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## Automatising 13 C-fluxomics flux calculations through a workflow hosted on the Workflow4Metabolomics Galaxy platform

Loïc Le Grégam, Pierre Millard, Serguei Sokol, Yann Guitton, Gildas Le Corguillé, Fabien Jourdan, Floriant Bellvert, Jean-Charles Portais

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Loïc Le Grégam, Pierre Millard, Serguei Sokol, Yann Guitton, Gildas Le Corguillé, et al.. Automatising 13 C-fluxomics flux calculations through a workflow hosted on the Workflow4Metabolomics Galaxy platform. Analytics 2022, RFMF; AFSEP; AFSM, Sep 2022, Nantes (Cité des Congrès), France. hal-04352460

**HAL Id: hal-04352460**

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Submitted on 19 Dec 2023

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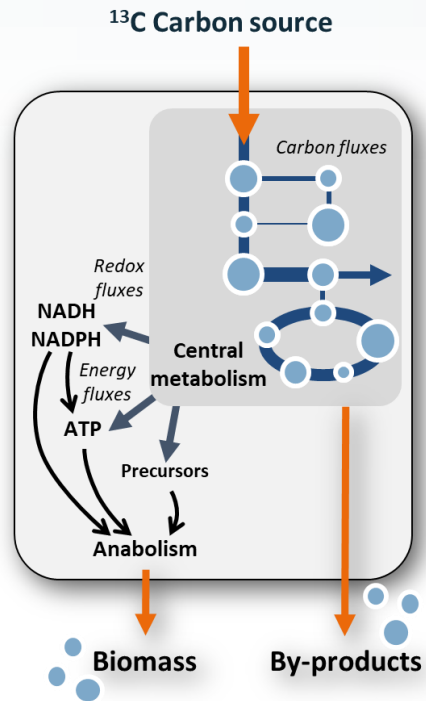
# An automatised $^{13}\text{C}$ -fluxomics workflow

Automatising flux calculations through a workflow hosted on the Workflow4Metabolomics Galaxy platform

**Loïc Le Grégam**, Pierre Millard, Serguei Sokol, Yann Guitton, Gildas Le Corguillé, Sébastien Hutinet, Sophie Colombie, Fabien Jourdan, Floriant Bellvert, Jean-Charles Portais

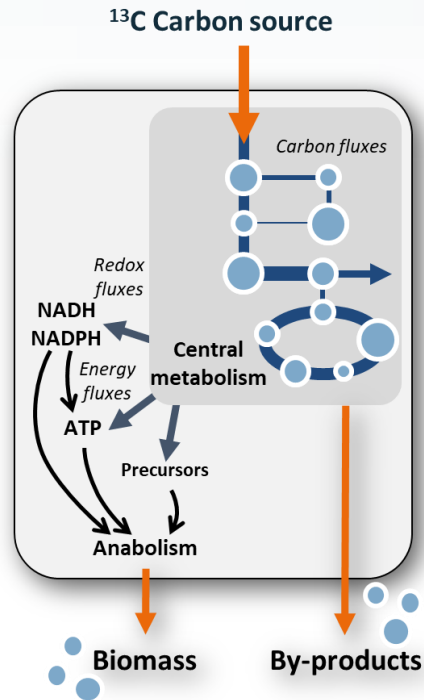
# Quantifying fluxes: the basics

A flux can be defined as the in vivo rates of biochemical reactions.

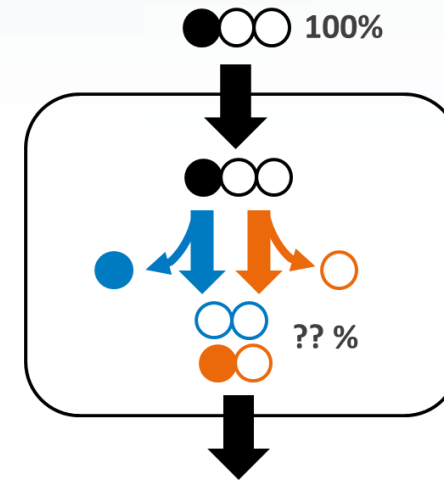


# Quantifying fluxes: the basics

A flux can be defined as the in vivo rates of biochemical reactions.



Fluxes cannot be measured directly!

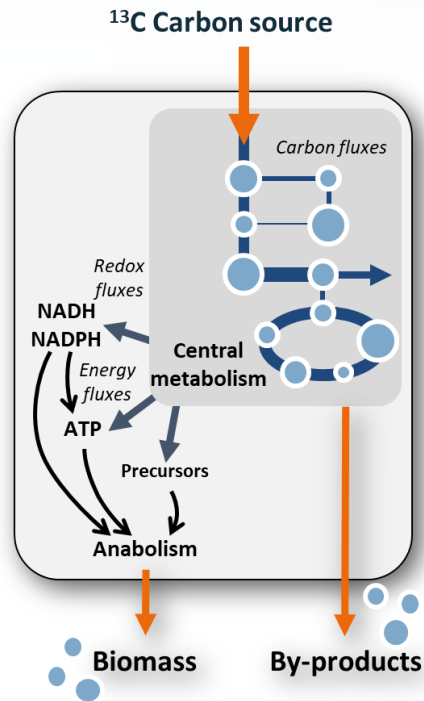


**Data that is needed:**

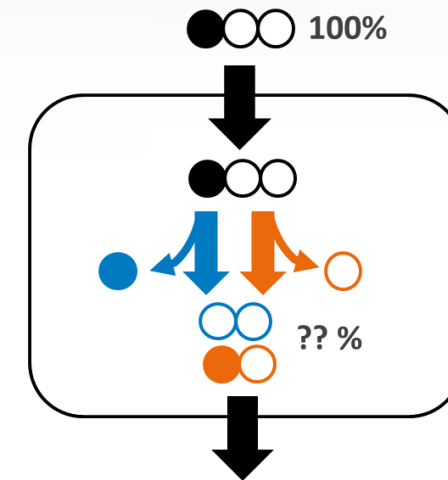
- Stoichiometric model
- Input-output rates (i.e. extracellular fluxes)
- Labeling distribution

# Quantifying fluxes: the basics

A flux can be defined as the in vivo rates of biochemical reactions.



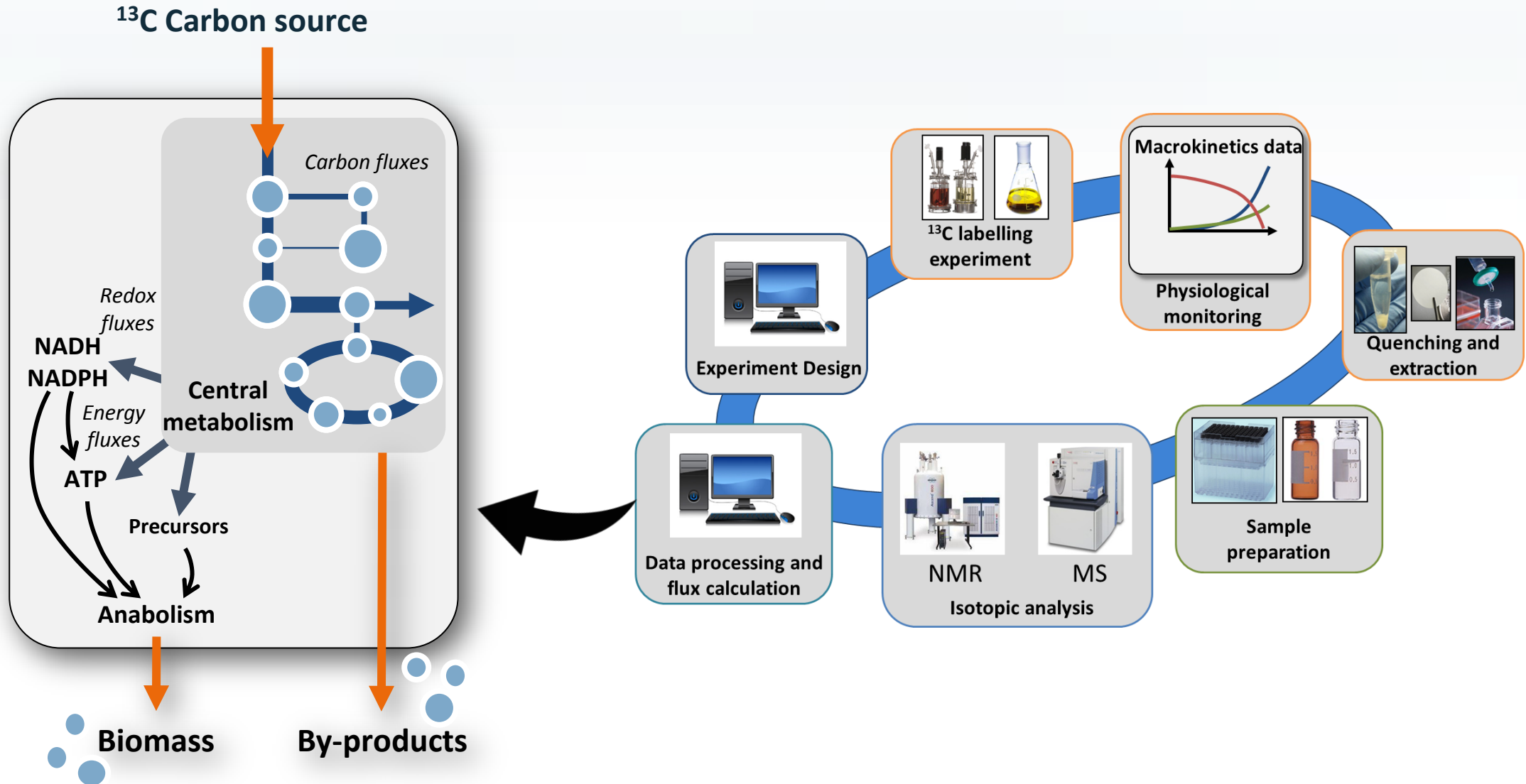
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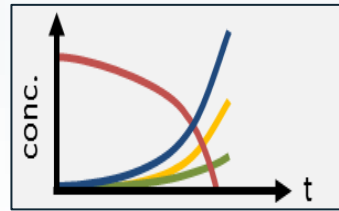
**Data that is needed:**

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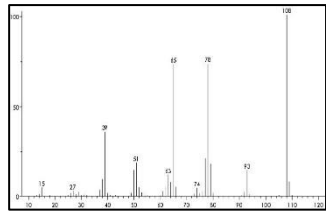
# Quantifying fluxes: A complex workflow



# Quantifying fluxes: data processing & flux calculation



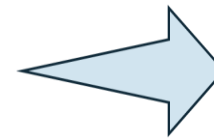
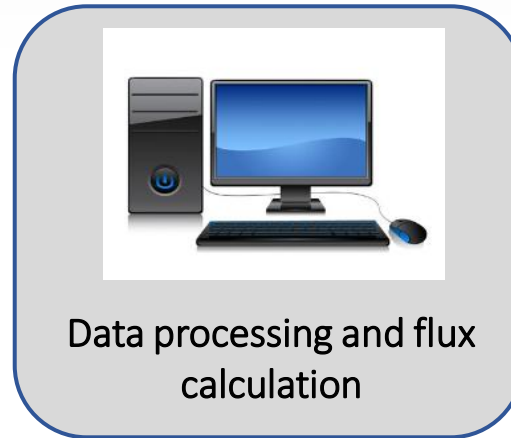
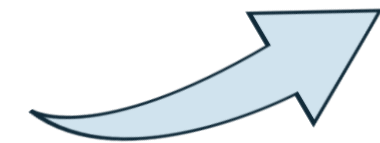
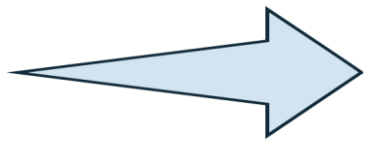
Growth data



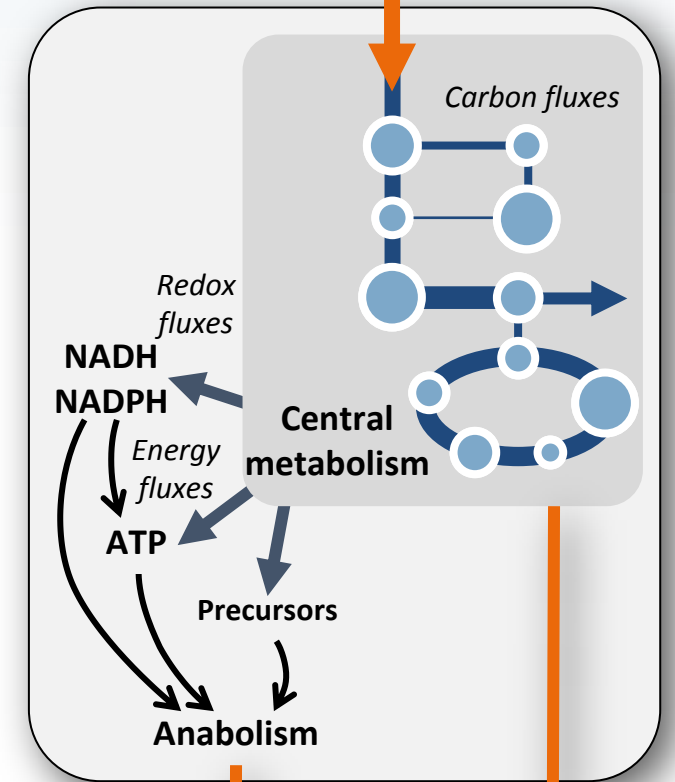
Isotopic data



Metabolic model

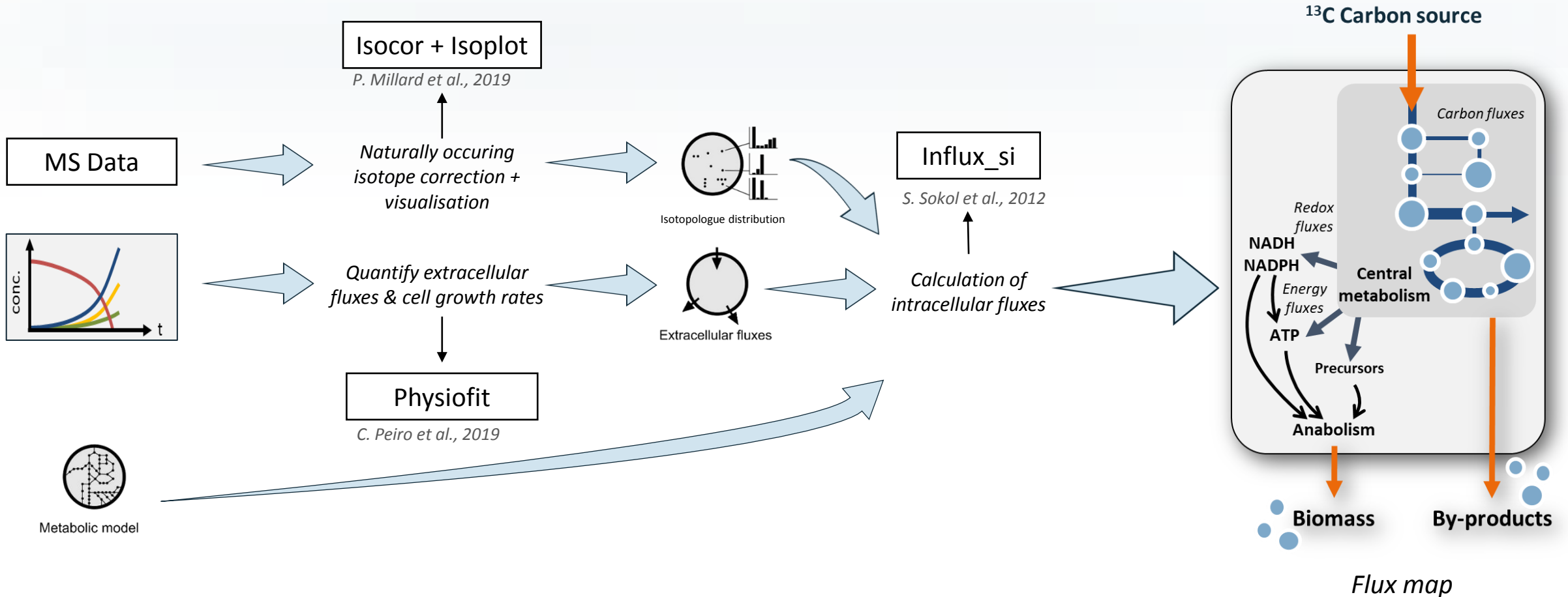


$^{13}\text{C}$  Carbon source



Many complex steps and multiple approaches  
→ High level of expertise needed

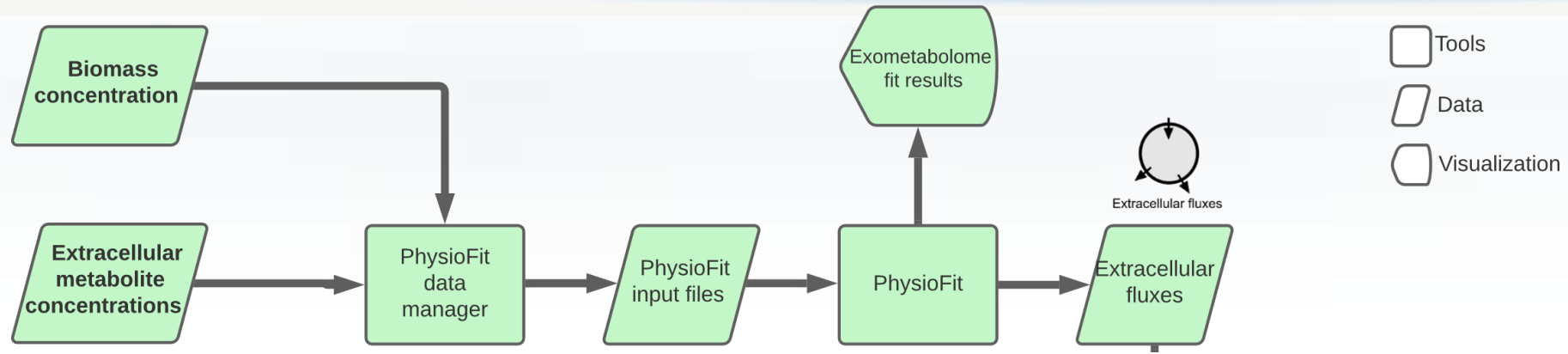
# Quantifying fluxes: current (manual) pipeline for flux calculation



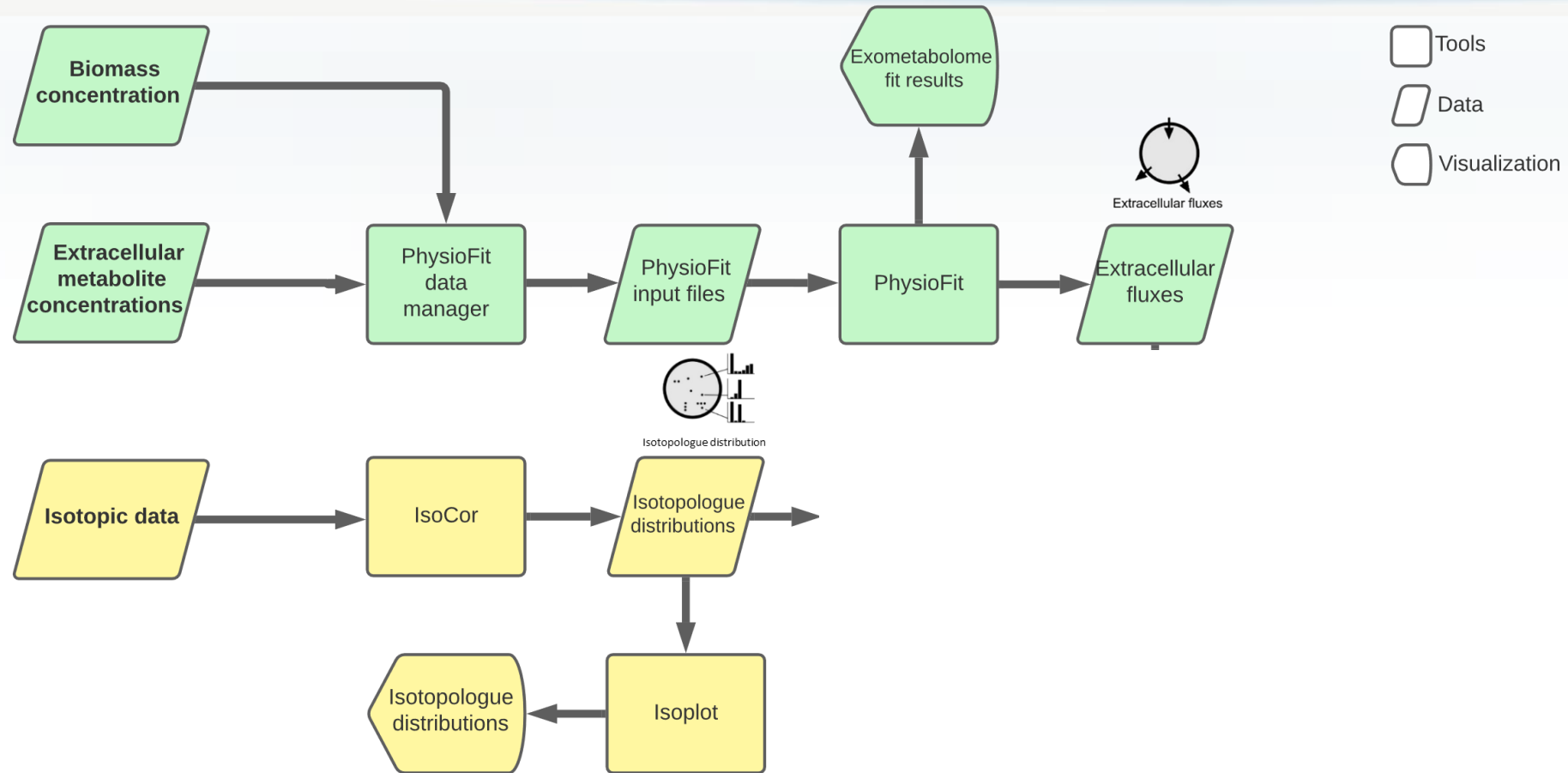
Objective: streamline the process to increase reproducibility, robustness and throughput  
-> Development of an automatised <sup>13</sup>C workflow



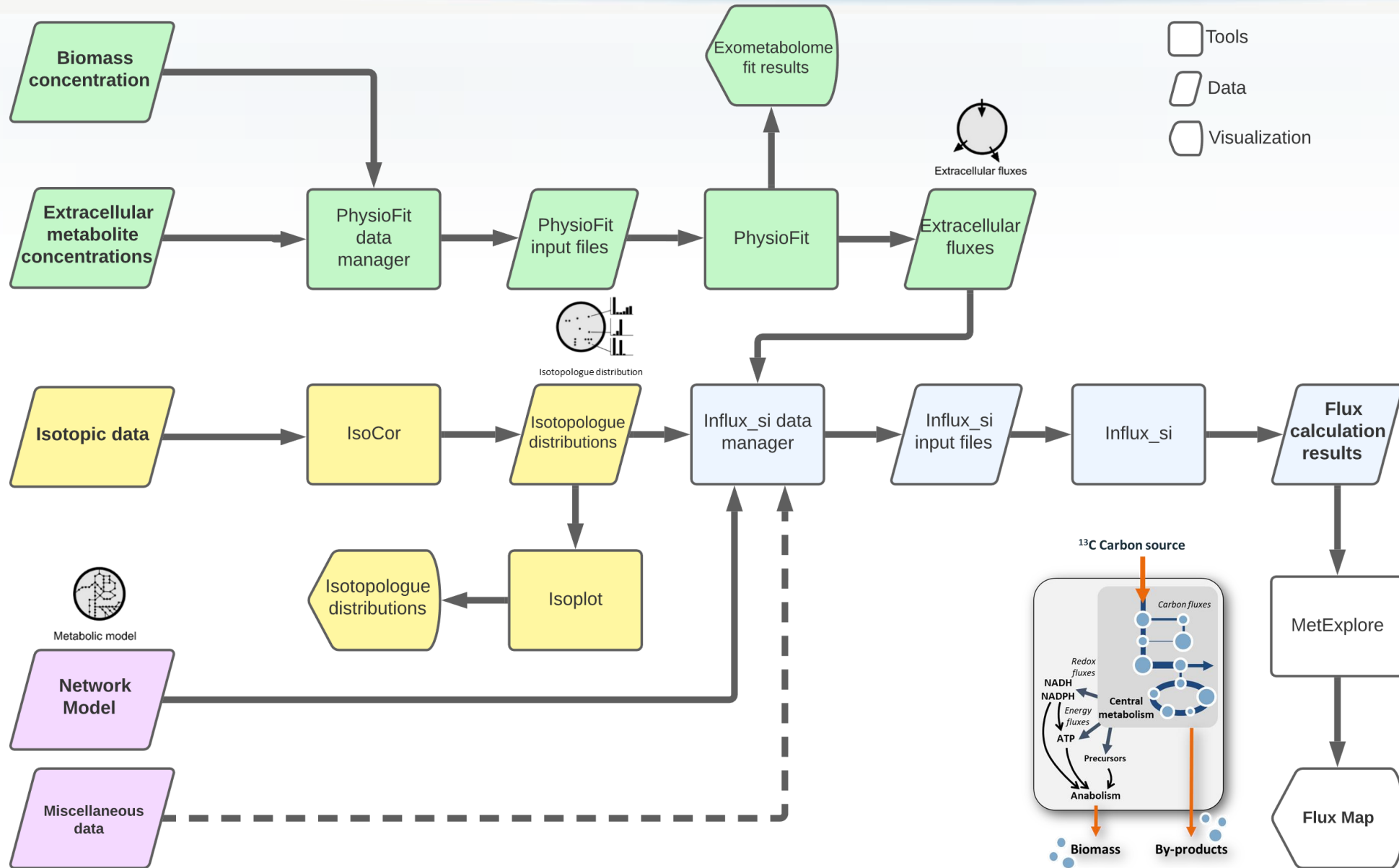
# Proposed $^{13}\text{C}$ -fluxomics workflow



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# Proposed $^{13}\text{C}$ -fluxomics workflow



# Galaxy – Workflow4Metabolomics (W4M)

*User oriented*

*Open source*

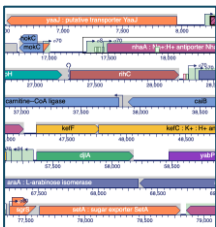
*Web-based*



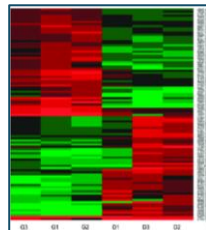
*E. Afgan et al., 2018*



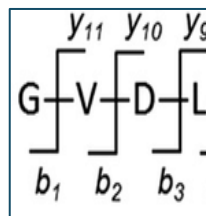
*Genomics*



*Transcriptomics*



*Proteomics*



# Galaxy – Workflow4Metabolomics (W4M)

User oriented  
Open source  
Web-based

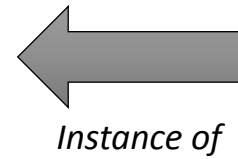


*E. Afgan et al., 2018*

Data pre-processing & processing  
Statistical analysis  
Interpretation



Workflow4metabolomics



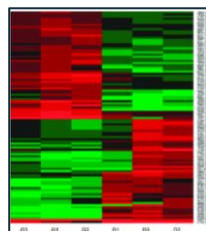
Instance of

*Giacomoni et al., 2014*

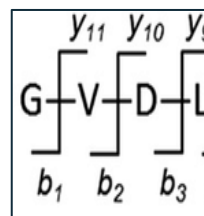
Genomics



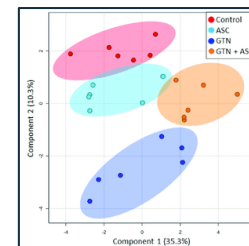
Transcriptomics



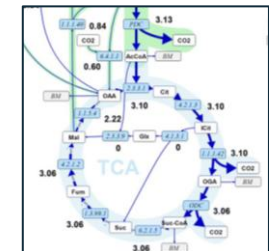
Proteomics



Metabolomics



Fluxomics

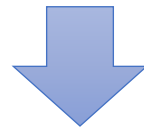


# Steps for uploading tools to W4M

Upload to  
Bioconda



Elaboration of  
the XML  
wrapper



Test and  
release

# Steps for uploading tools to W4M

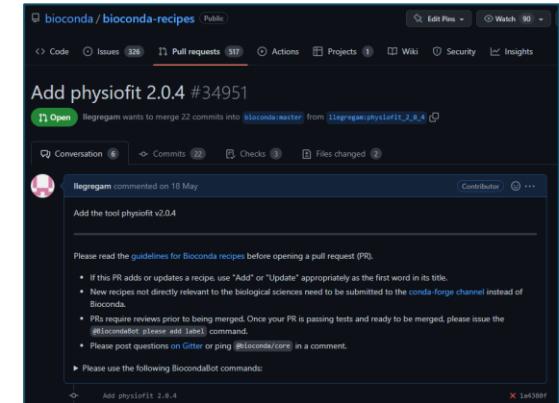
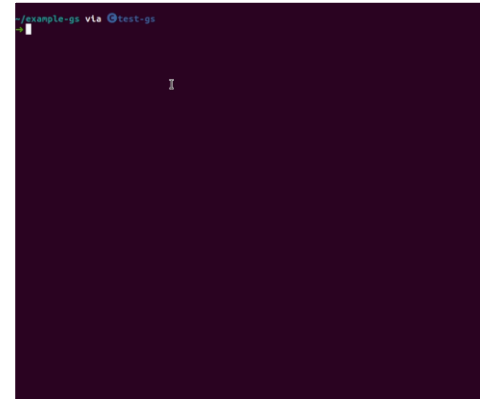
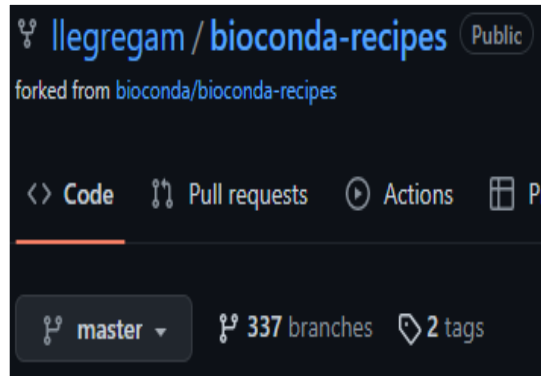
Upload to Bioconda

Step 1: Create fork of the **Bioconda-recipes** repository

Step 2: **Clone** the repository and create recipe using *grayskull* package

Step 3: Add the *meta.yml*, commit, push the changes to Bioconda-recipes and pull-request

Elaboration of the XML wrapper



Test and release



# Steps for uploading tools to W4M

Upload to Bioconda

Elaboration of the XML wrapper

Test and release

```
1 <tool id='isoplot' name='Isoplot: Generate plots from isocor output' version='1.3.0+galaxy1' profile='20.01'>
2   <requirements>
3     <requirement type='package' version='1.3.0'>isoplot</requirement>
4   </requirements>
5   <command><![CDATA[
6     isoplot '$datafile' 'galaxy' '$format' --value '$value' --template '$template_file' $SP.barplot $SP.meaned_barplot
7     $SP.static_heatmap $SP.static_clustermap $IP.interactive_barplot $IP.interactive_meanplot $IP.interactive_heatmap
8   #if $Sunstack:
9     -s
10  #end if
11  #if $verbosity:
12    -v
13  #end if
14  #if $annotation:
15    -a
16  #end if
17  -g -z '$plots_output' > $data_output 2> '$log_output'
18  ]]></command>
19  <inputs>
20    <param name='datafile' type='data' format='csv,tabular' multiple='true' label='Upload data that has been corrected by Isocor (.tsv format)' />
21    <param name='template_file' type='data' format='csv,xlsx' multiple='true' label='Upload template file containing plot metadata (.xlsx format)' argument='--template' />
22    <!--param name='run_name' type='text' label='Run name' /-->
23    <param name='format' type='select' label='Plot format'>
24      <option value='pdf'>pdf</option>
25      <option value='jpeg'>jpeg</option>
26      <option value='png'>png</option>
27      <option value='svg'>svg</option>
28      <option value='html'>html</option>
29    </param>
30    <param name='value' type='select' label='Data to plot' >
31      <option value='corrected_area'>Corrected Area</option>
32      <option value='isotopologue_fraction'>Isotopologue Fraction</option>
33      <option value='mean_enrichment'>Mean Enrichment</option>
34    </param>
```

The wrapper is an **XML file** that contains the configuration for the Graphical User interface that will be displayed on W4M and the logic for launching the tool (**command-line interface launch**)





# Steps for uploading tools to W4M

Upload to Bioconda

This last phase is executed using the *Planemo* tool developed by the *Galaxy* team to **ease the process** of uploading tools onto the platform. Features include:

PLANEMO

Elaboration of the  
XML wrapper

**XML Linting :** `$ planemo lint`

**Running tool tests:** `$ planemo test --galaxy_root=./galaxy randomlines.xml`

**Viewing in Galaxy interface:** `$ planemo serve`

Test and  
release

# Slide with W4M workflow example

TODO

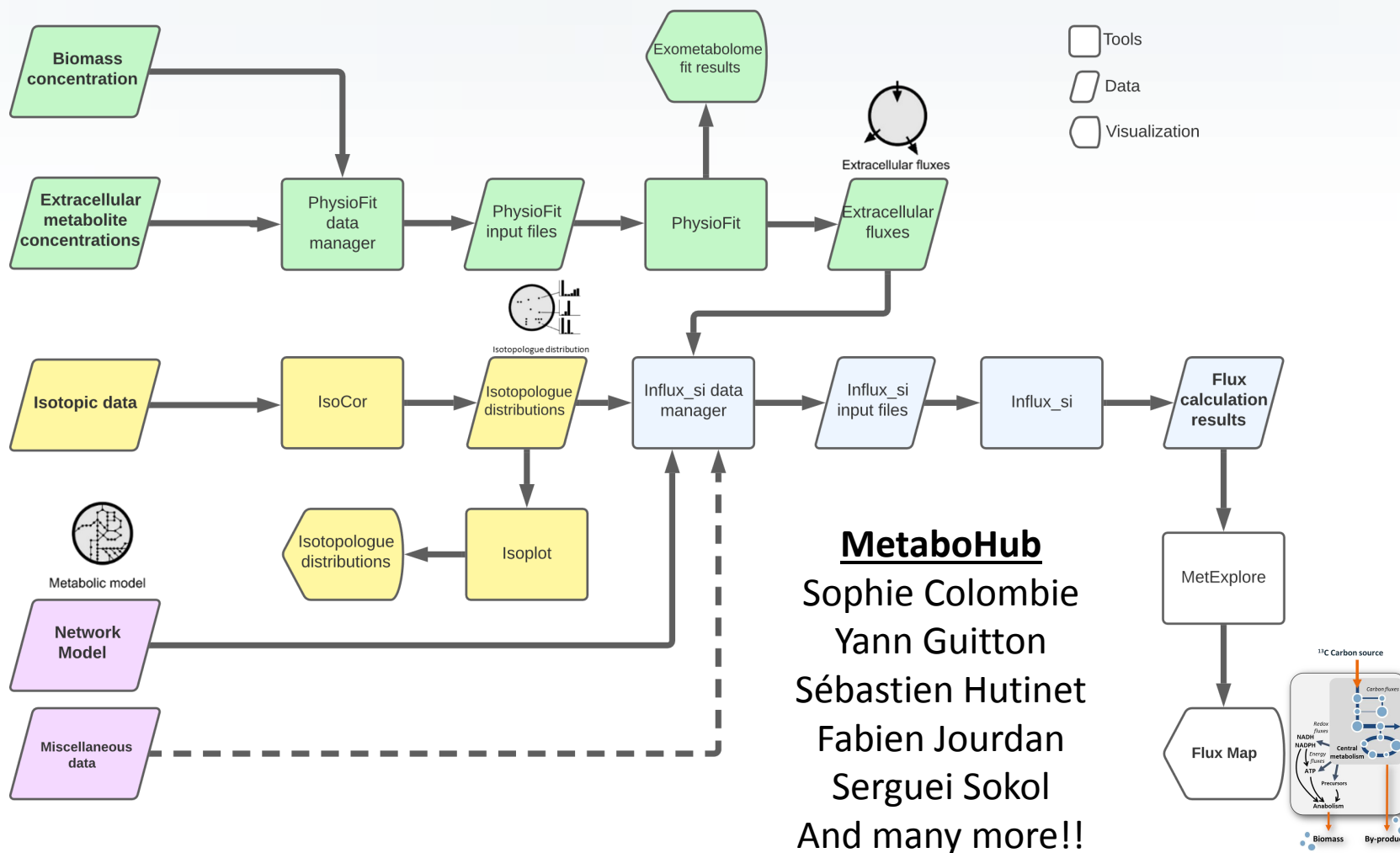
# Conclusion

- ➔ The **lack of interoperality** between tools meant **high expertise** was needed for flux calculation
- ➔ The workflow renders flux calculation more **reproducible, repeatable** and **increases throughput**.
- ➔ **Easy access and user-friendly** interface through W4M
- ➔ Uploading workplan is well detailed → faster developments in the future

# Outlook

- ➔ Extension to other  $^{13}\text{C}$  fluxomics approaches (instationary, scalable, NMR-based, etc)
- ➔ Extension with preliminary computational steps (quantification by MS and/or NMR, grouping of isotopic data, etc)
- ➔ Validation and application to investigate glucose & acetate co-metabolism in *E. coli* (requires large number of flux maps)

# Acknowledgments



## MetaToul FluxoMet

Floriant Bellvert  
 Cécilia Bergès  
 Noémie Butin  
 Edern Cahoreau  
 Jean-Charles  
 Lara Galès  
 Hanna Kulyk  
 Nina Lager-Lachaud  
 Lindsay Peyriga  
 Etienne Rifa  
 Amandine Rocher

## MetaSys team

Pierre Millard  
 Stéphanie Heux

