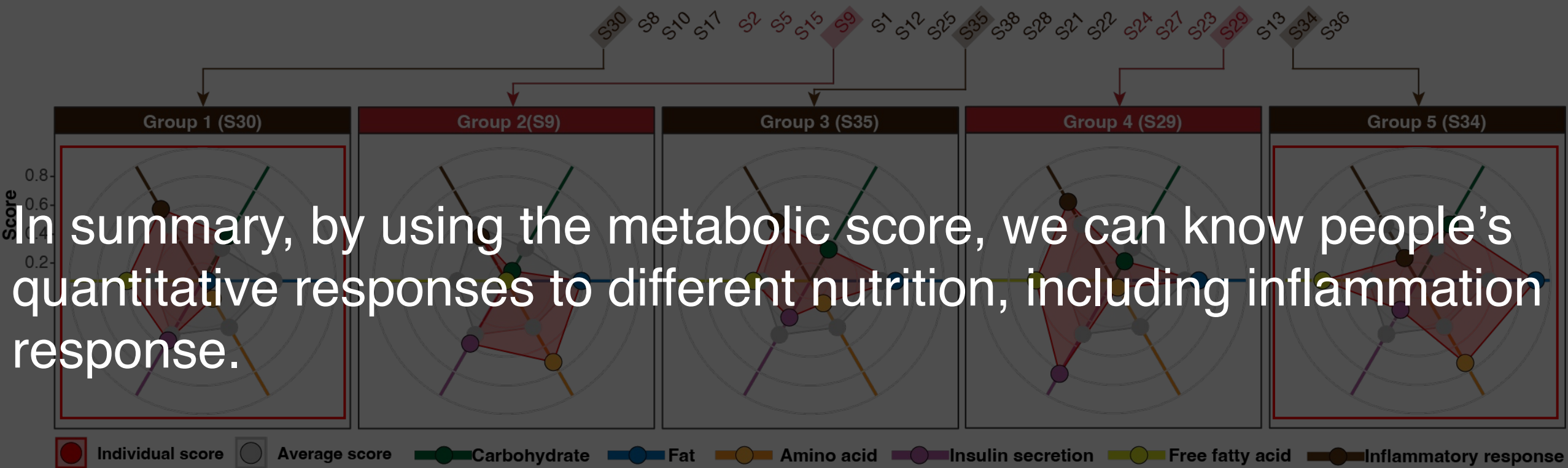


Quantify People's Responses to Different Nutrition



These differences may be due to several different underlying mechanisms, including levels of enzymes or gut microbiome required to process particular molecules in the Ensure shake.

Quantify People's Responses to Different Nutrition



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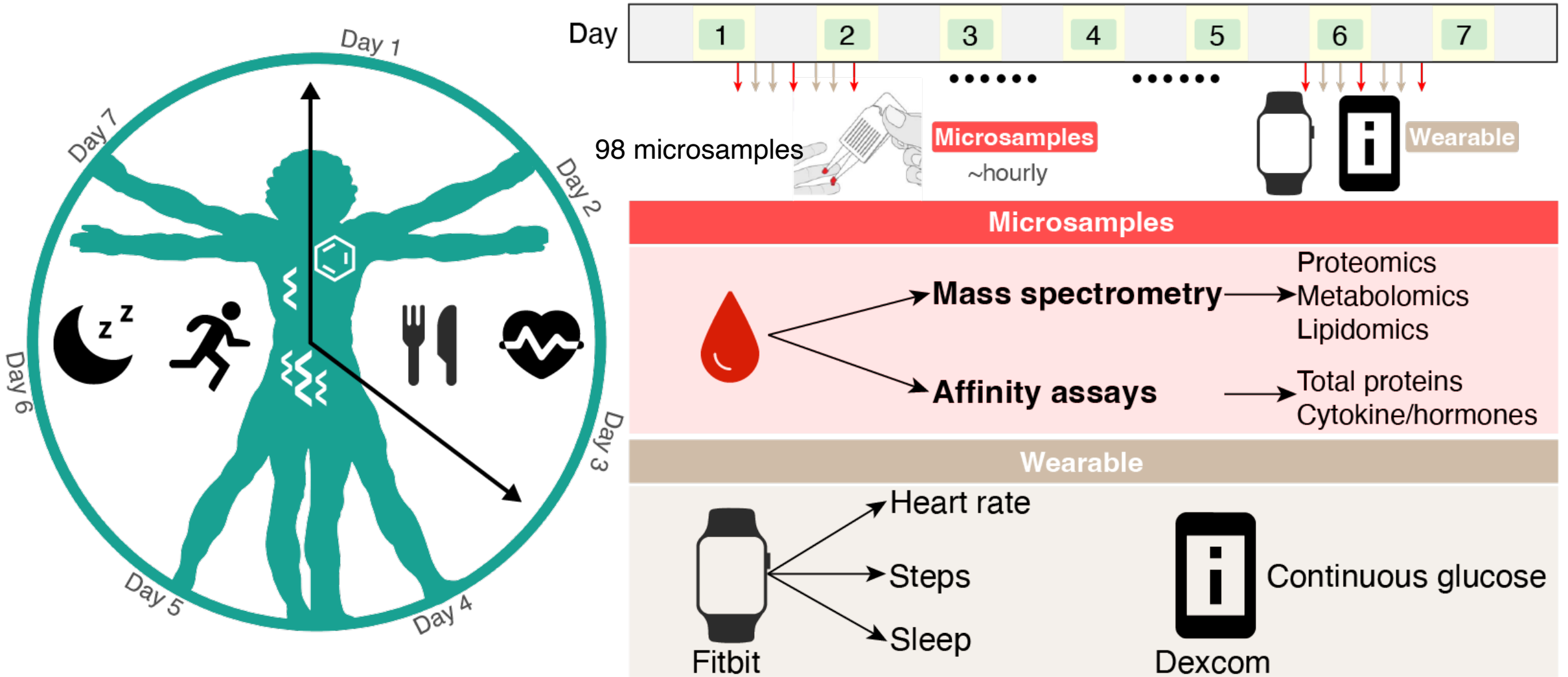
Case Study #2

24/7 Personalized Whole Physiome Profiling

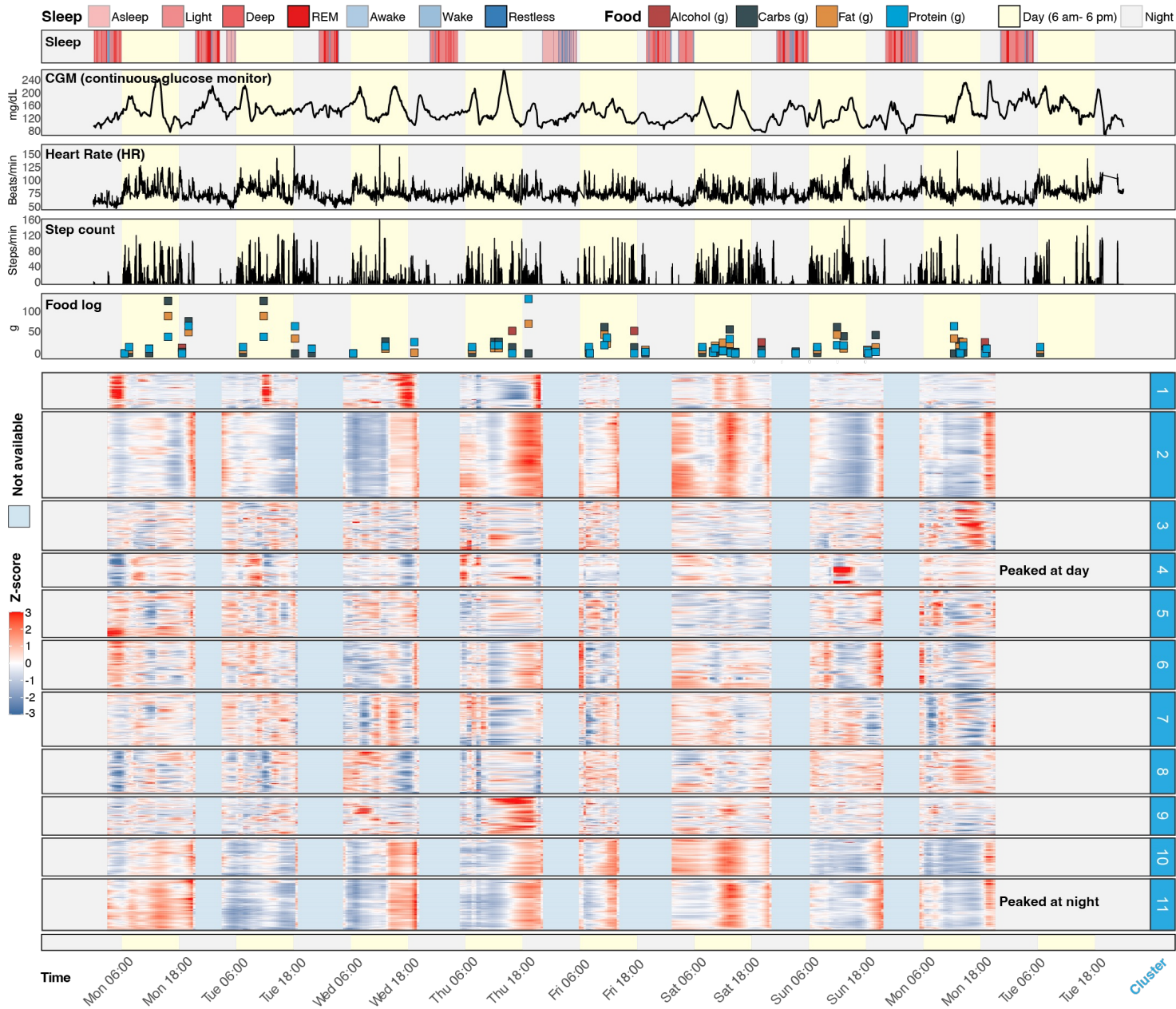
Electrolytes	Na, K, Ca, Mg, AG
Diabetes	HbA1c, ALB, GLU, UACB, CR, ALCRU
Cardiovascular disease	CHOL, LDLHDL, HDL, HDL, HDL, HDL
Hepatic	ALKP, BU, AL, TBIL
Immune system	LYM, LYMAB, MONO, MONOAB, NE, UTAS IGM, EOS, EOS, BASO, BASO, WBC, RBC, CRP
Hematologic	mRen PLT, GLOB, TP, HGB, HCT, RDW, MCH, MCV, RBC, MCHC



Study Design and Overview



Data Summary



CGM: continuous glucose monitoring

HR: heart rate

Step

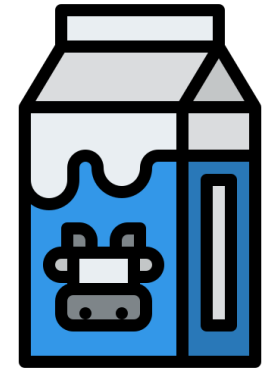
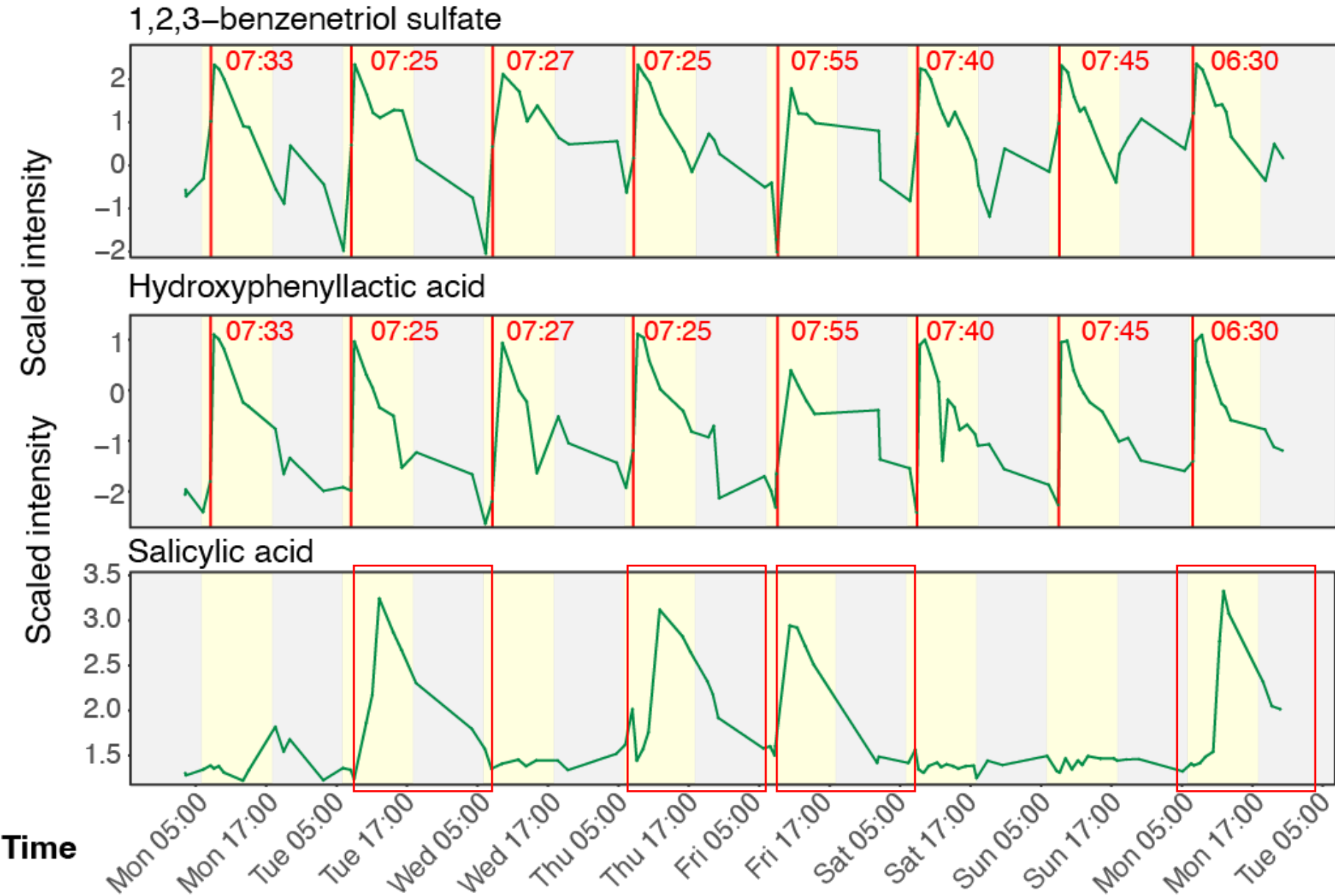
Sleep: asleep, light, deep, ram, awake, awake and restless

Food: food log

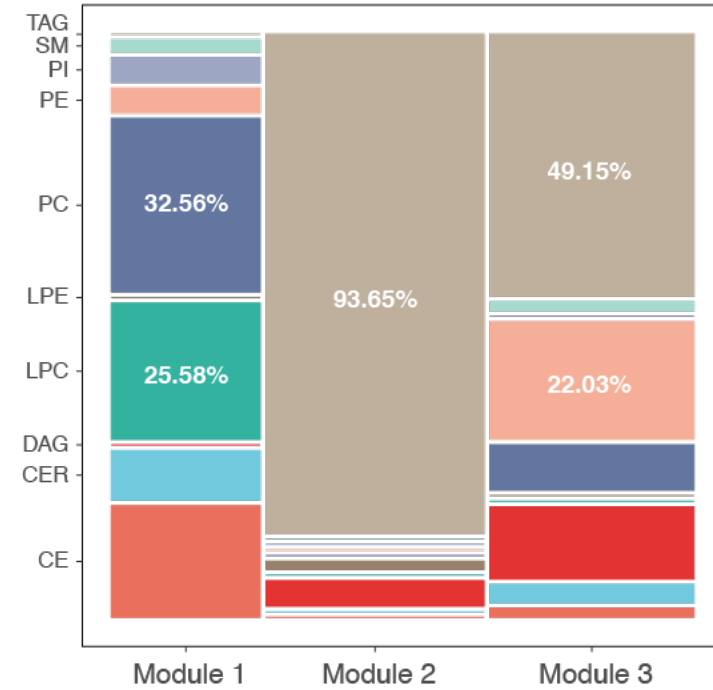
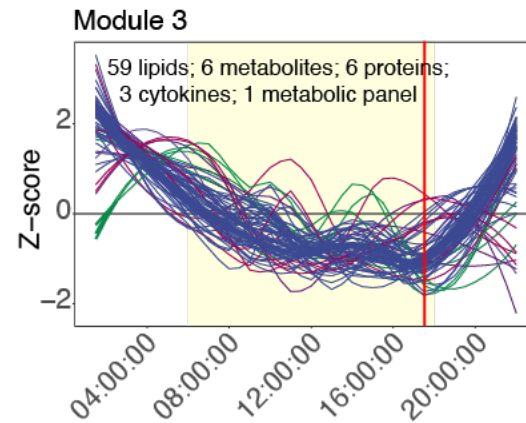
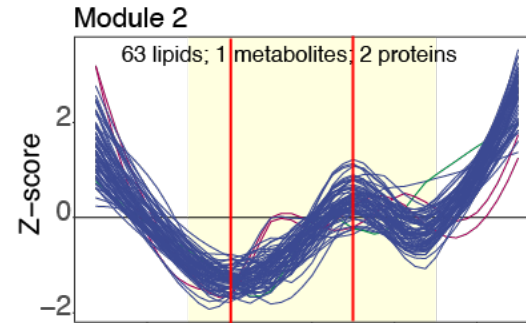
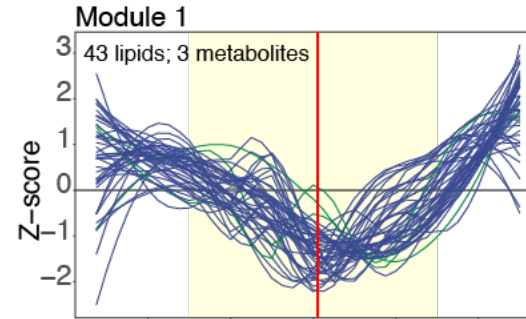
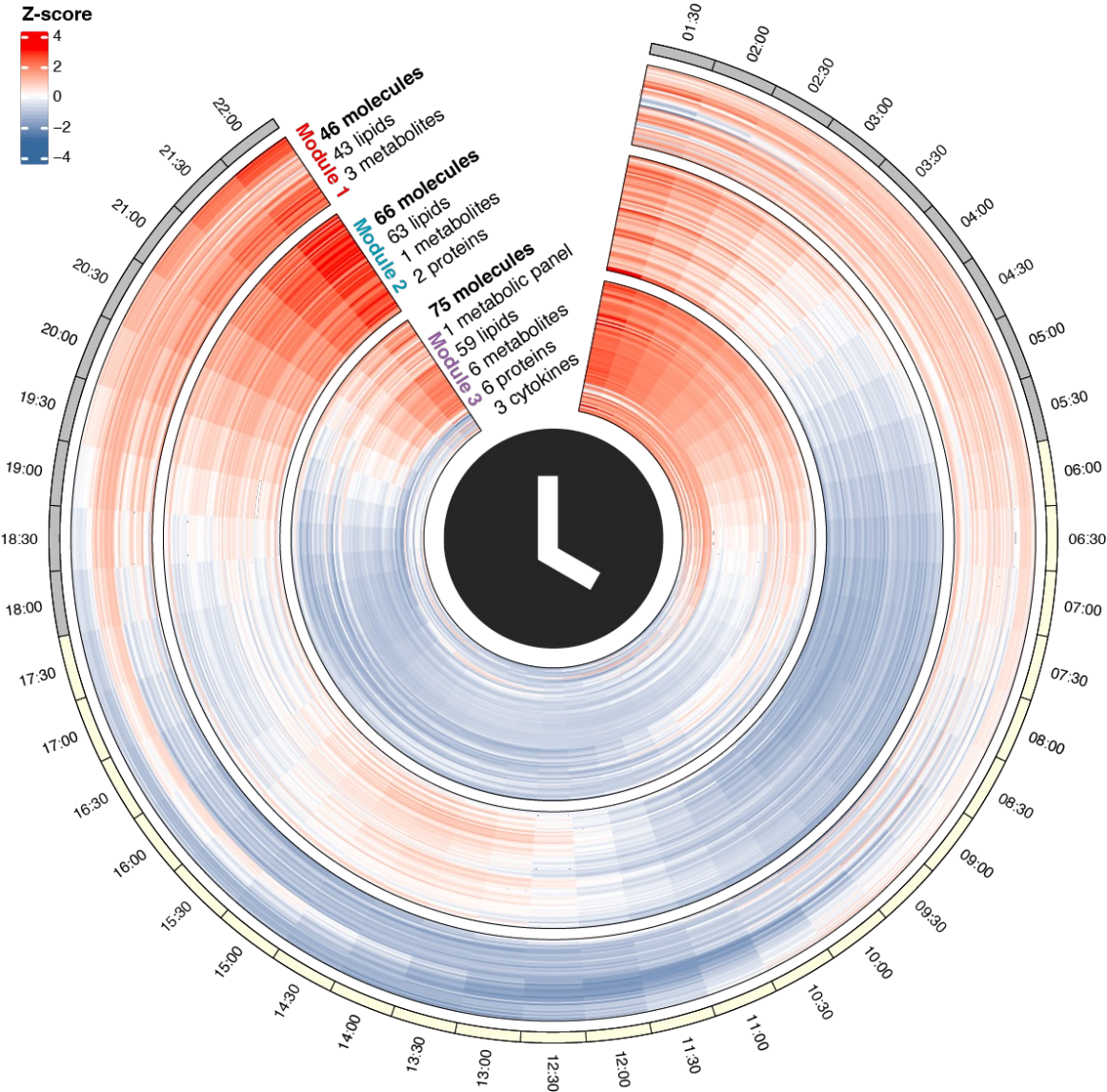
Wearable data

Multi-omics data

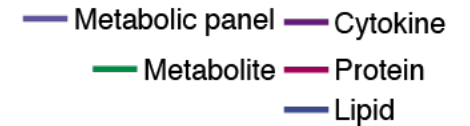
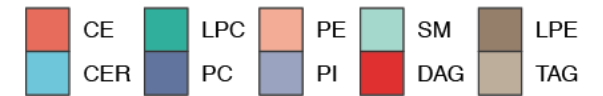
Multi-Omics Data Reflects the Food Intake



Circadian Rhythms of Internal Molecules In Human Blood



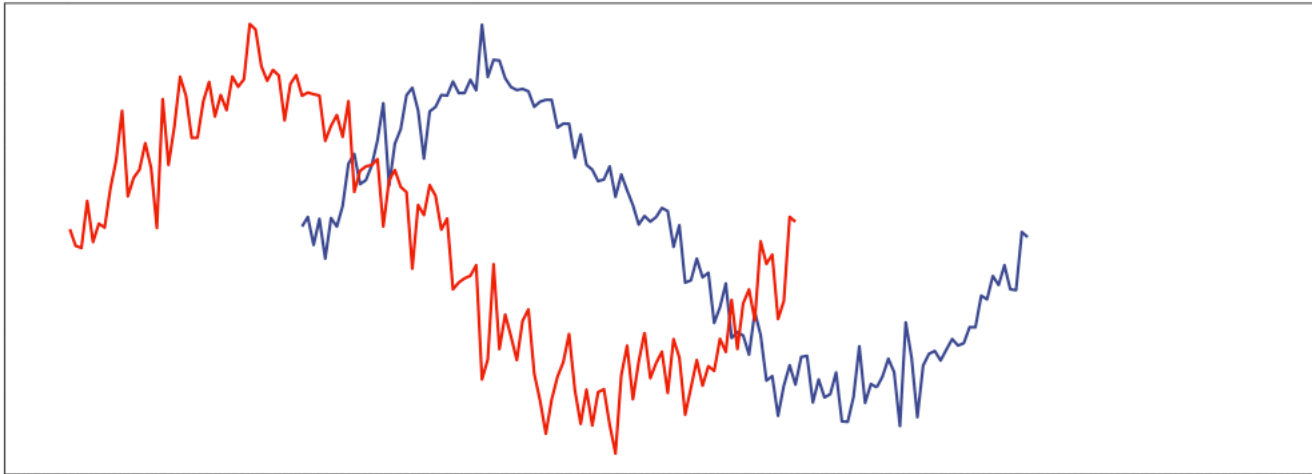
Lipid class



Potential Causal Associations Between Wearable and Molecules

Lagged Correlation

Shift time: -40



Advantage:

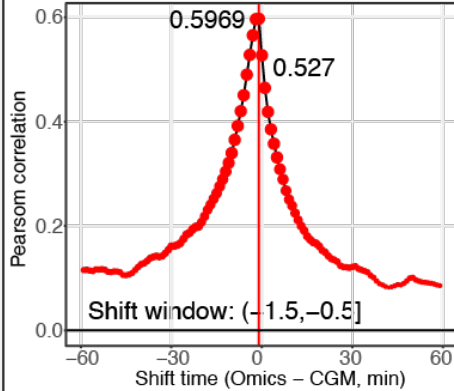
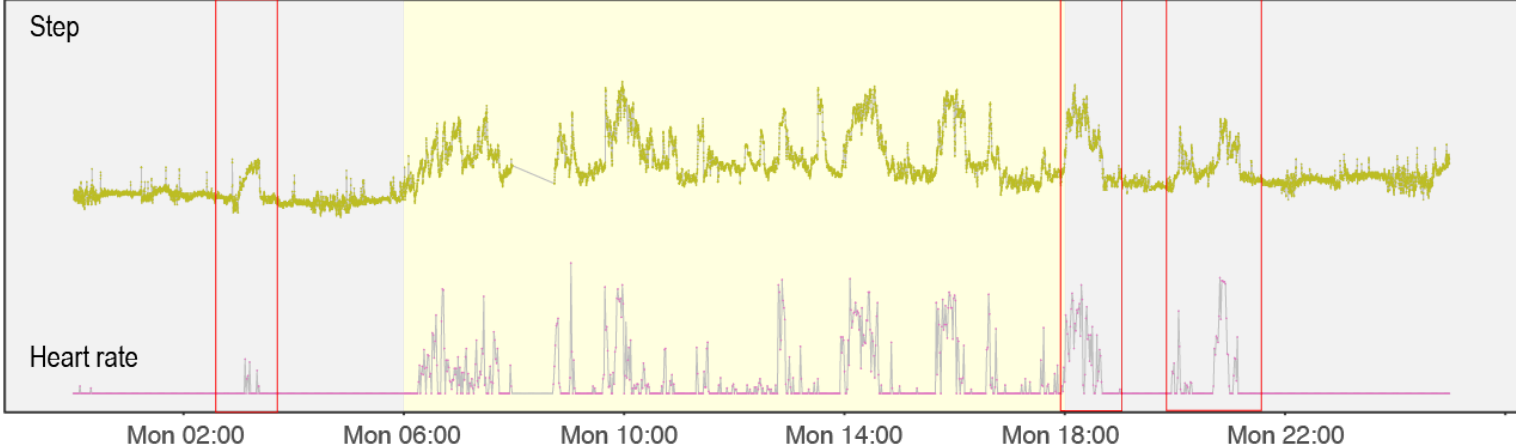
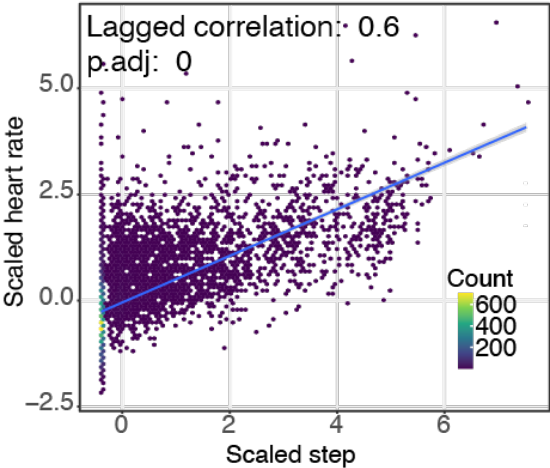
1. Can catch the nonsynchronous associations between wearable and omics data.
2. Can also catch the synchronous associations between wearable and omics data.
3. **Can get some causal associations between wearable and omics data.**

Requirement:

1. High resolution sampling.
2. Enough time points.

Microsampling makes the lagged correlation algorithm possible.

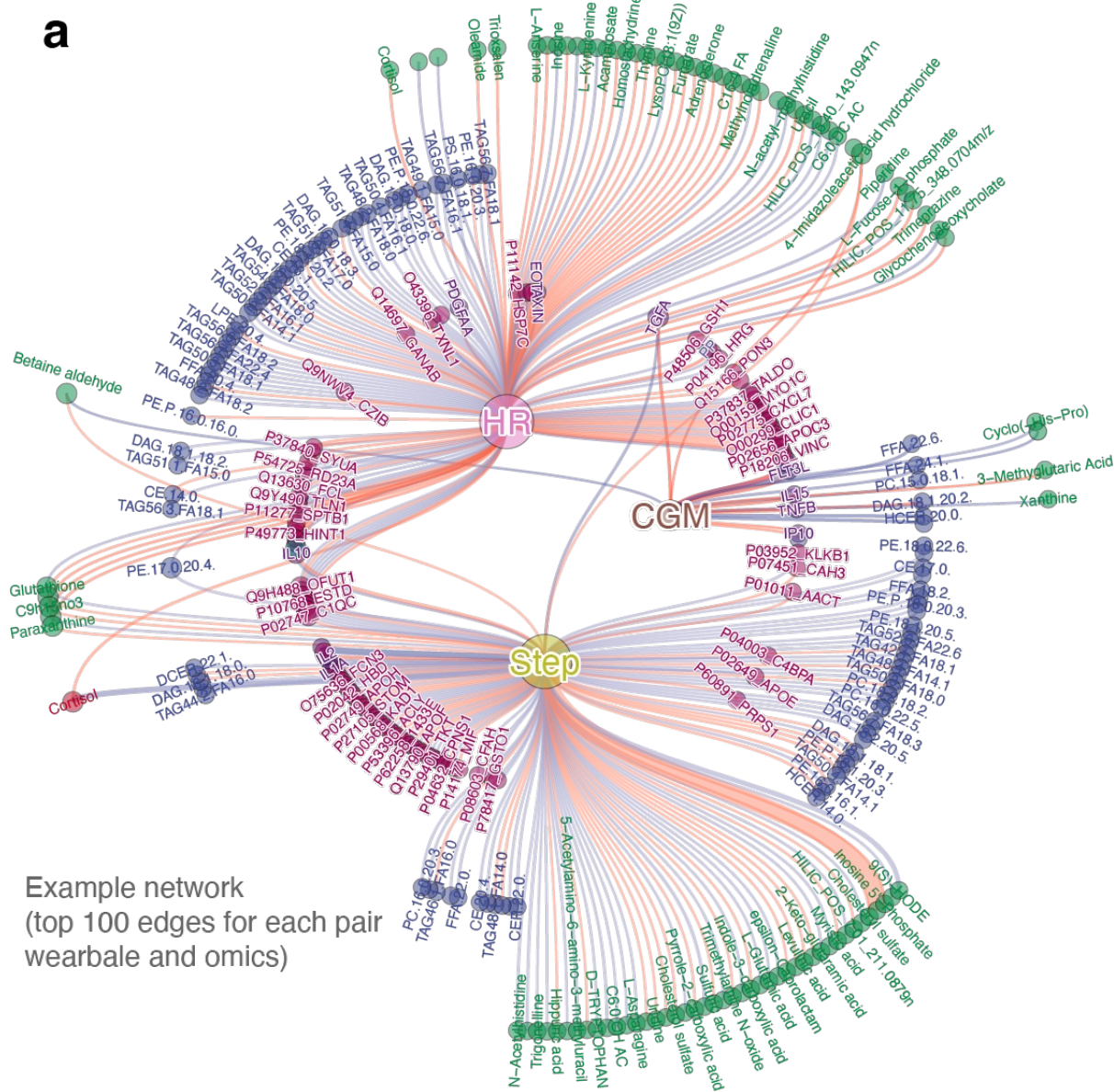
Example: Step versus Heart Rate



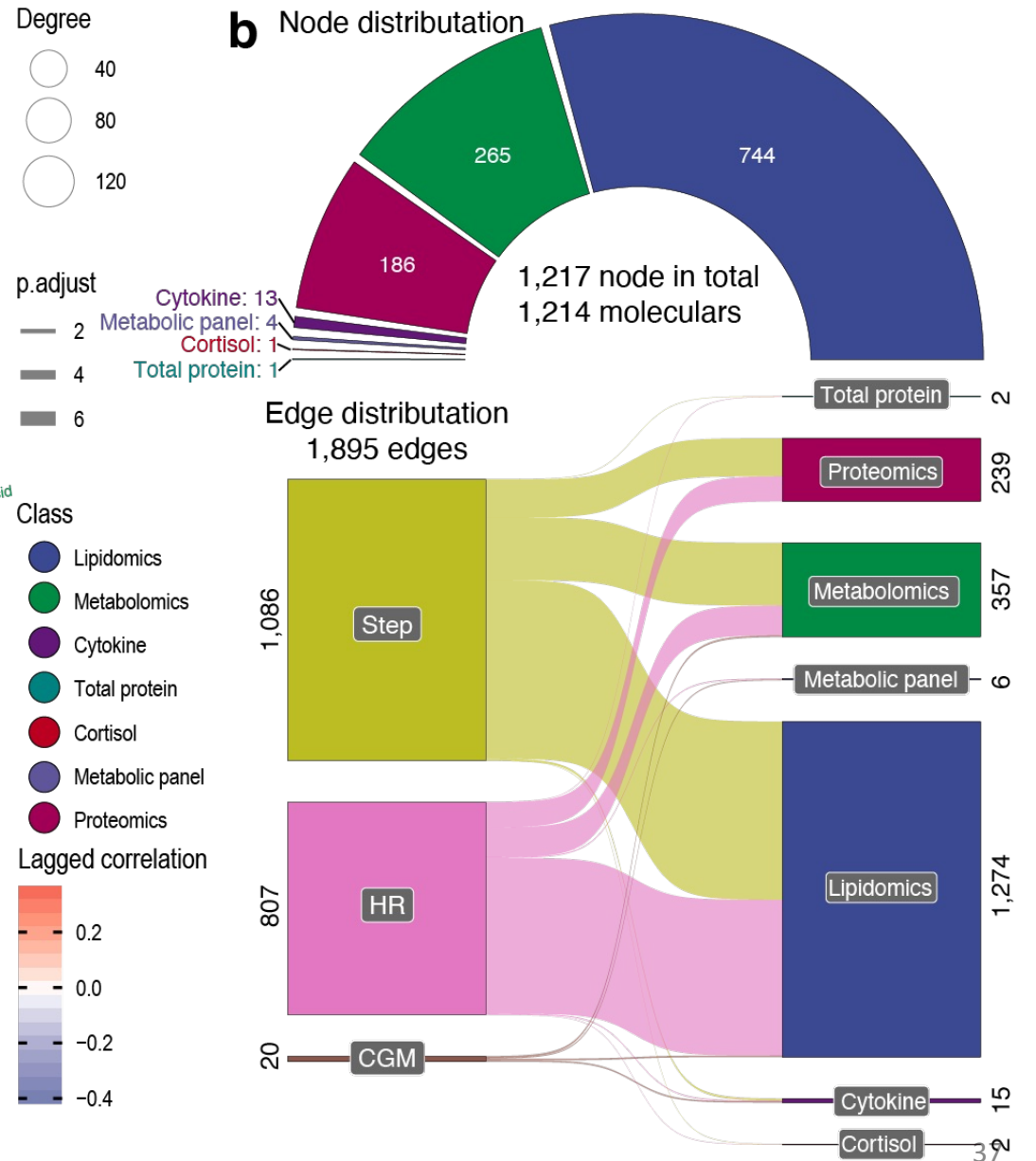
Step is a little bit before the heart rate (step increase the heart rate).

Wearable and Internal Molecular Association Network

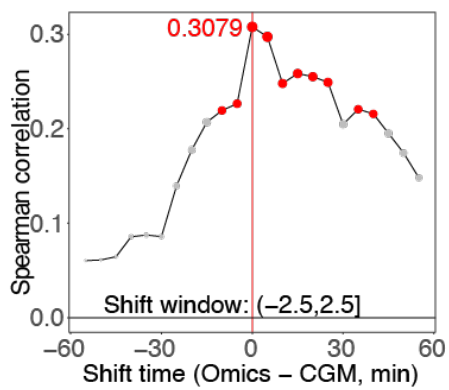
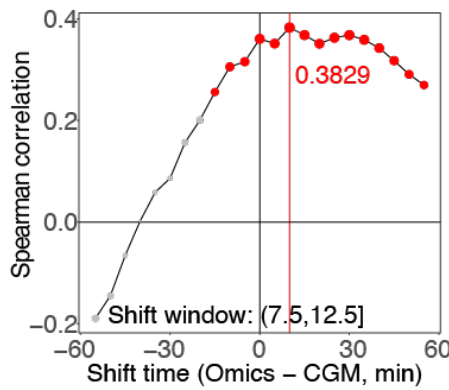
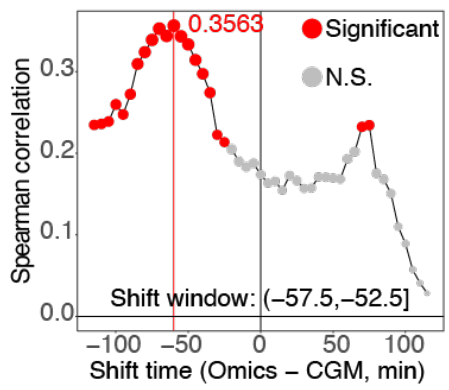
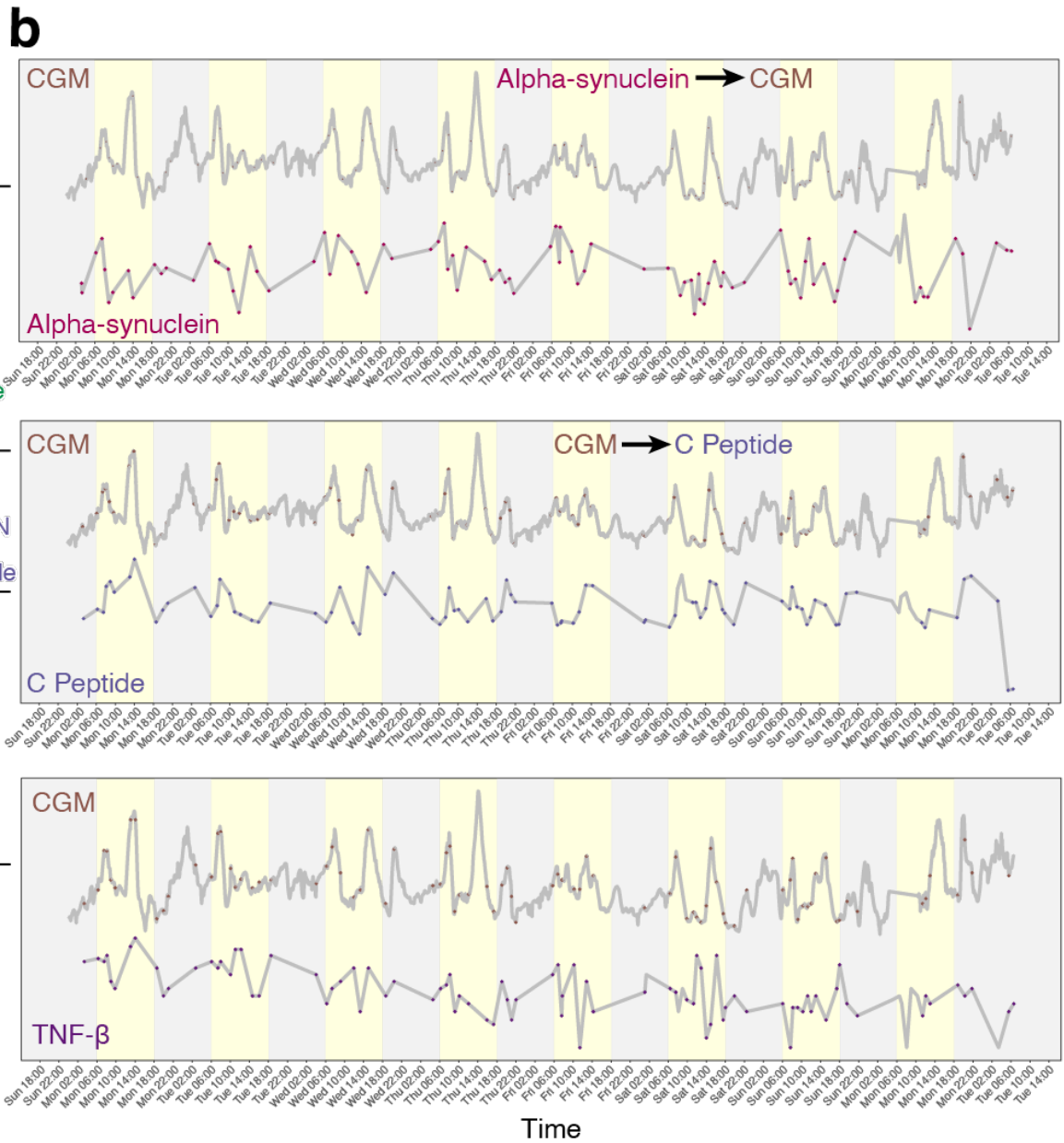
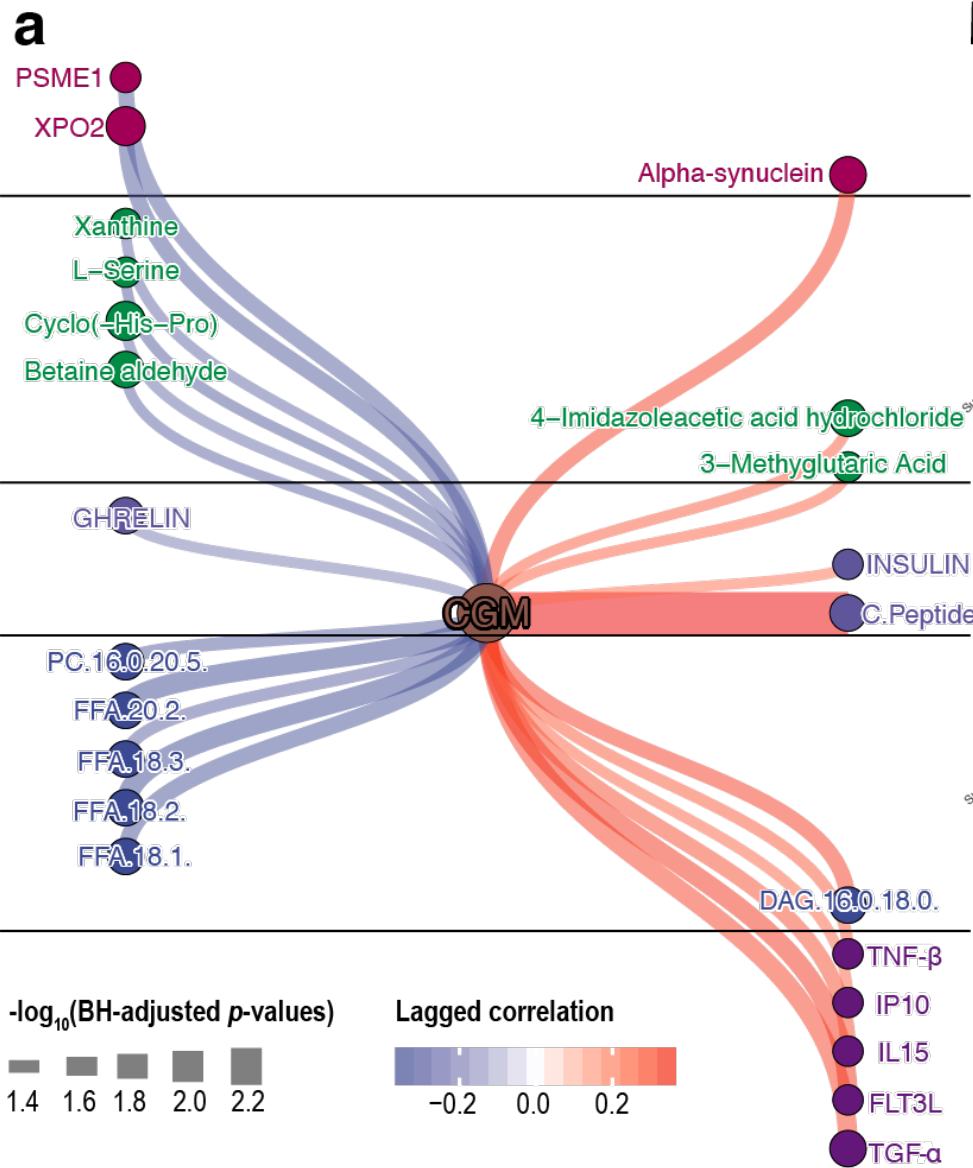
a



b Node distribution



Glucose Subnetwork



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Summary

- </> **A multi-omics** microsampling approach enables the measurement of thousands of metabolites, lipids, cytokines, and proteins in frequently collected 10 μ l blood samples.
- </> **A methodology** achieves fully remote, scalable, high-temporal-resolution omics and sensor monitoring.
- </> **It has** the potential for large-scale comprehensive, dynamic molecular and digital biomarker discovery and monitoring as well as health profiling.
- </> **A new** algorithm can be used to discover potential causal relationships.
- </> **By integrating** high frequent microsampling multi-omics and wearable data, we can achieve personalized health status monitoring in the future.

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Snyder lab

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Dr. Chuchu Wang
Dr. Jessalyn Ubellecker



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National Institutes
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Thank you for your attention!

Q&A

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