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TOWARDS A DIAGNOSIS OF NON-CELIAC GLUTEN SENSITIVITY:

the contribution of metabolomics for monitoring metabolites produced by *in vitro* digestates of bread



Houssein ZHOUR¹, Mélyny GENOT², Marie-Agnes PEYRON², Melanie PETERA¹, Veronique SANTE-LHOUELLIER³, Stephanie DURAND¹, Delphine CENTENO¹, Emmanuelle BANCEL⁴, Catherine RAVEL⁴, Estelle PUJOS-GUILLOT¹

¹Université Clermont Auvergne, INRAE, UNH, Plateforme d'Exploration du Métabolisme, MetaboHUB Clermont, 63000 Clermont-Ferrand, France

² Human Nutrition Unit (UNH), (INRAE), Université Clermont Auvergne, F-63000 Clermont-Ferrand, France

³QuaPA, UR 370, (INRAE), 63122 Saint Genès Champanelle

⁴Genetics Diversity and Ecophysiology of Cereals, (INRAE), Université Clermont-Auvergne, 63000 Clermont-Ferrand, France

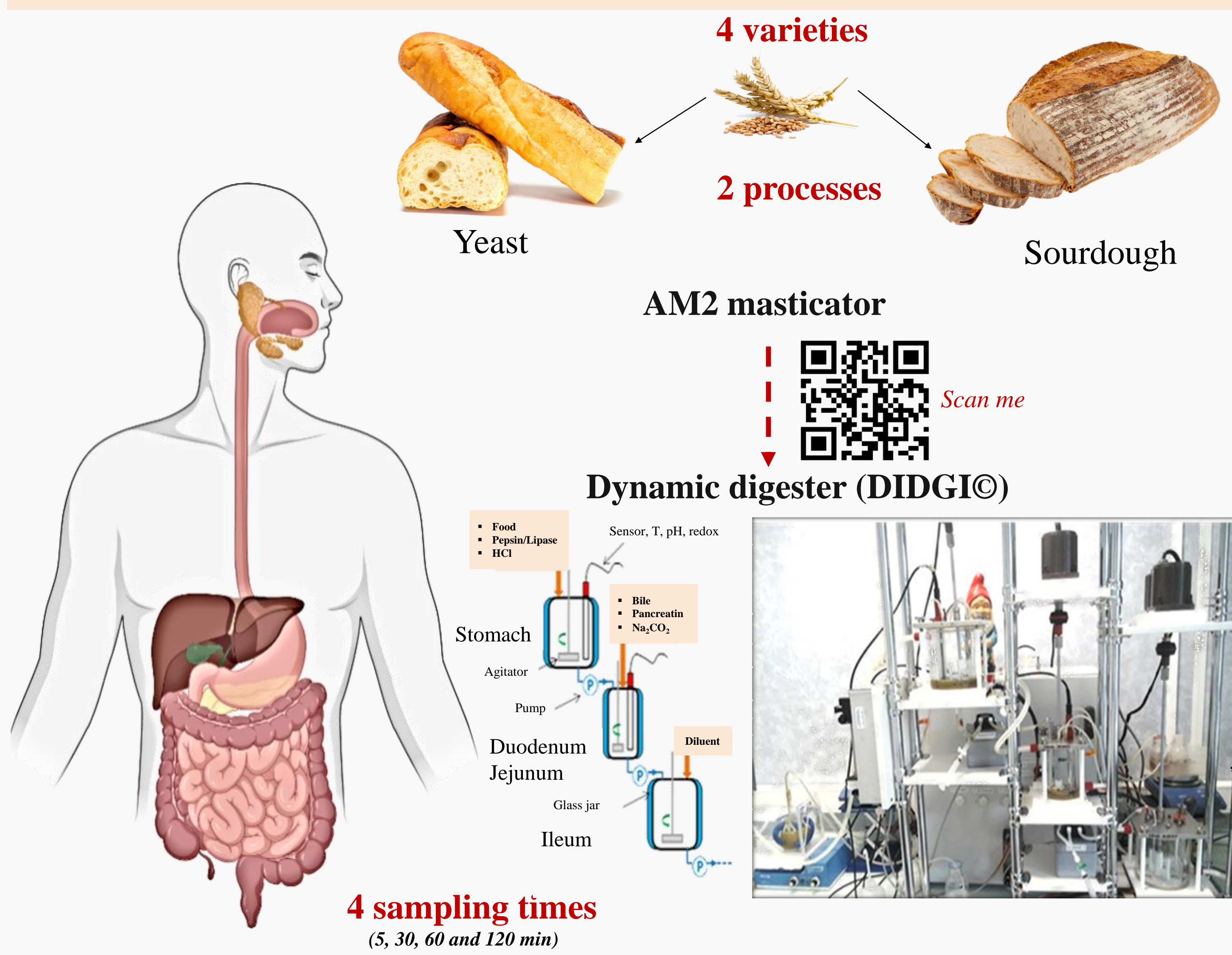
INTRODUCTION

- Over the past decade, the non-celiac wheat sensitivity (NCWS) is more and more self-diagnosed, which makes the gluten-free diet more frequent, without objective clinical criteria.
- NCWS is poorly understood and challenging to diagnose in contrast to celiac disease because of a lack of clinical indicators.
- One objective in this study was to monitor metabolites produced by *in vitro* digestates using an untargeted metabolomics approach.
 - Finding biomarkers associated with this phenotype is critical for an accurate diagnosis and innovative patient management.



PREPARATION OF THE STOMACH AND INTESTINAL DIGESTATES

- A recent approach with *in vitro* investigation was applied to study the overall digestive process of different breads, combining tools from the oral step thanks to the AM2 masticator apparatus, until the end of digestion thanks to a dynamic digester (DIDGI©) mimicking the physiology of the adult gastrointestinal tract "GIT".



RESULTS

Untargeted metabolomic analysis (ESI+) of gastric bread digestates

Effect of the digestion time:

Results reveal that metabolic profiles of gastric digestates allow discriminating the sampling time. Hence the effectiveness of our *in vitro* digestion system is shown.

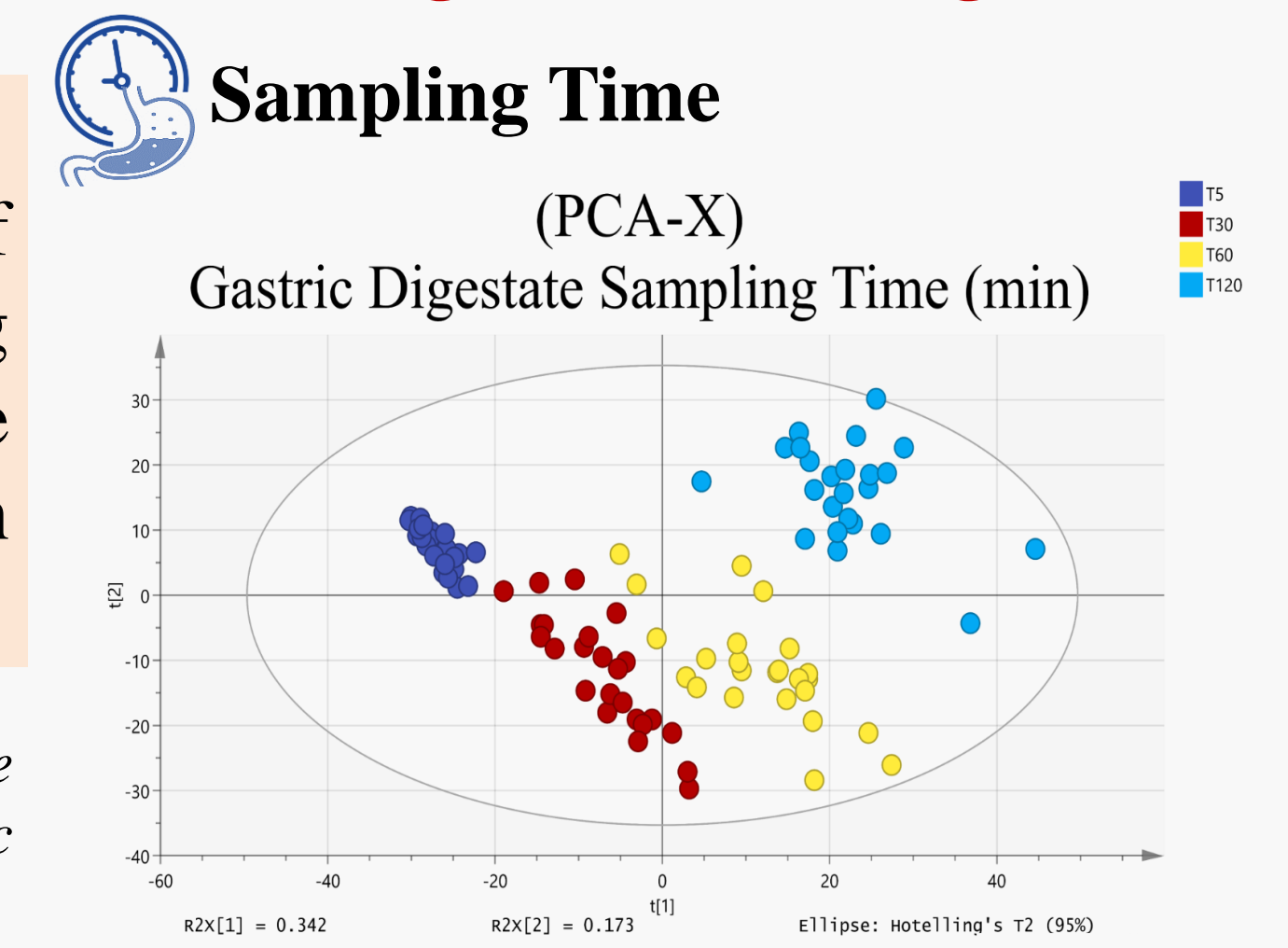


Fig.1 Principal component analysis (PCA) of the metabolite - related features identified in gastric digestate taken after 5, 30, 60 and 120 min.

OPLS-DA analyses can clearly discriminate between:

the wheat varieties used, particularly the V39 variety, and the two processes (Yeast and Sourdough). This shows the influence of bread type on digestion and therefore on the production of metabolites.

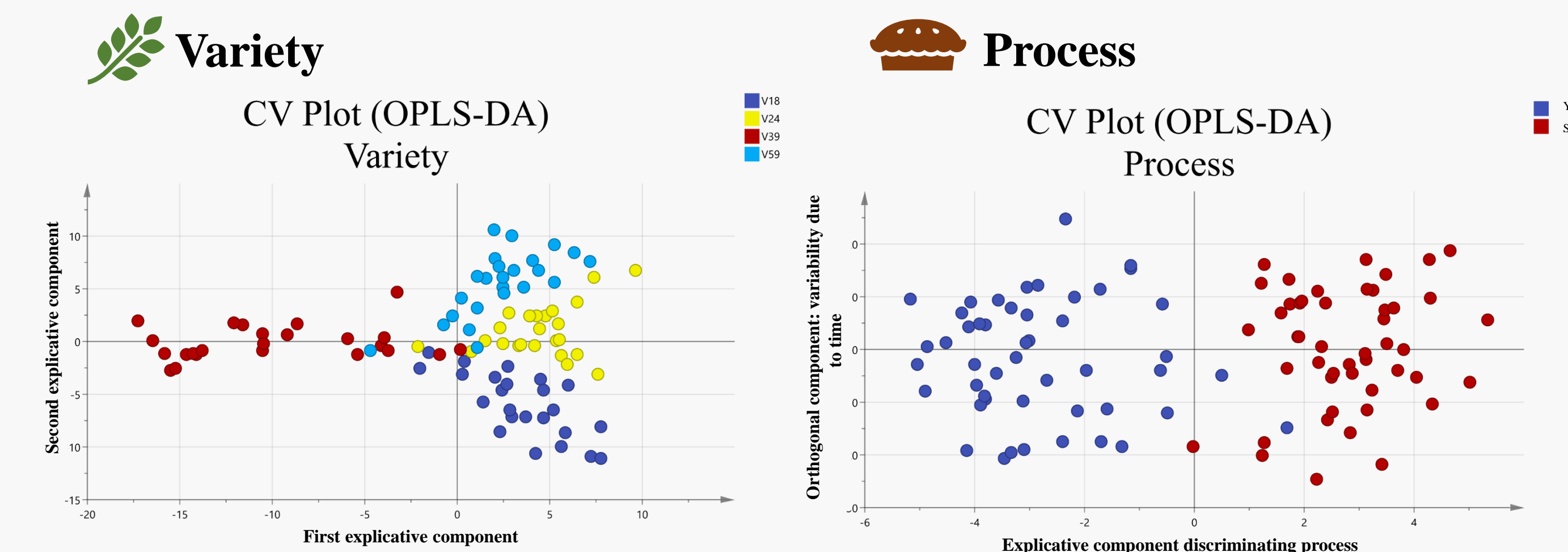


Fig.2 Cross-validated scores plot of the OPLS-DA model built to discriminate between the four varieties (v18, v24, v39 and v59) and the two processes (Y: Yeast and S: Sourdough).

Univariate statistical analysis whole dataset as well as per time point:

Significantly different metabolites were identified depending on the variety and the process.

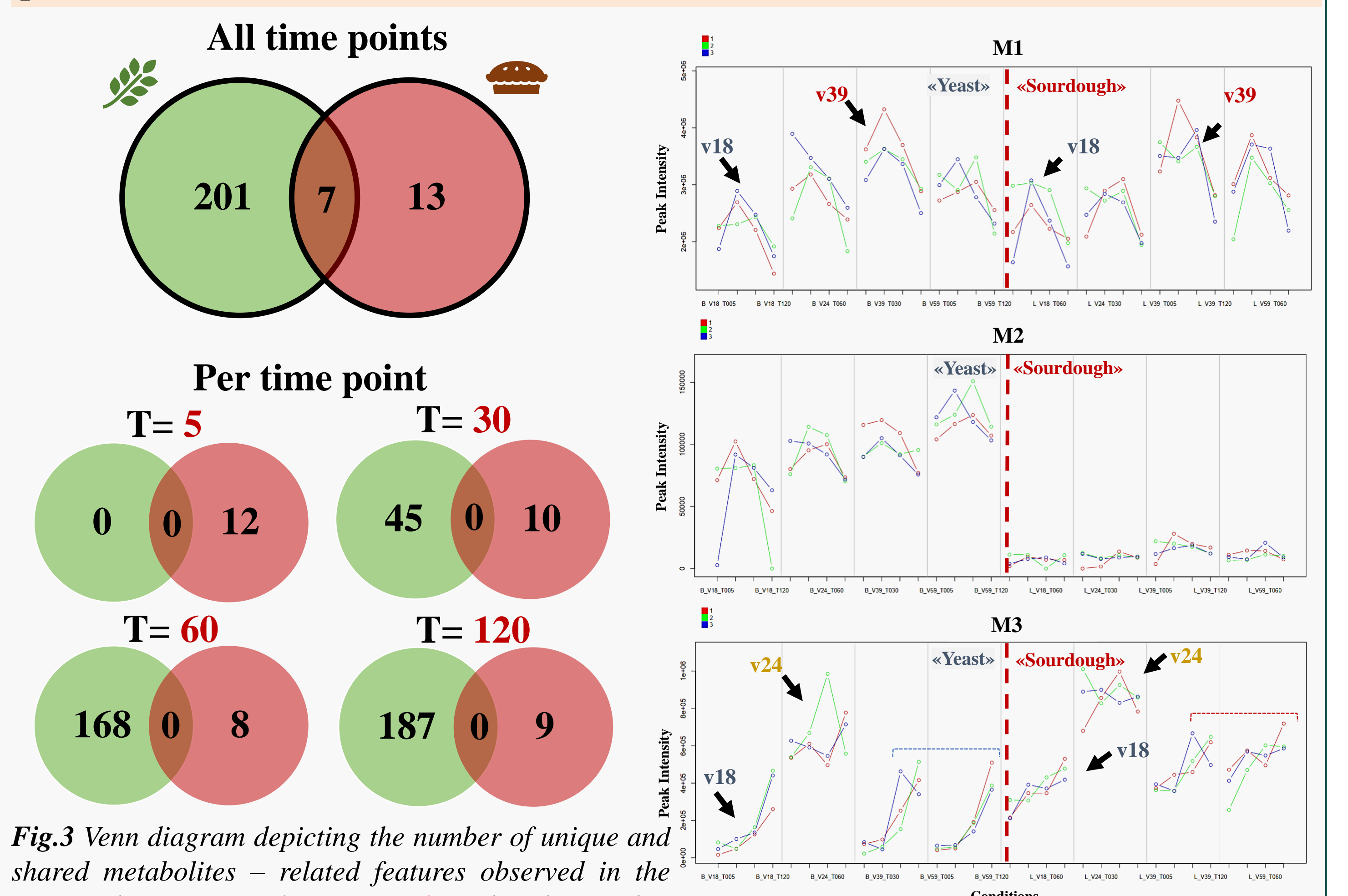
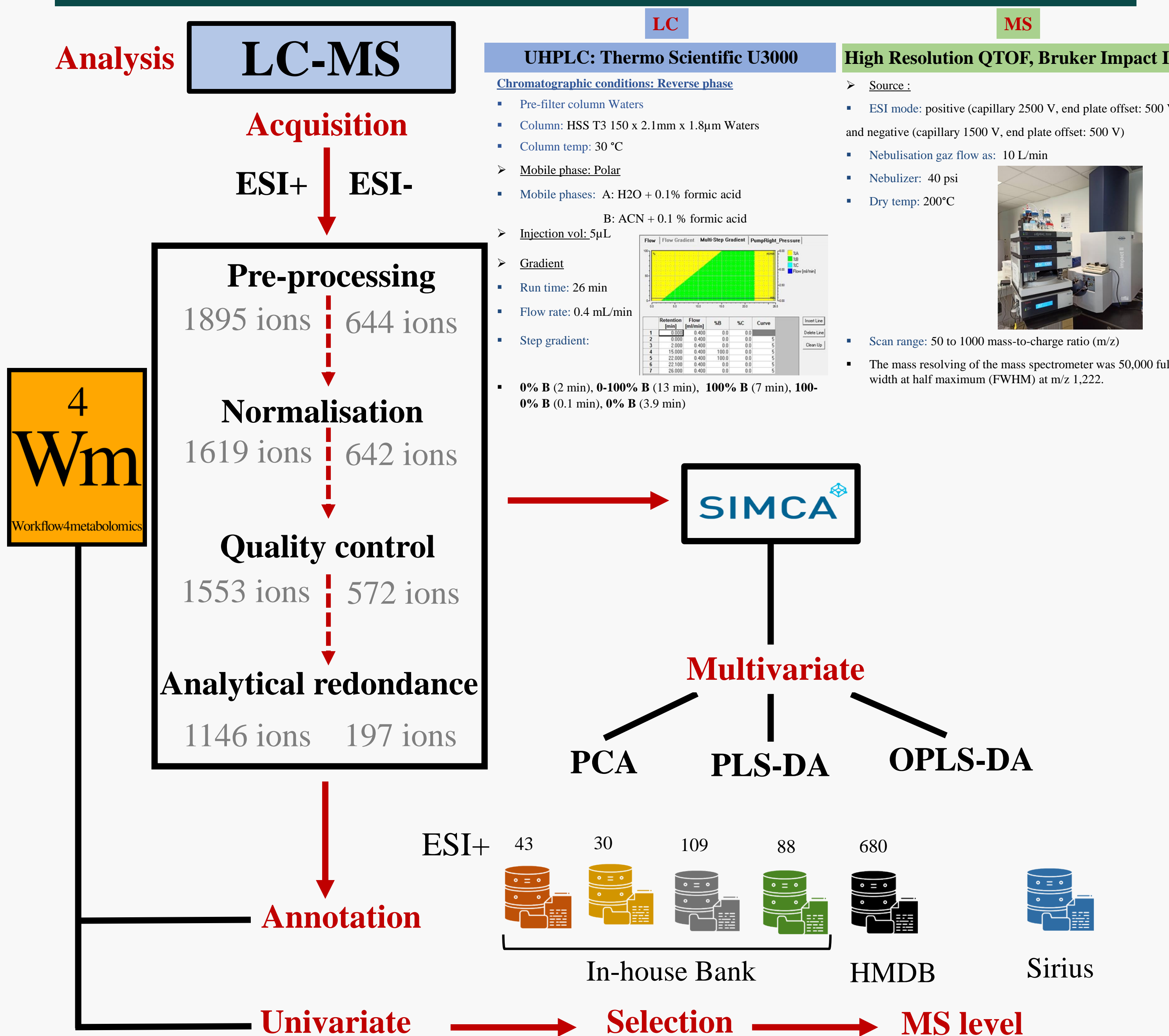


Fig.3 Venn diagram depicting the number of unique and shared metabolites - related features observed in the gastric digestate. In the green/red circles the number indicates metabolites which are differentially presented between varieties/processes. The metabolites were found modulated following univariate statistical analysis (P-value <0.05).

Fig.4. Examples of metabolites (M1, M2 and M3) that significantly modulate three biological replicates denoted by the numbers 1, 2 and 3 colored red, green and blue respectively.

Shared significant metabolites are present across varieties and processes, although no overlap could be highlighted when observing data time by time.

METABOLOMIC ANALYSIS



CONCLUSION AND PERSPECTIVES

These first results show modulations in certain metabolites identified according to the type of bread digested. This reveals the impact of type of bread on the digestibility and allows us to emphasize the contribution of metabolomic approach for monitoring the metabolites produced by *in vitro* digestates.

The upcoming metabolomic analysis of intestinal digestates can help us understand the evolution and emergence of metabolites, and the biological interpretation of significant metabolites can contribute to identify metabolic pathways through *in vivo* experiments or clinical studies.