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An automated workflow for high-throughput ¹³C-fluxomics



Loïc Le Grégam^{1,2}, Serguei Sokol^{1,2}, Yann Guitton^{3,4}, Fabien Jourdan^{2,5}, Floriant Bellvert^{1,2}, Jean-Charles Portais^{2, 6}, Pierre Millard^{1,2}

1 - Toulouse Biotechnology Institute, TBI-INSA de Toulouse INSA/CNRS 5504-UMR INSA/INRA 798, 5504 Toulouse, France – INSA - Institut National des Sciences Appliquées – France 2 - MetaboHUB-MetaToul, National Infrastructure of Metabolomics and Fluxomics, 31077 Toulouse, France – Institut National des Sciences Appliquées – Toulouse – France 3 - MetaboHUB-Grand-Ouest – MetaboHUB – France 4 - Laboratoire d'étude des Résidus et Contaminants dans les Aliments – Ecole Nationale Vétérinaire, Agroalimentaire et de l'alimentation Nantes-Atlantique, Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement, INRAE – France 5 - ToxAlim – Université Toulouse III – Paul Sabatier, Ecole Nationale Vétérinaire de Toulouse, Institut National Polytechnique (Toulouse), Ecole d'Ingénieurs de Purpan, Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement – France 6 - Geroscience and rejuvenation research center – Université Toulouse III – Paul Sabatier, EFS, Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique – France



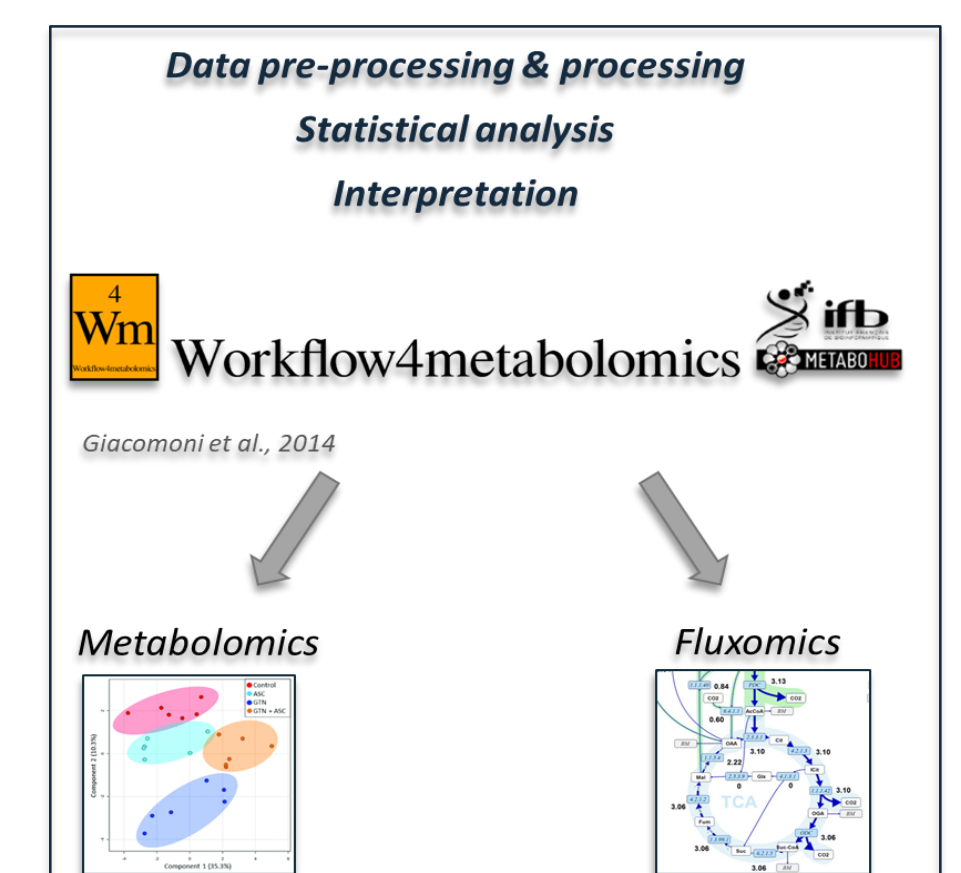
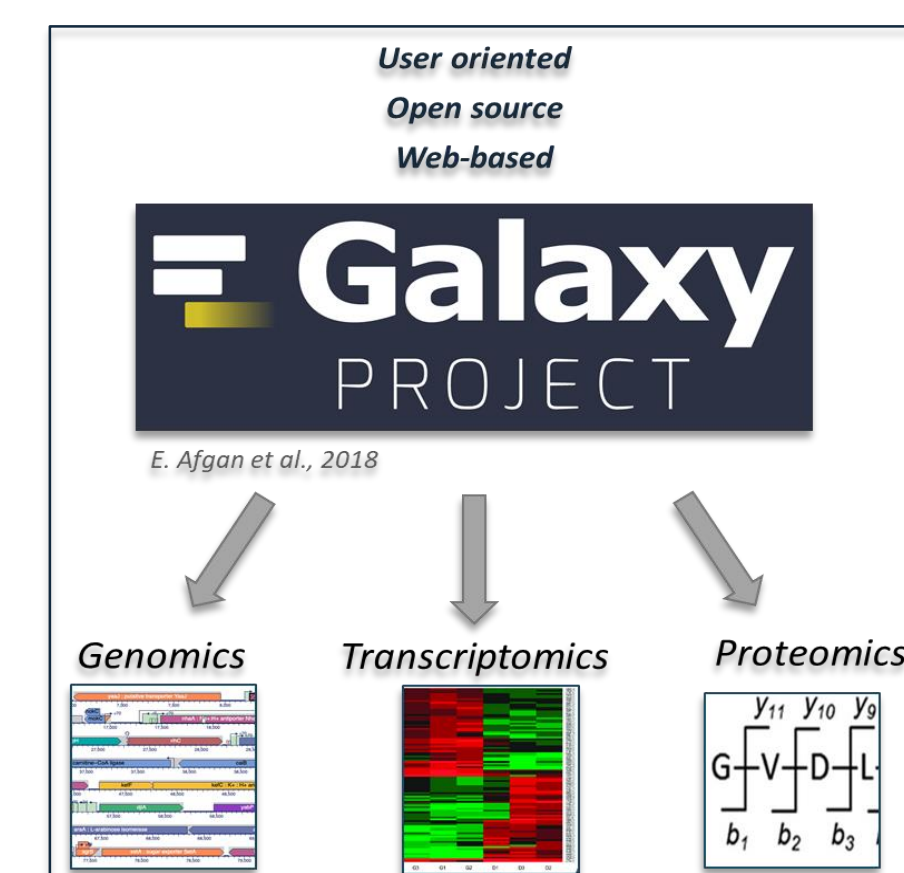
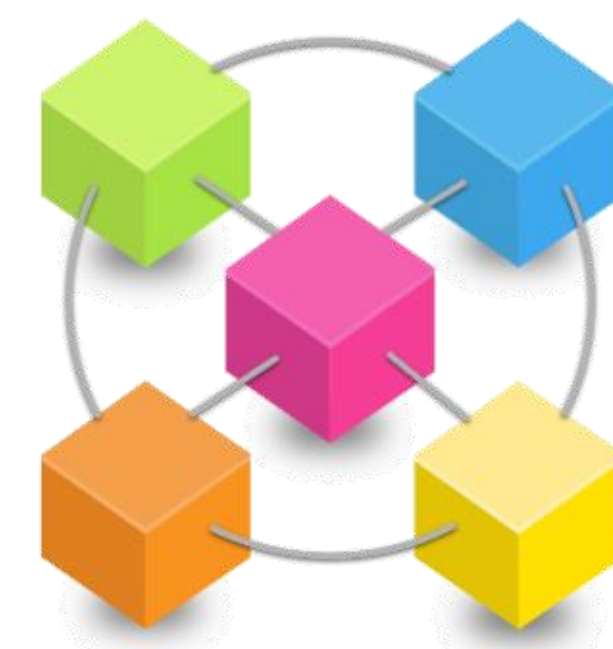
Introduction

The goal of isotope-based fluxomics approaches is to quantify metabolic fluxes in living organisms. ¹³C-fluxomics provides a detailed phenotypic description of the actual metabolic state of studied organisms. To achieve this, a combination of several experimental and computational steps is required. However, the complexity of the computational steps, coupled with the need to select the right software while manually ensuring data interoperability, makes the process error-prone, time-consuming, and hard to reproduce effectively.

The objective of this project is to overcome these limitations by providing a flexible, reproducible, user-friendly, and high-throughput ¹³C-fluxomics workflow that integrates the tools needed for flux calculation.

Material and Methods

Microservices



Integration of a minimal set of tools for stationary ¹³C-fluxomics on Workflow4Metabolomics.

Flexible architecture eases implementation of upstream computational steps and thus the integration of additional approaches.

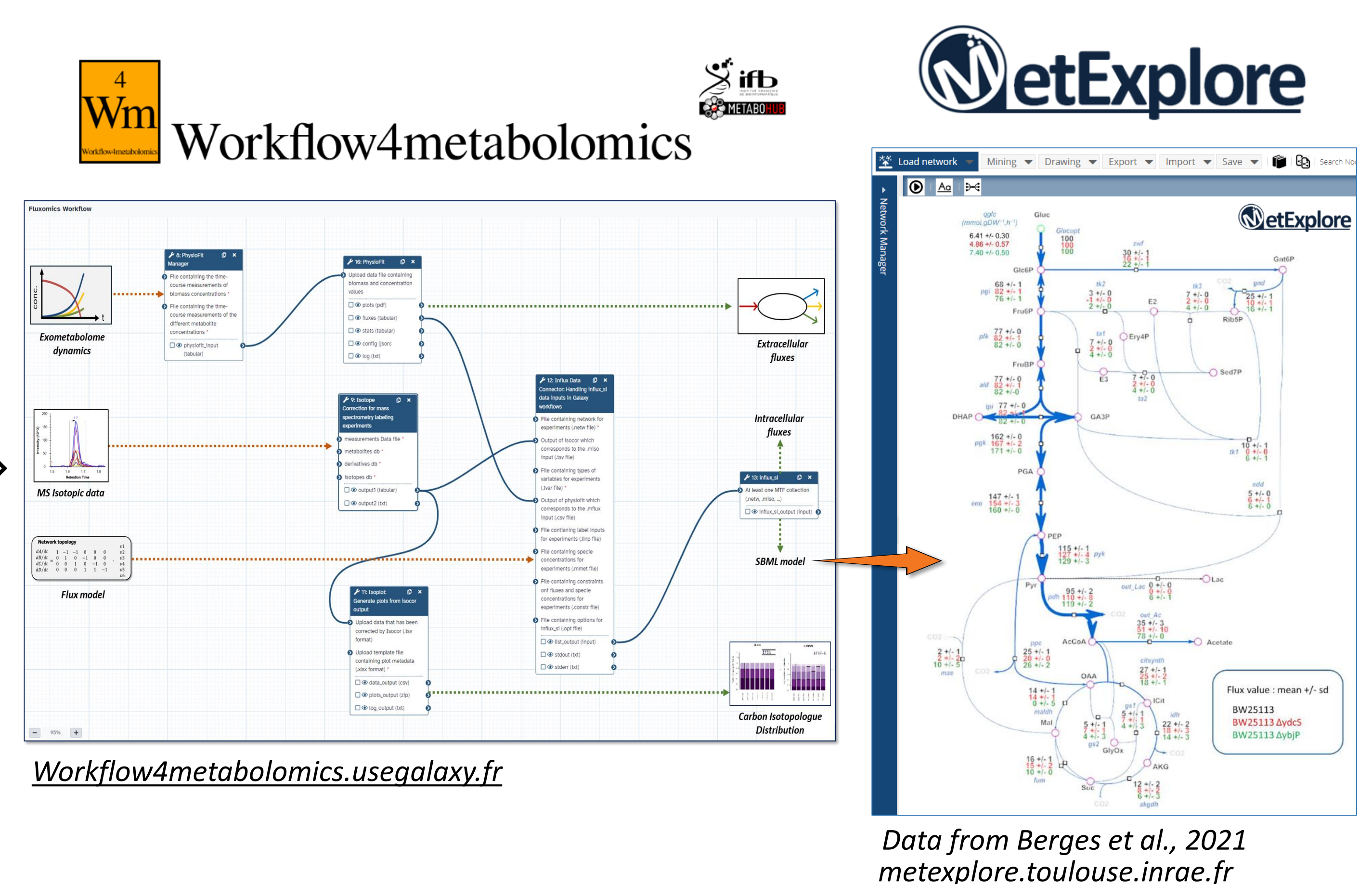
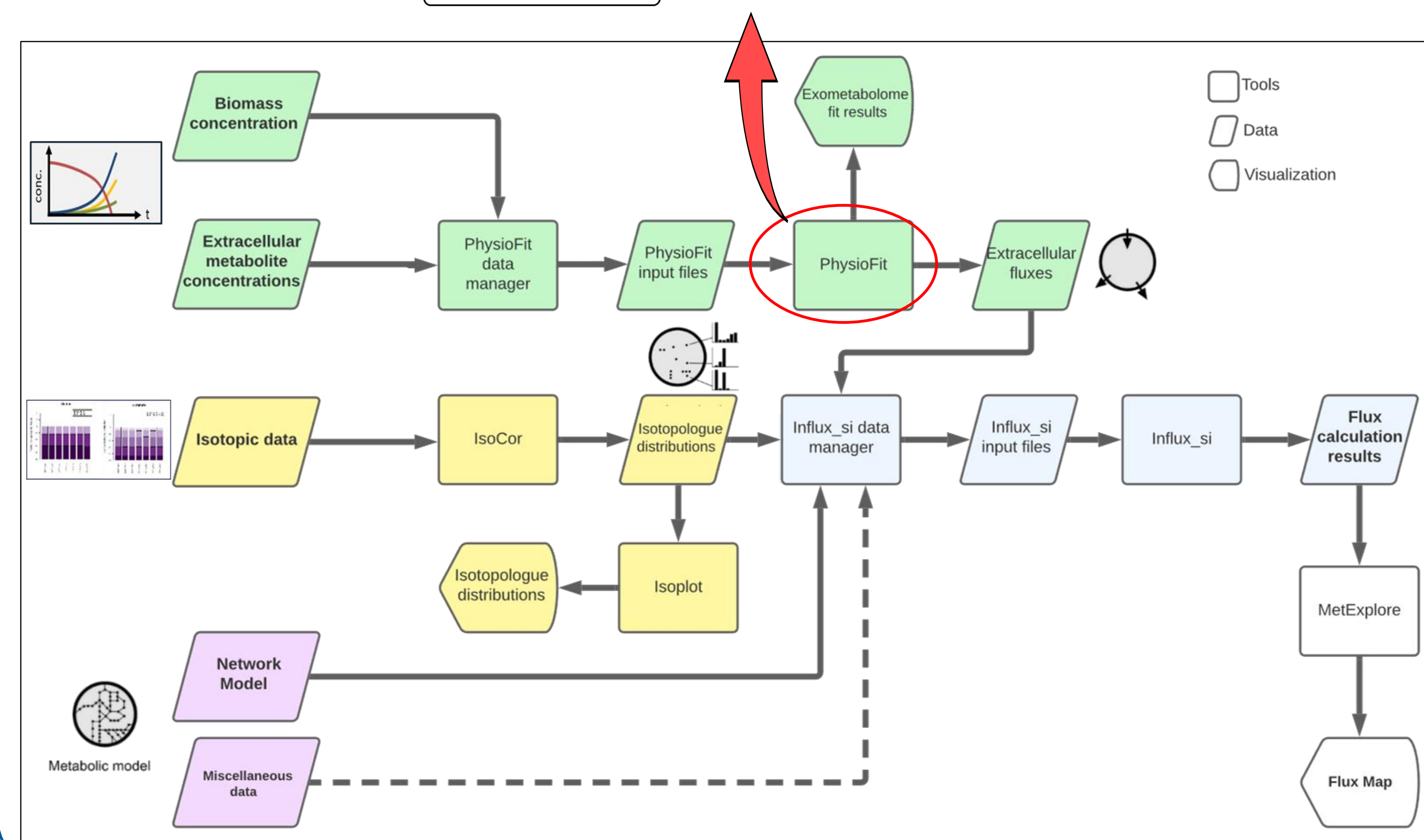
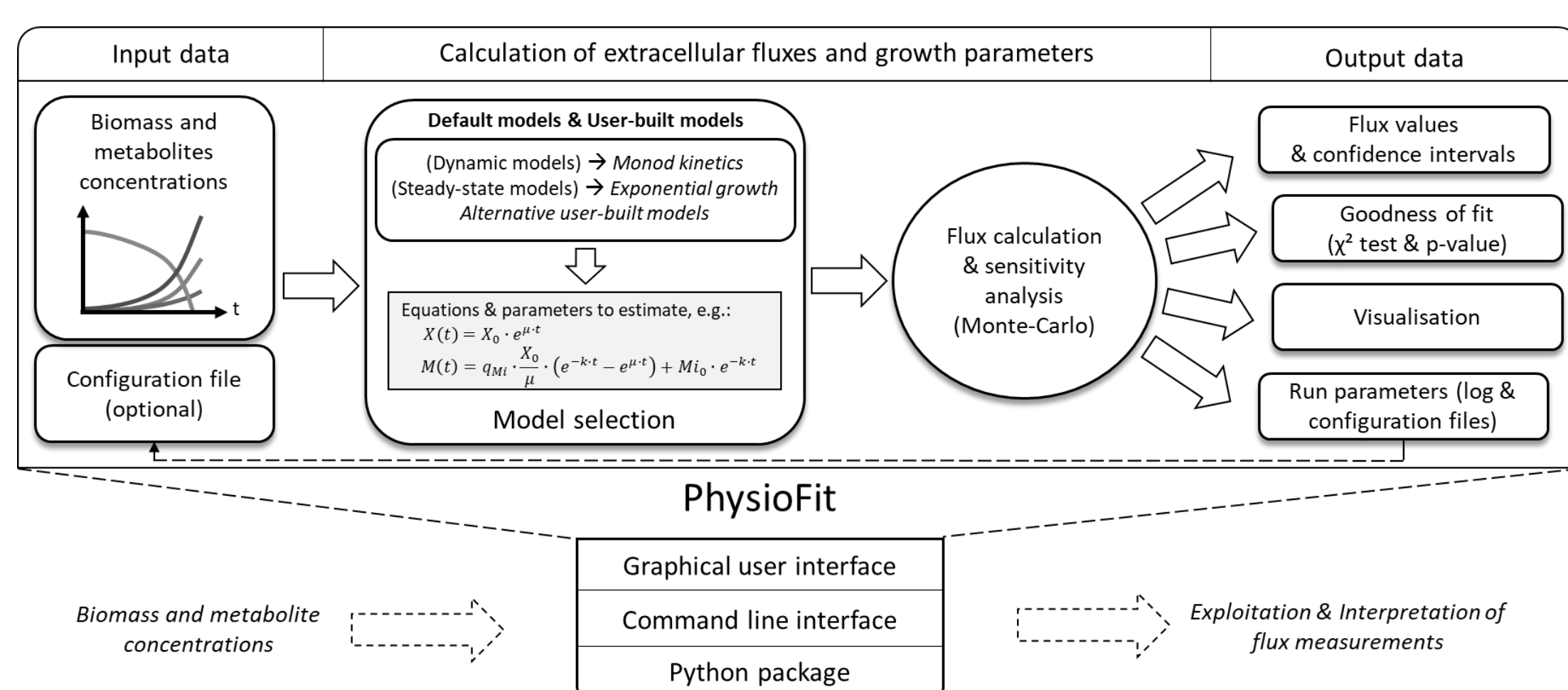
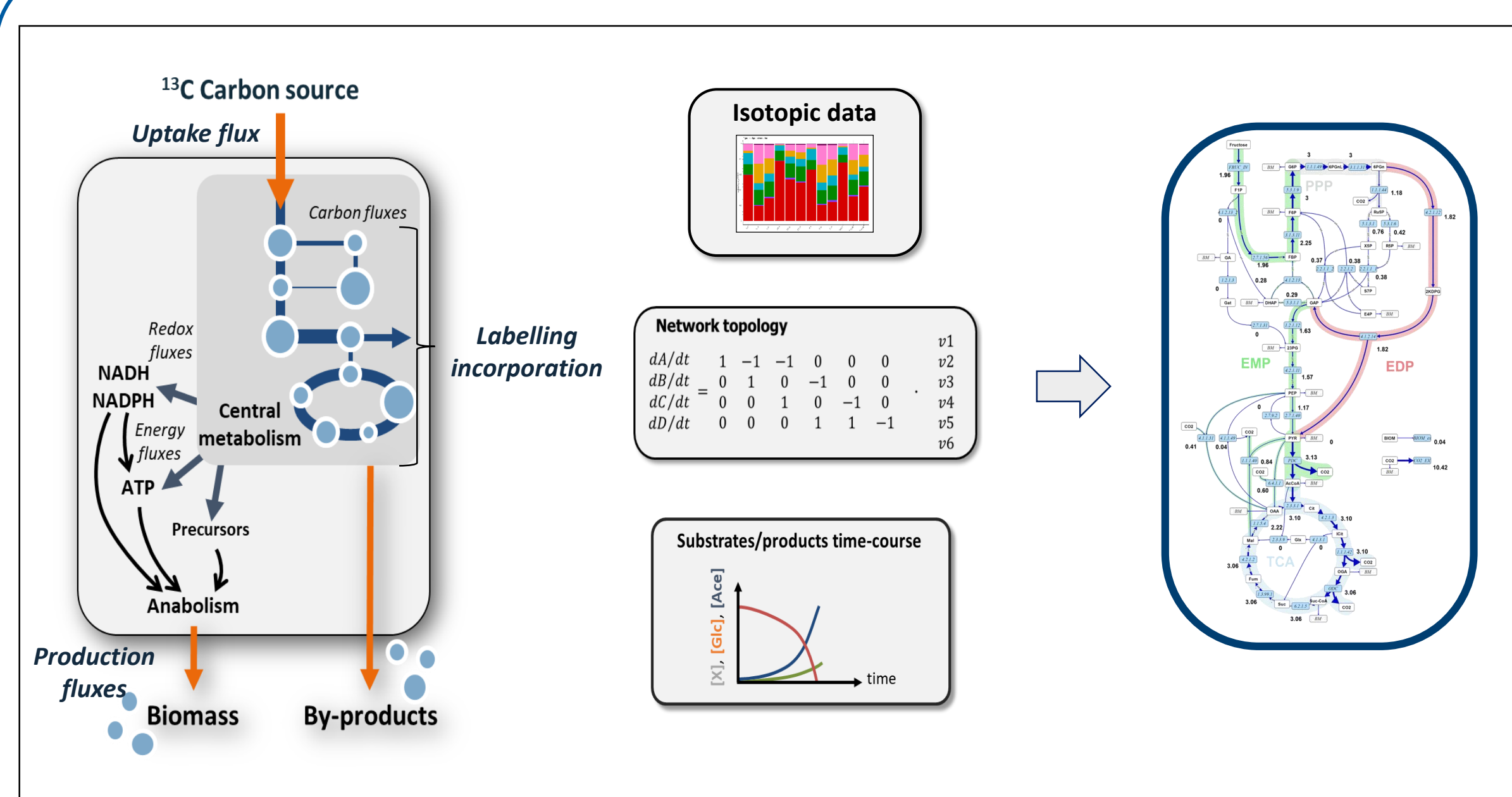
Results and discussion

The data needed for flux calculation:

- Flux Model:** Model containing information on the reactions within the network (stoichiometry and carbon transitions) as well as information on the labelled substrate(s), constraints on the model, etc
- Isotopic data:** Carbon Isotopologue Distribution measurements from different metabolites of the metabolic network
- Extracellular flux measurements:** Uptake and production fluxes calculated from biomass and extracellular metabolite dynamics

Interoperability of tools is key for building the workflow. Each tool can be used alone, or in tandem with other software. Logs and configuration files ensure reproducibility.

Implementation of PhysioFit, a software to quantify extracellular fluxes and growth parameters. LINKS -->



Conclusions

Reproducible and high-quality ¹³C-fluxomics experiments are critical for functional studies of metabolic systems, as well as for identifying metabolic levers to optimize biotechnological processes for drug development, industrial applications and fundamental understanding of metabolism. The development of an automated workflow for data processing and flux calculation enables reproducible, high-throughput experimental metabolic flux analysis. The flexible microservice architecture allows for future integration of new approaches and customization, helping scientists apply it to a wide range of biological questions and keeping this work relevant for years to come.

References

- [1] *influx_s: increasing numerical stability and precision for metabolic flux analysis in isotope labelling experiments*, Sokol et al., 2012
- [2] *Workflow4Metabolomics: a collaborative research infrastructure for computational metabolomics*, Giacomoni et al., 2015
- [3] *Recent advances in high-throughput ¹³C-fluxomics*, Heux et al., 2017
- [4] *IsoCor: isotope correction for high-resolution MS labeling experiments*, Millard et al., 2018
- [5] *Exploring the Glucose Fluxotype of the E. coli y-ome using high-resolution fluxomics*, Bergès et al., 2021
- [6] *PhysioFit: a software to quantify cell growth parameters and extracellular fluxes*, Le Grégam et al., 2024