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# Real-time metabolomics on *E. coli* cell cultures



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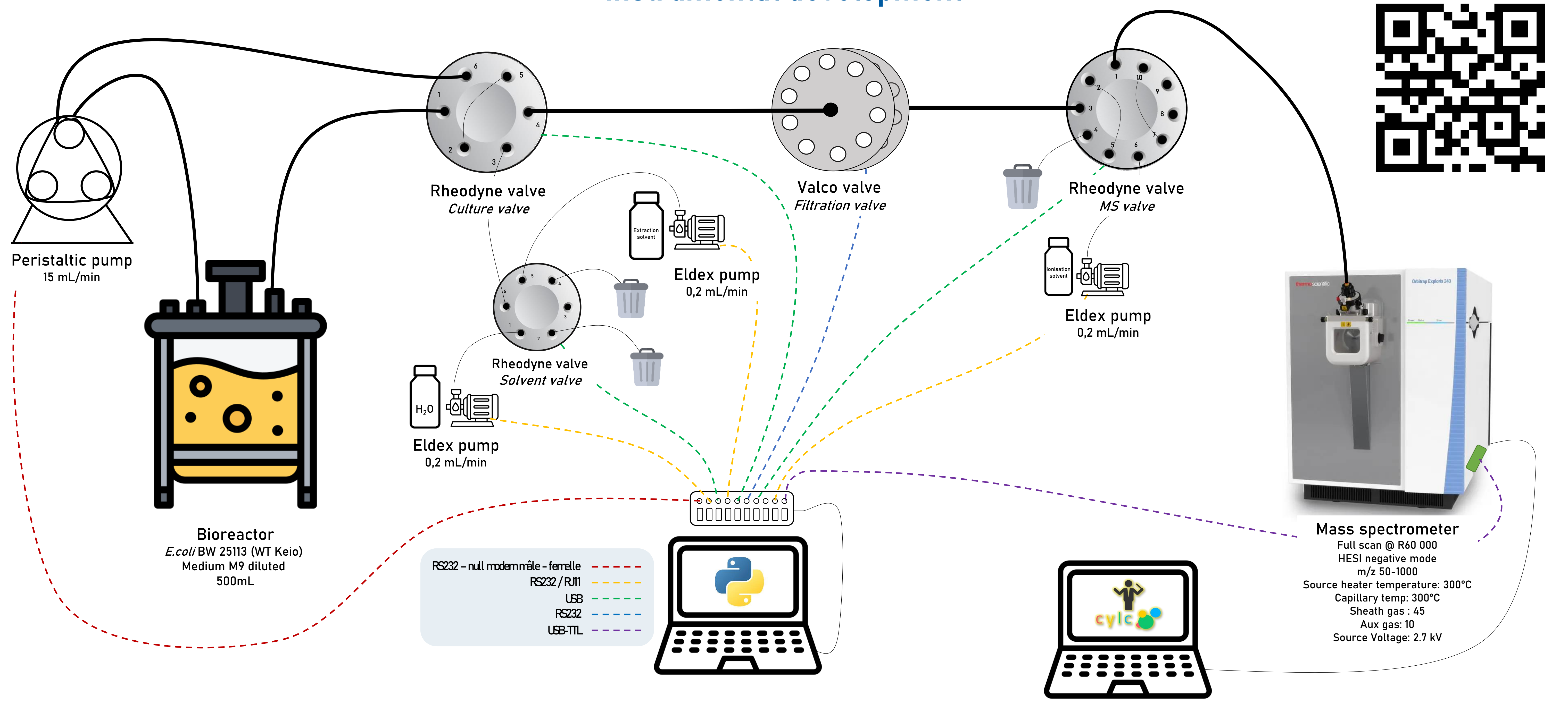
<sup>2</sup>MetaboHUB-MetaToul, National Infrastructure of Metabolomics Fluxomics (ANR-11-INBS-0010), 31077 Toulouse, France – INSA – Institut National des Sciences Appliquées – France

<sup>3</sup>Institut National des Sciences Appliquées – Toulouse – Institut National des Sciences Appliquées, Université de Toulouse – France

## Introduction

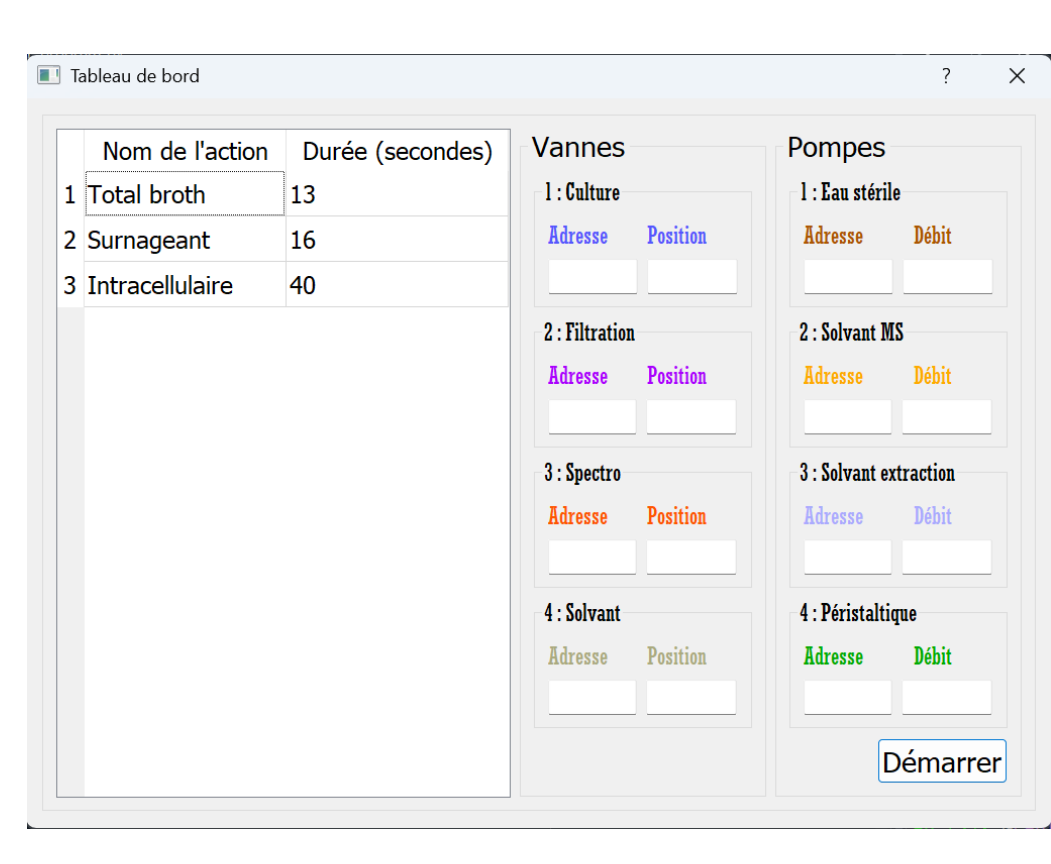
Fermentation monitoring is a powerful tool for bioprocess development, optimisation and control. Several parameters can be tracked including temperature, dissolved oxygen, pH, metabolites, etc... As metabolites represent the final step of biological regulation, they are key indicators. Metabolic changes can occur very rapidly, and traditional metabolomic analyses are time-consuming. Therefore, online high-resolution time course analysis is required. To achieve this, we adapt a real-time metabolomic workflow from instrumental development (Cortada-Garcia, et al., 2022) to automated reprocessing, enabling feedback to the fermenter in real time to optimise bioprocesses.

## Instrumental development



## Software development

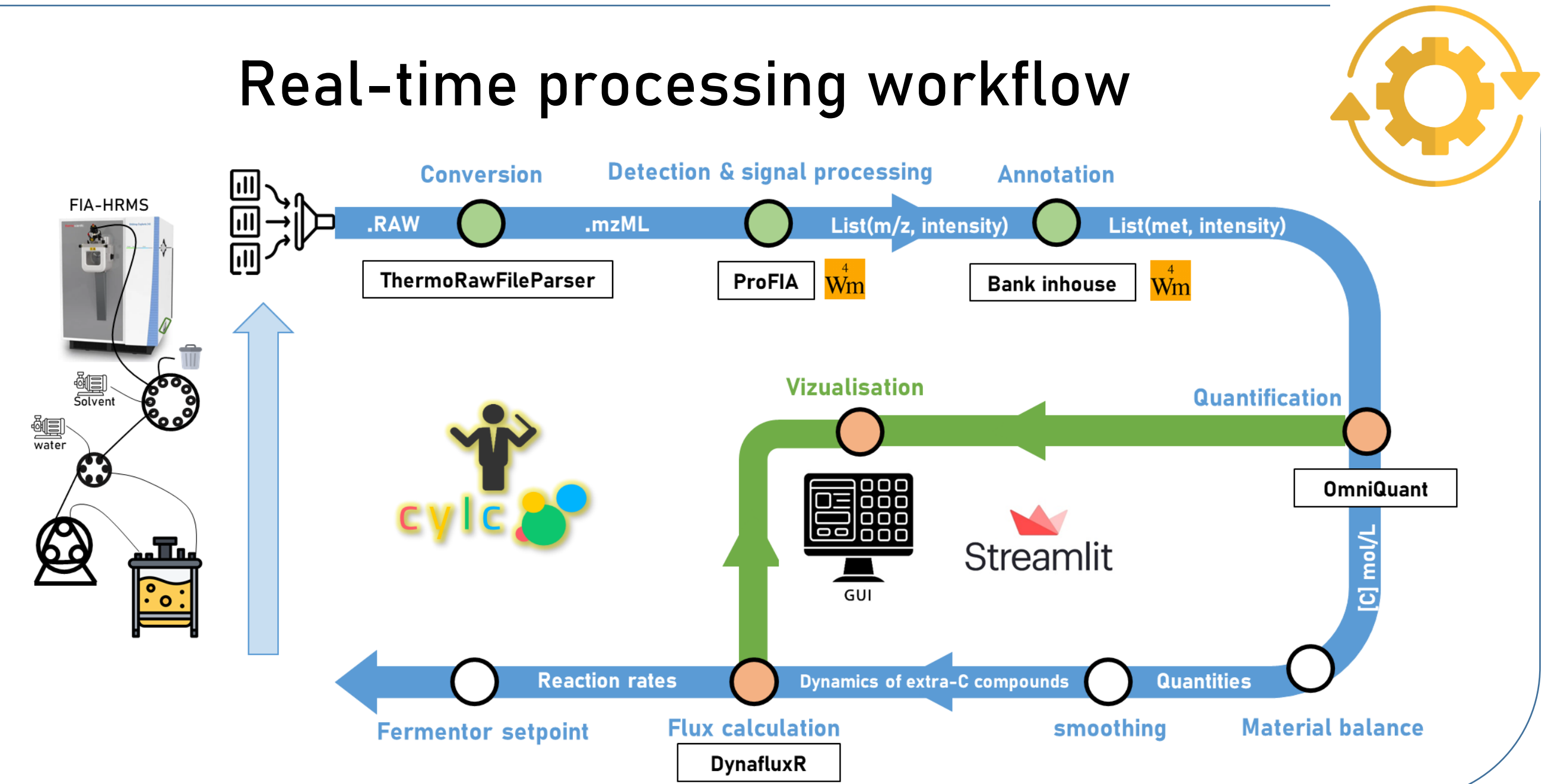
### One tool controls all modules



- ✓ Source code driving and synchronizing all modules
- ✓ Intuitive graphical interface
- ✓ User guide (GitHub)
- ✓ Modular and adaptable to different designs

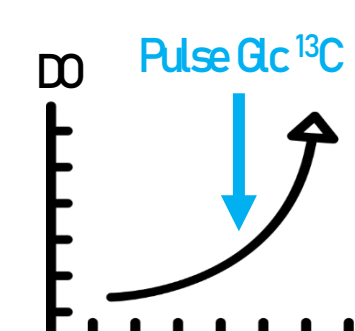
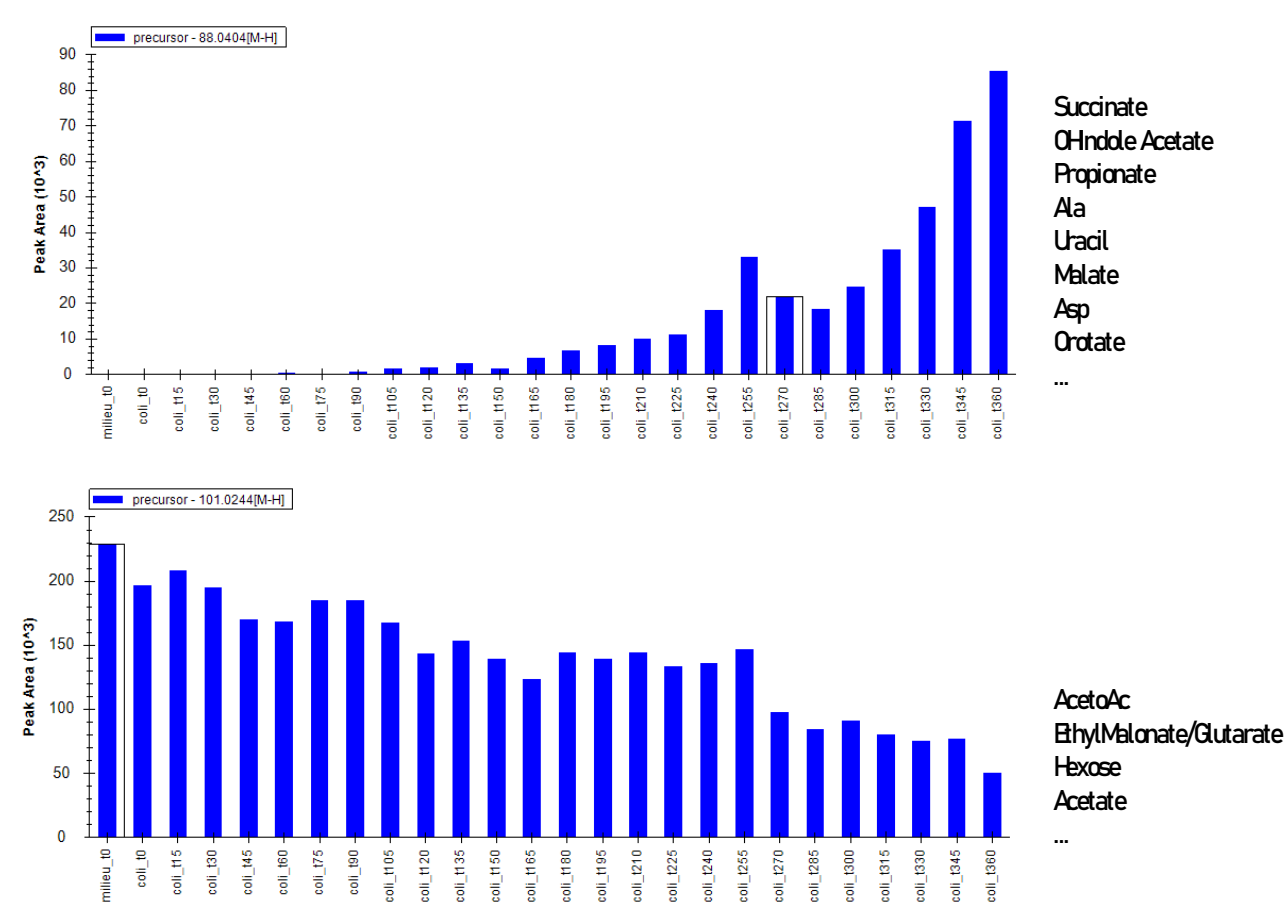


### Real-time processing workflow

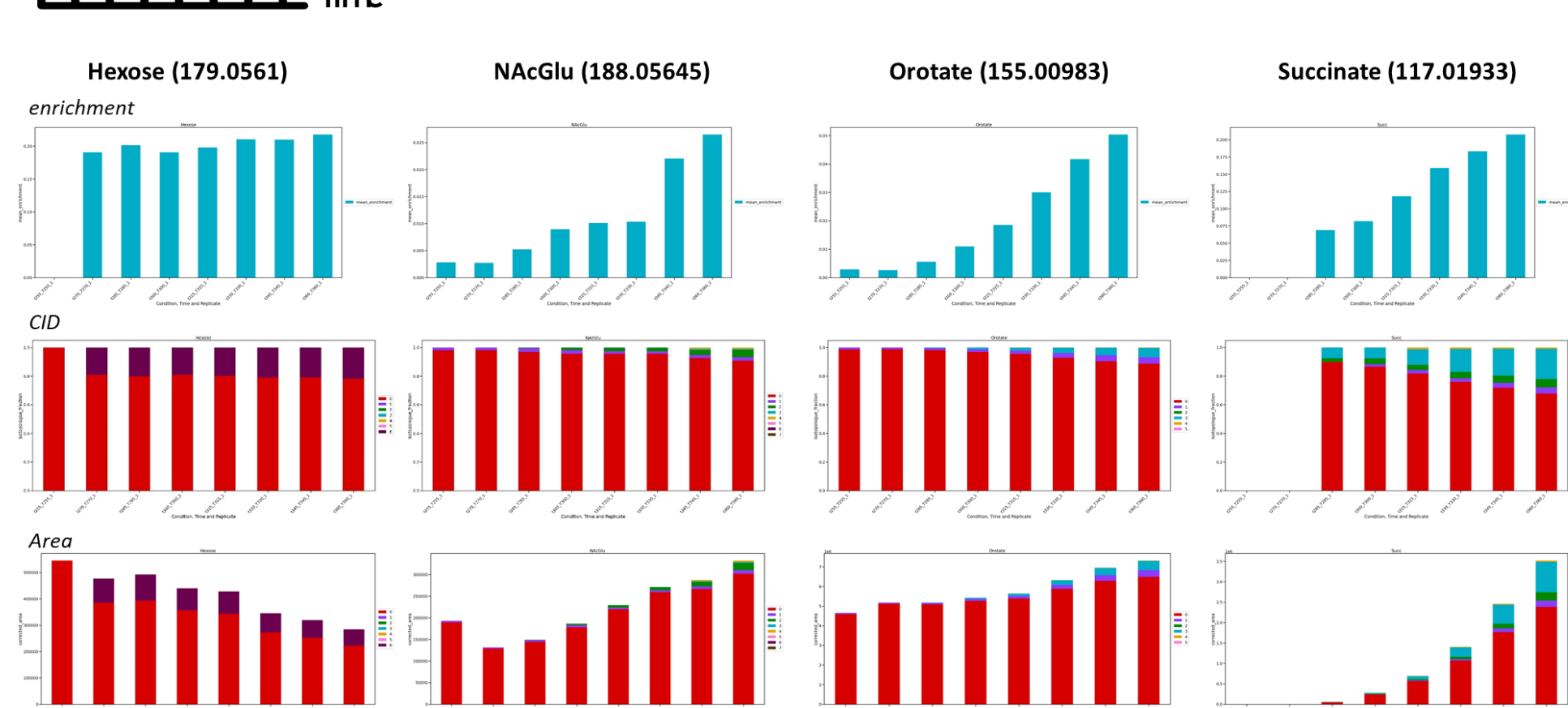


## Results & Discussion

<sup>12</sup>C: 33/283 compounds detected  
(no normalization by DO)



<sup>13</sup>C: 24/33 compounds labeled  
(no normalization by DO)



### Metabolome coverage :

- Improve metabolome coverage : FIA parameters optimization
- Validate metabolites identification with offline points (IC-HRMS & NMR)

### Metabolome quantification :

- Relative quantification in progress : addition of non-metabolised internal standard in cell culture -> MOPS
- Next step : Absolute quantification with NMR benchtop in series or external calibration curve...

### Other applications :

- Transpose to other types of cell cultures, such as adherent cells (cf. HepatOtwins project)

## References

- [1] On-line targeted metabolomics for real-time monitoring of relevant compounds in fermentation processes. Cortada-Garcia *et al.* 2023
- [2] On-line untargeted metabolomics monitoring of an Escherichia coli succinate fermentation process. Cortada-Garcia *et al.* 2022

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