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

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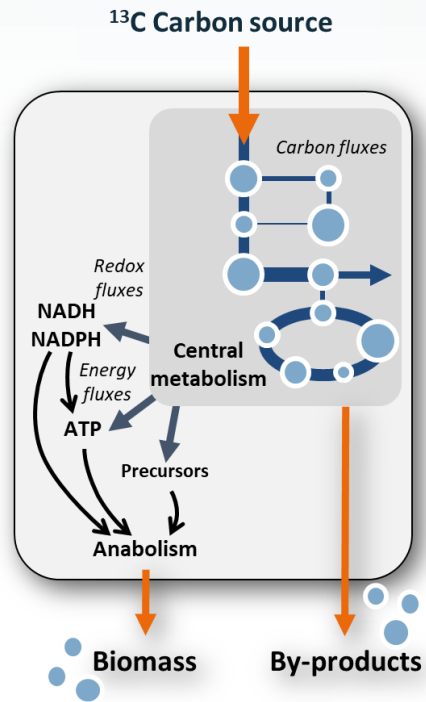
An automatised ^{13}C -fluxomics workflow

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

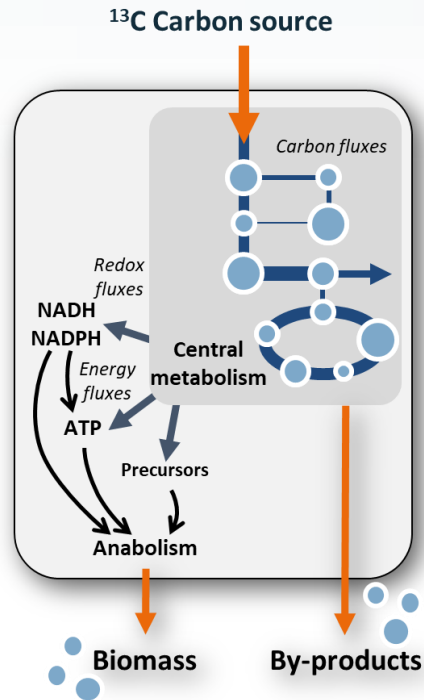
Quantifying fluxes: the basics

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

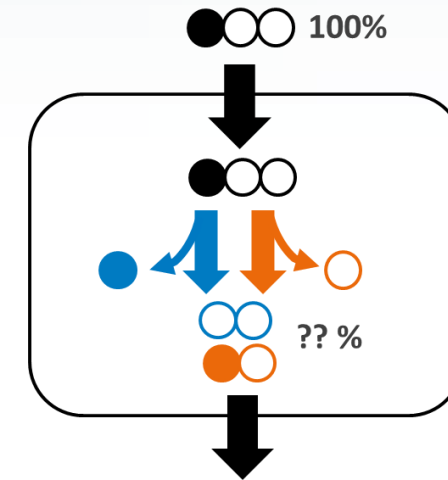


Quantifying fluxes: the basics

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



Fluxes cannot be measured directly!

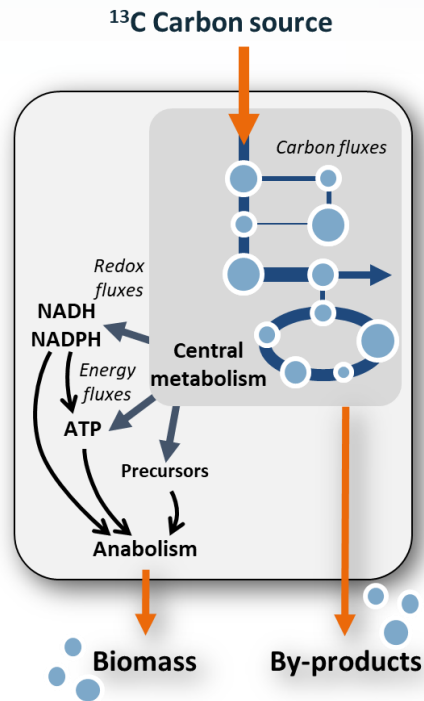


Data that is needed:

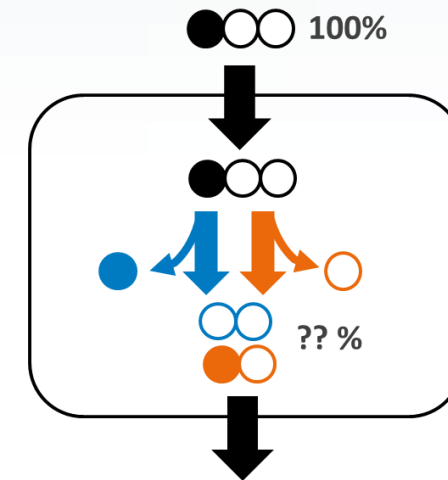
- Stoichiometric model
- Input-output rates (i.e. extracellular fluxes)
- Labeling distribution

Quantifying fluxes: the basics

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



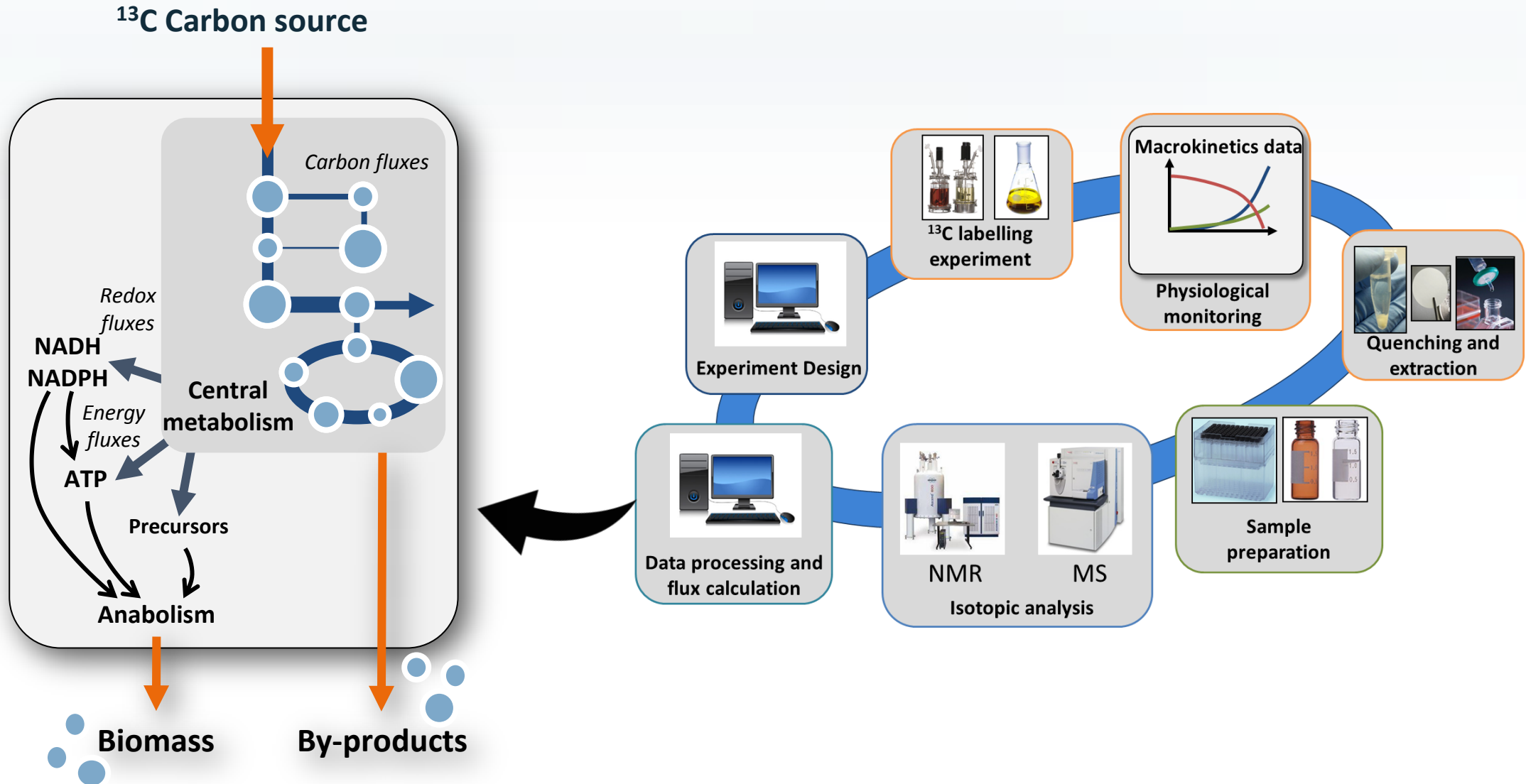
Fluxes cannot be measured directly!



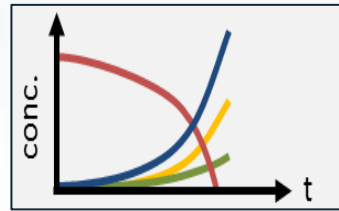
Data that is needed:

- Stoichiometric model
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- Labeling distribution

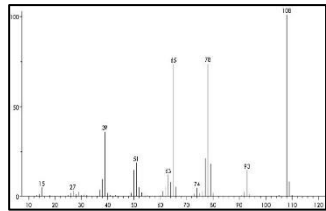
Quantifying fluxes: A complex workflow



Quantifying fluxes: data processing & flux calculation



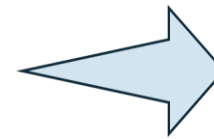
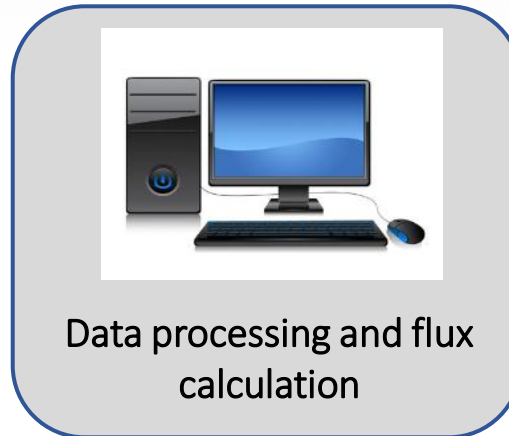
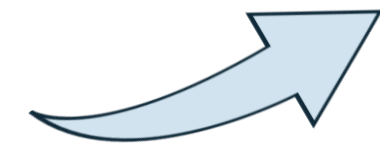
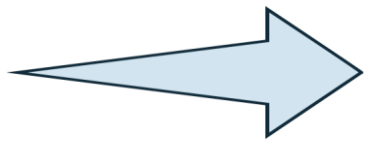
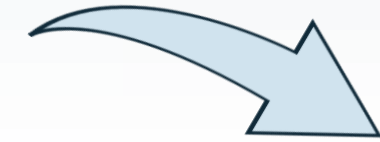
Growth data



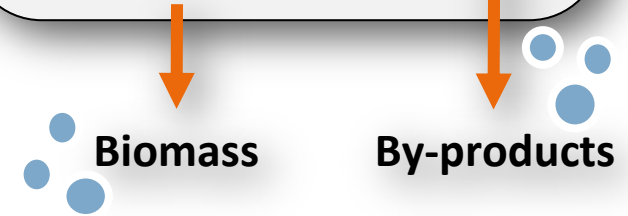
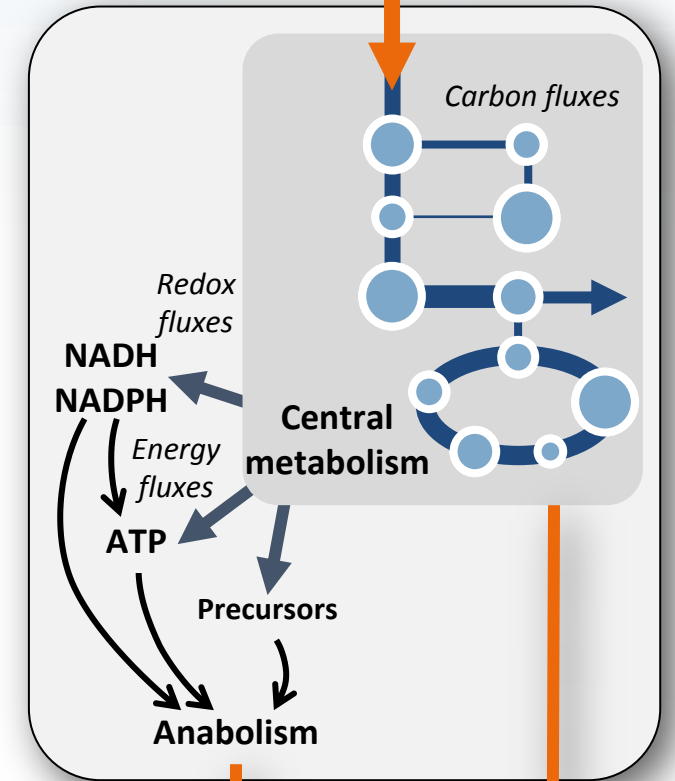
Isotopic data



Metabolic model



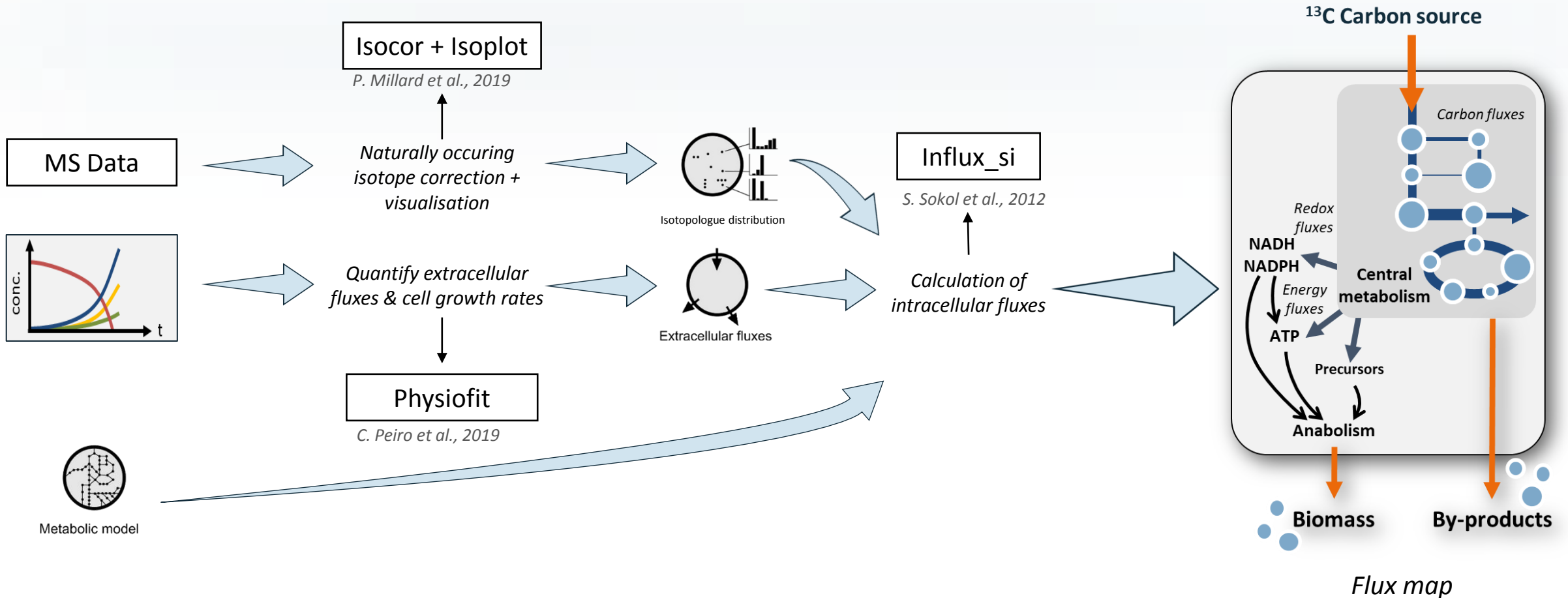
^{13}C Carbon source



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

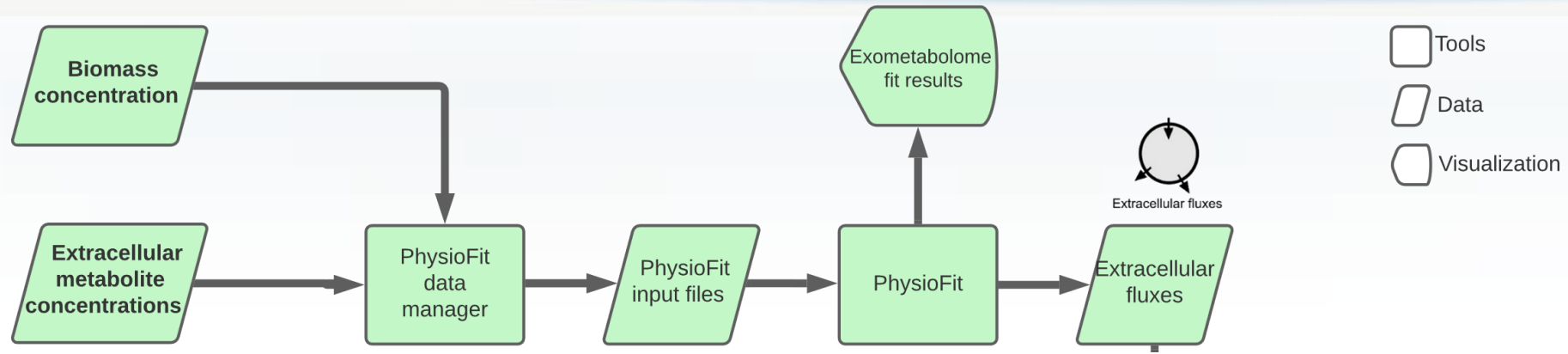


Quantifying fluxes: current (manual) pipeline for flux calculation

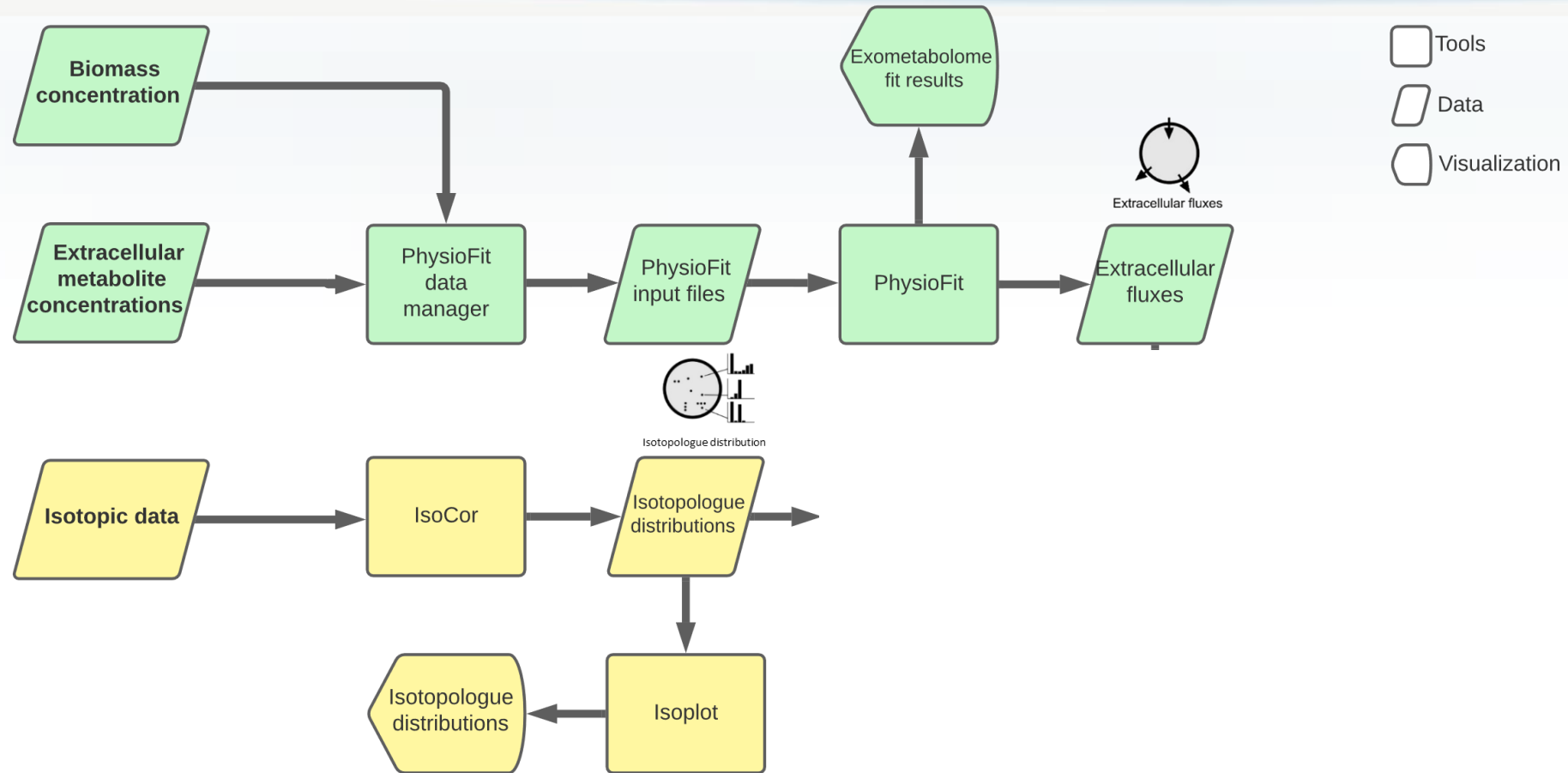


Objective: streamline the process to increase reproducibility, robustness and throughput
-> Development of an automatised ^{13}C workflow

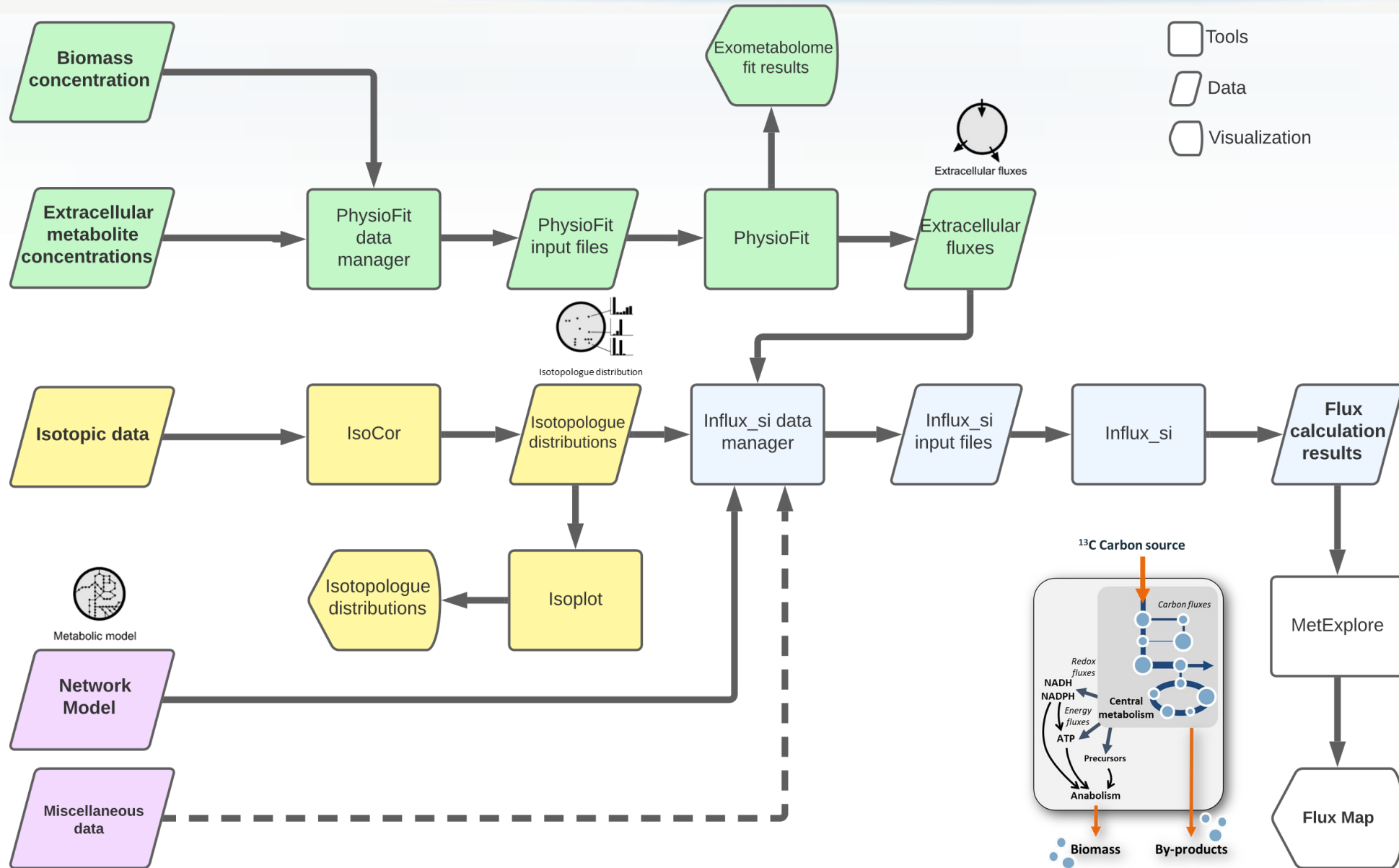
Proposed ^{13}C -fluxomics workflow



Proposed ^{13}C -fluxomics workflow



Proposed ^{13}C -fluxomics workflow



Galaxy – Workflow4Metabolomics (W4M)

User oriented

Open source

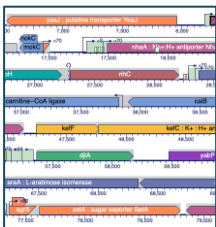
Web-based



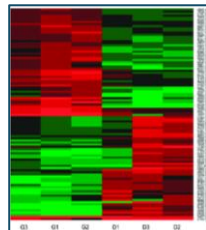
E. Afgan et al., 2018



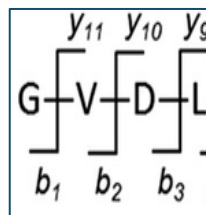
Genomics



Transcriptomics



Proteomics



Galaxy – Workflow4Metabolomics (W4M)

User oriented
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Web-based

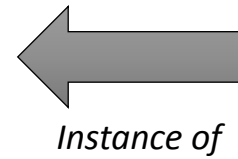


E. Afgan et al., 2018

Data pre-processing & processing
Statistical analysis
Interpretation



Workflow4metabolomics



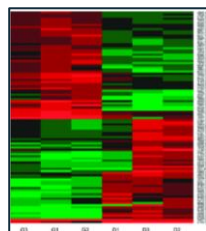
Instance of

Giacomoni et al., 2014

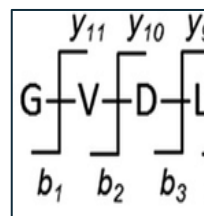
Genomics



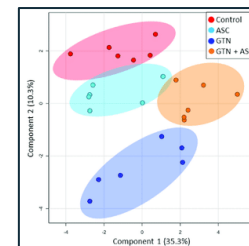
Transcriptomics



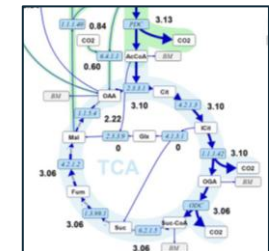
Proteomics



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

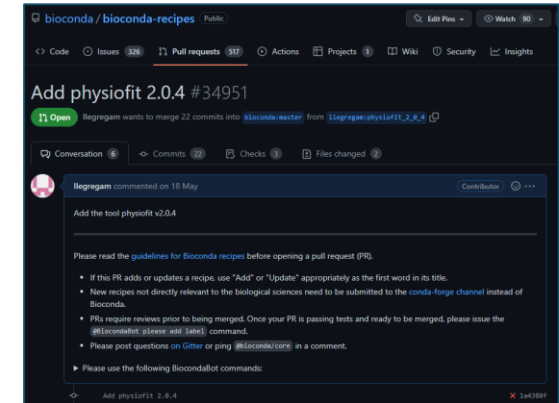
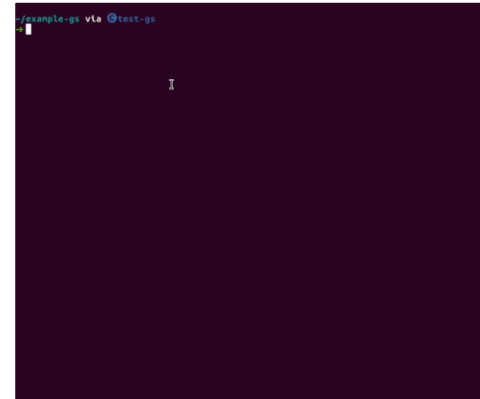
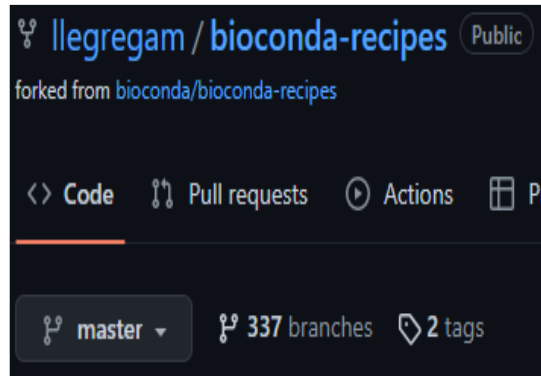
Upload to Bioconda

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



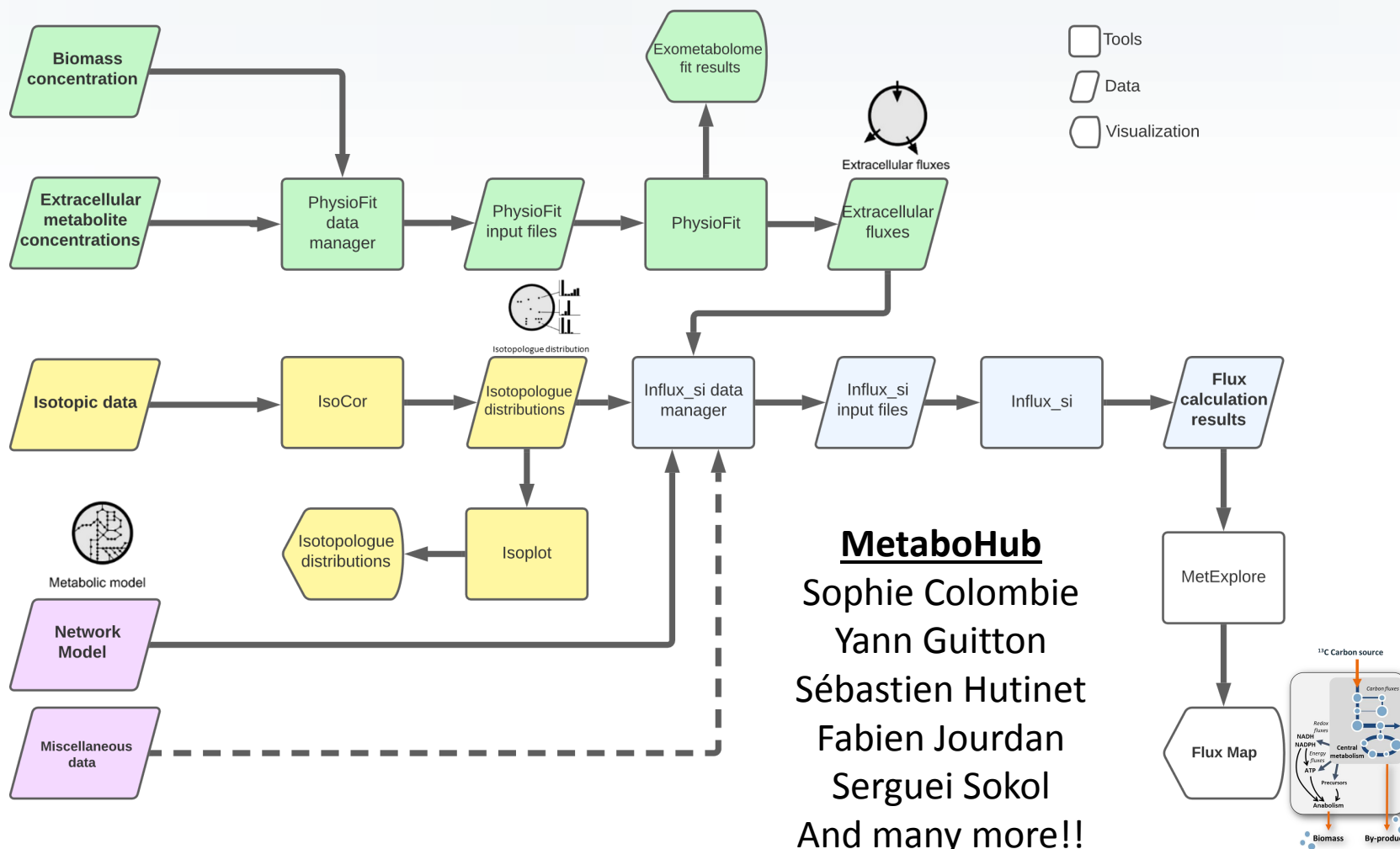
Conclusion

- ➔ 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}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
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Pierre Millard
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