

*DD-DeCaF: Bioinformatics Services for Data-Driven  
Design of Cell Factories and Communities*

# DD-DeCaF Workshop at DSM

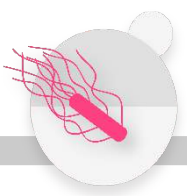
Session 4: Cameo and DD-DeCaF platforms  
Nikolaus Sonnenschein  
[niso@biosustain.dtu.dk](mailto:niso@biosustain.dtu.dk)  
DTU



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 686070

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Design of Cell Factories and Communities*

DEMO 11-Sep-2017



# Download slides

<https://goo.gl/sWRfGH>



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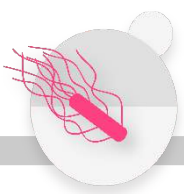
*DD-DeCaF: Bioinformatics Services for Data-Driven  
Design of Cell Factories and Communities*

DEMO 11-Sep-2017



**DTU Biosustain**

The Novo Nordisk Foundation Center for Biosustainability



# The problem with traditional metabolic engineering

## **Commercial:**

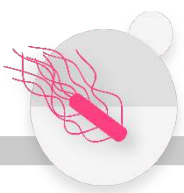
Product titre > 10 g/L  
>25 FTE for >5 years  
Cost >\$50M

## **Academic:**

Product titre < 100 mg/L  
2 FTE for 3 years  
Cost \$1M



Valley of Death



# Bridging the valley of death

Lab automation



Omics



**Commercial:**

Product titre > 10 g/L

Cost <\$20M

**Academic:**

Product titre < 100 mg/L

2 FTE for 3 years

Cost \$1M

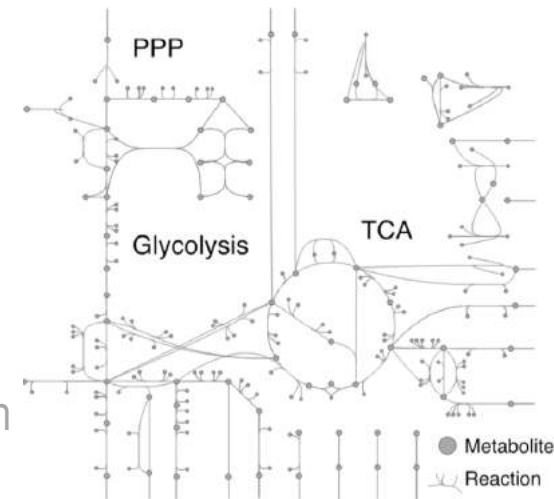


Systems biology  
guided design

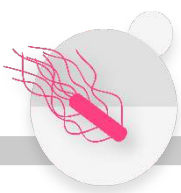


Valley of Death

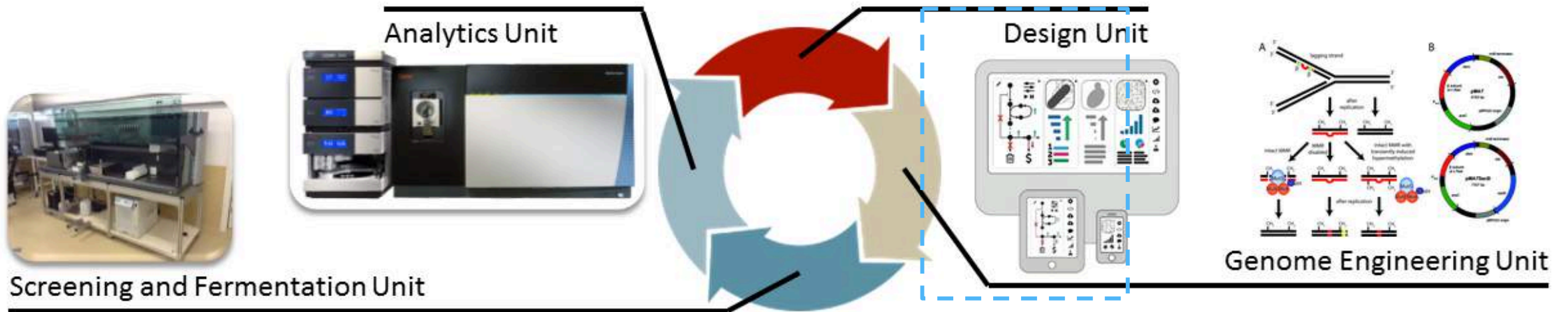
Metabolic pathway





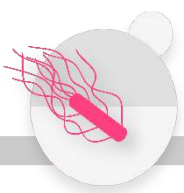


# iLoop Core Unit at DTU Biosustain

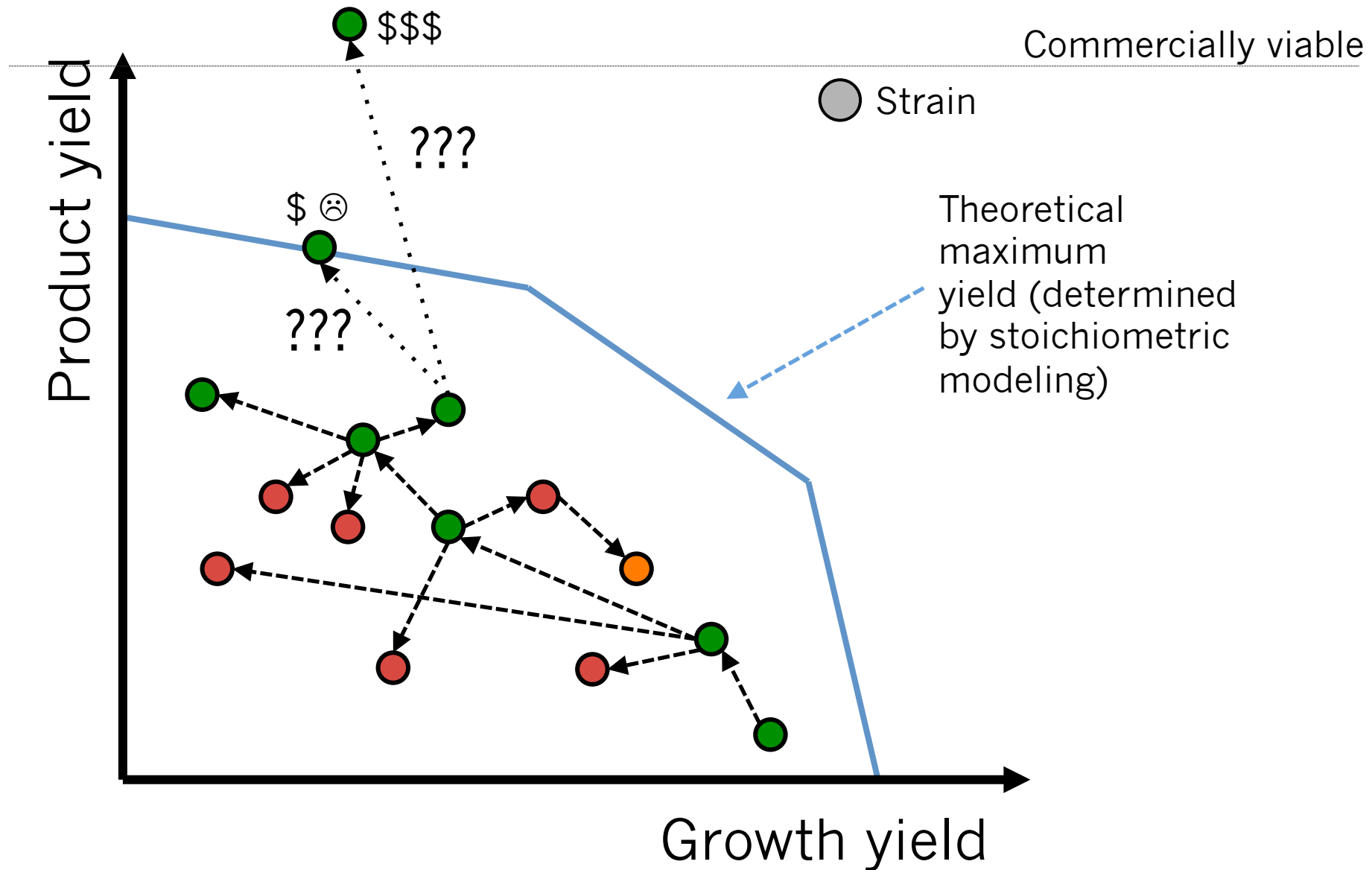


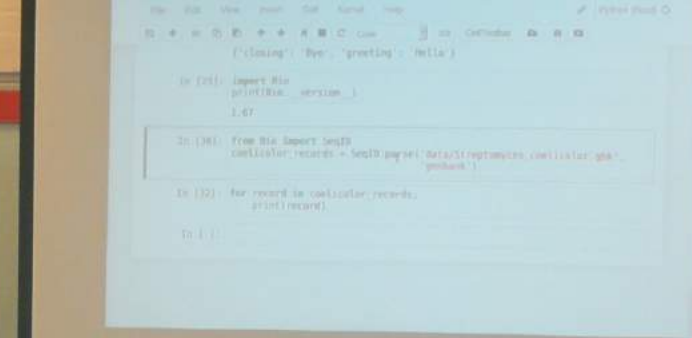
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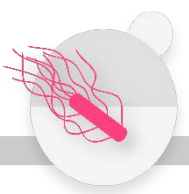
# The strain engineering problem





Software carpentry + Computational cell  
factory engineering course  
18–22 September, 2017 (annual course)





# <http://opencobra.github.io/cobrapy/>

Menu

Home

Releases

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# cobrapy



models



fluxes



algorithms

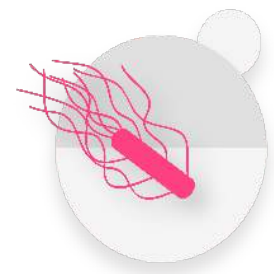
Star 90 contributors 24 release v0.6.1

**cobrapy** is a python package that provides a simple interface to metabolic constraint-based reconstruction and analysis.



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*DD-DeCaF: Bioinformatics Services for Data-Driven Design of Cell Factories and Communities*



*DD-DeCaF: Bioinformatics Services for Data-Driven  
Design of Cell Factories and Communities*

# cameo

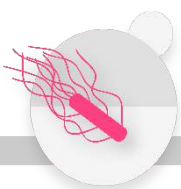
Computer Aided Metabolic Engineering  
and Optimization of Cell Factories

<http://cameo.bio>

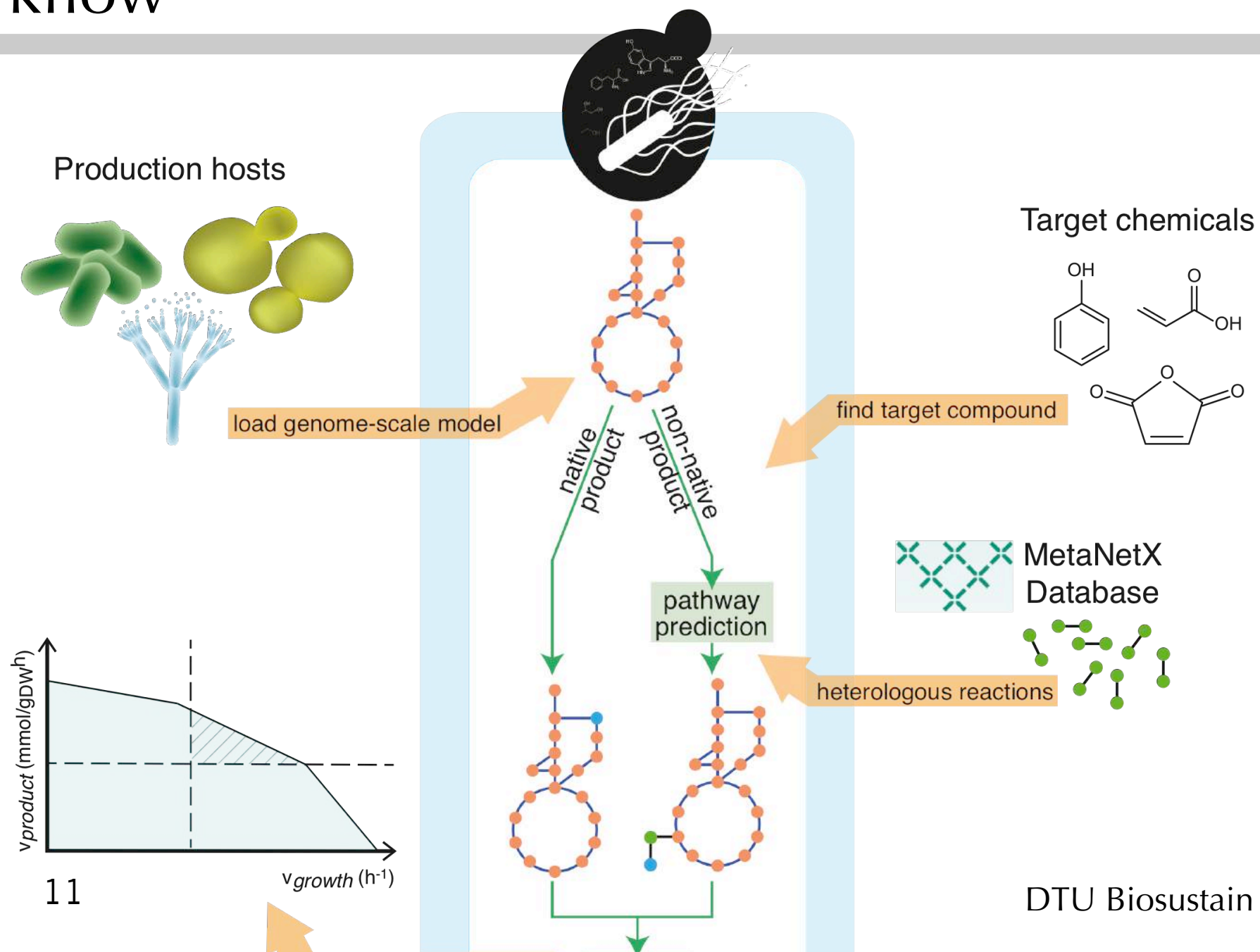


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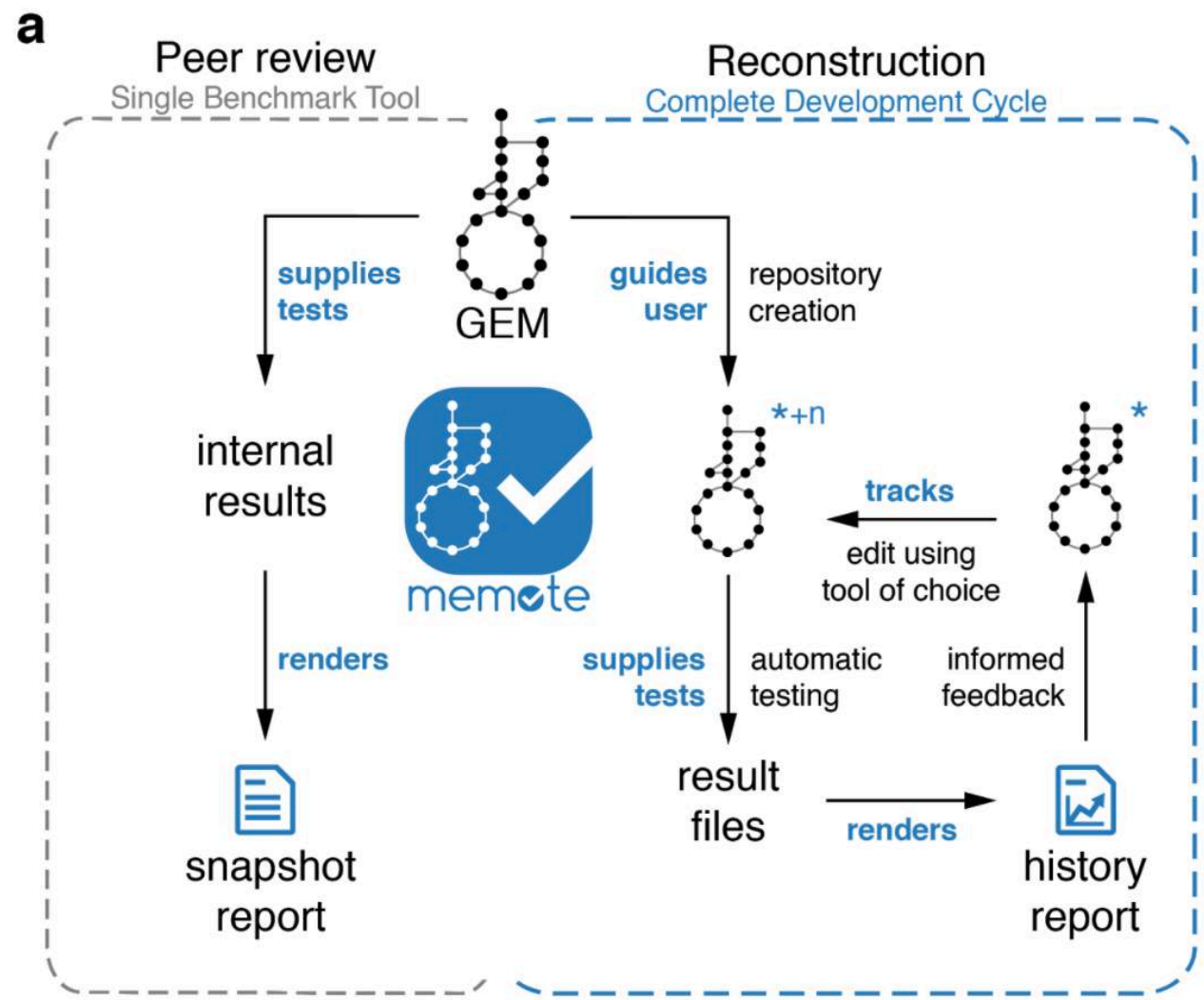
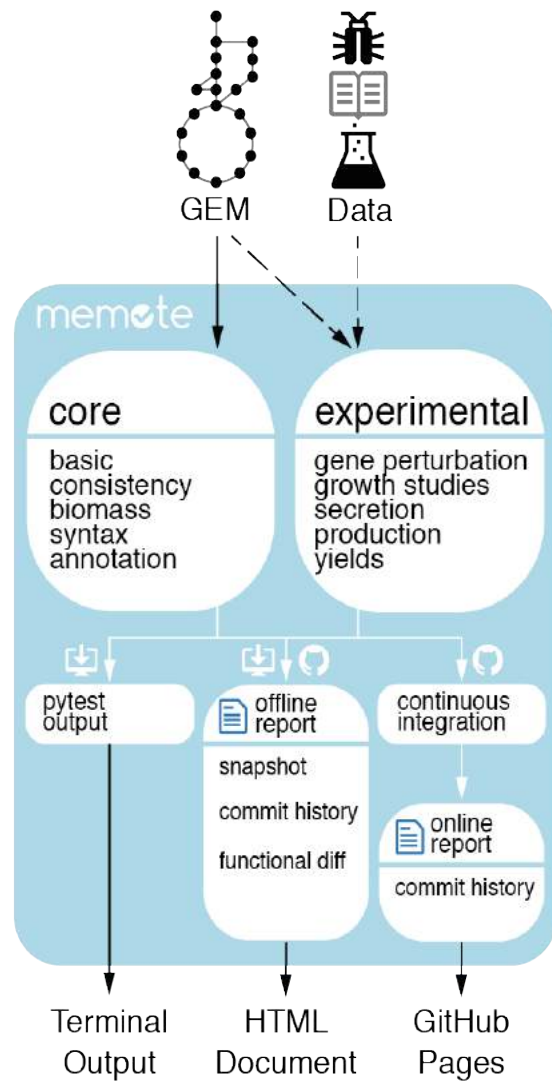


# Workflow





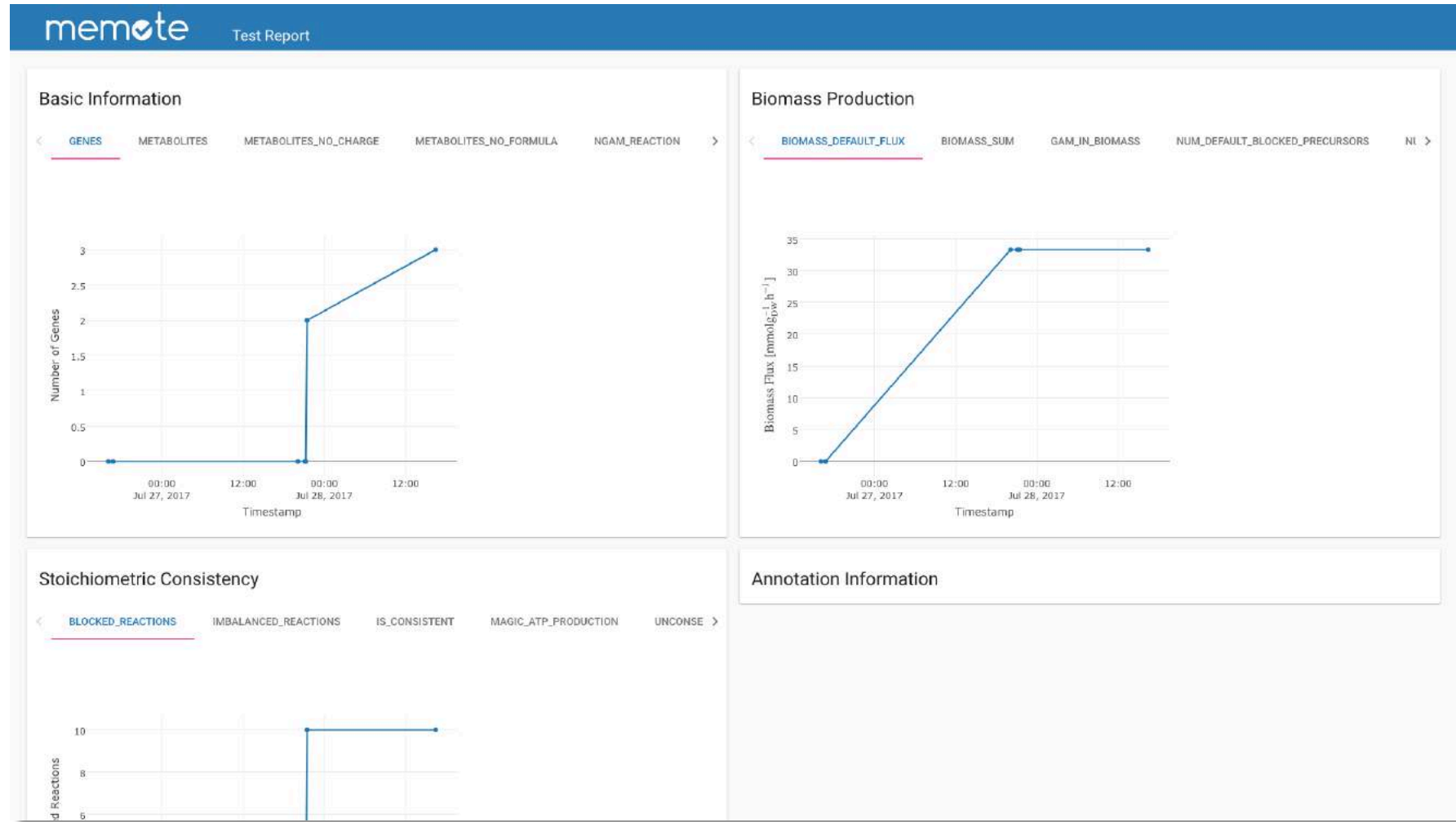
# Memote – metabolic model test suite





# Memote – metabolic model test suite

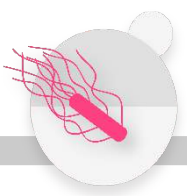
<https://christianlieven.github.io/memote-demo/>



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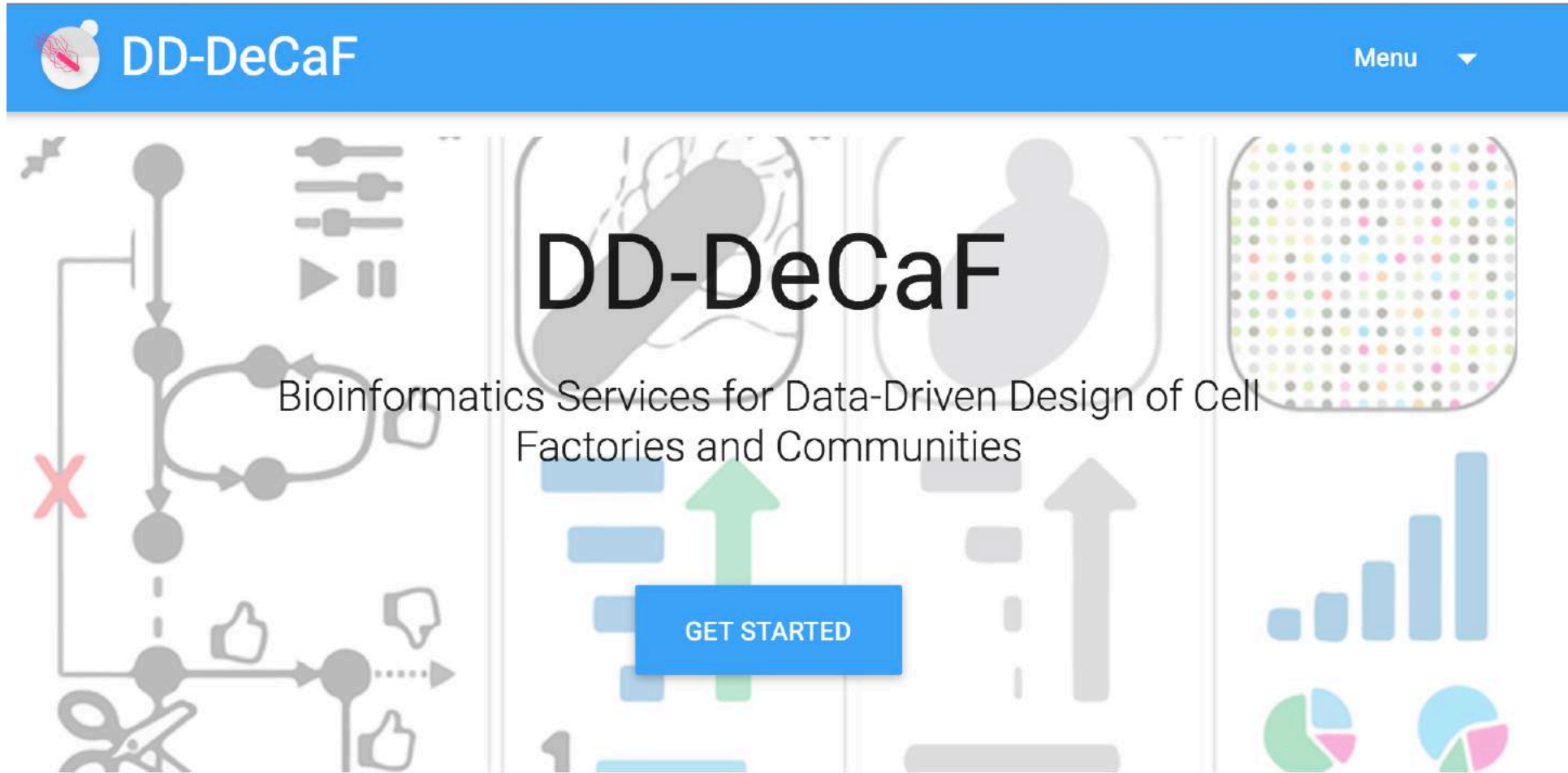
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Session 4 11-Sep-2017



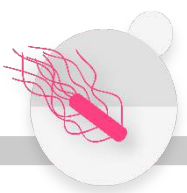
# H2020: Data-Driven Design of Cell Factories and Communities

<http://dd-decaf.eu/>

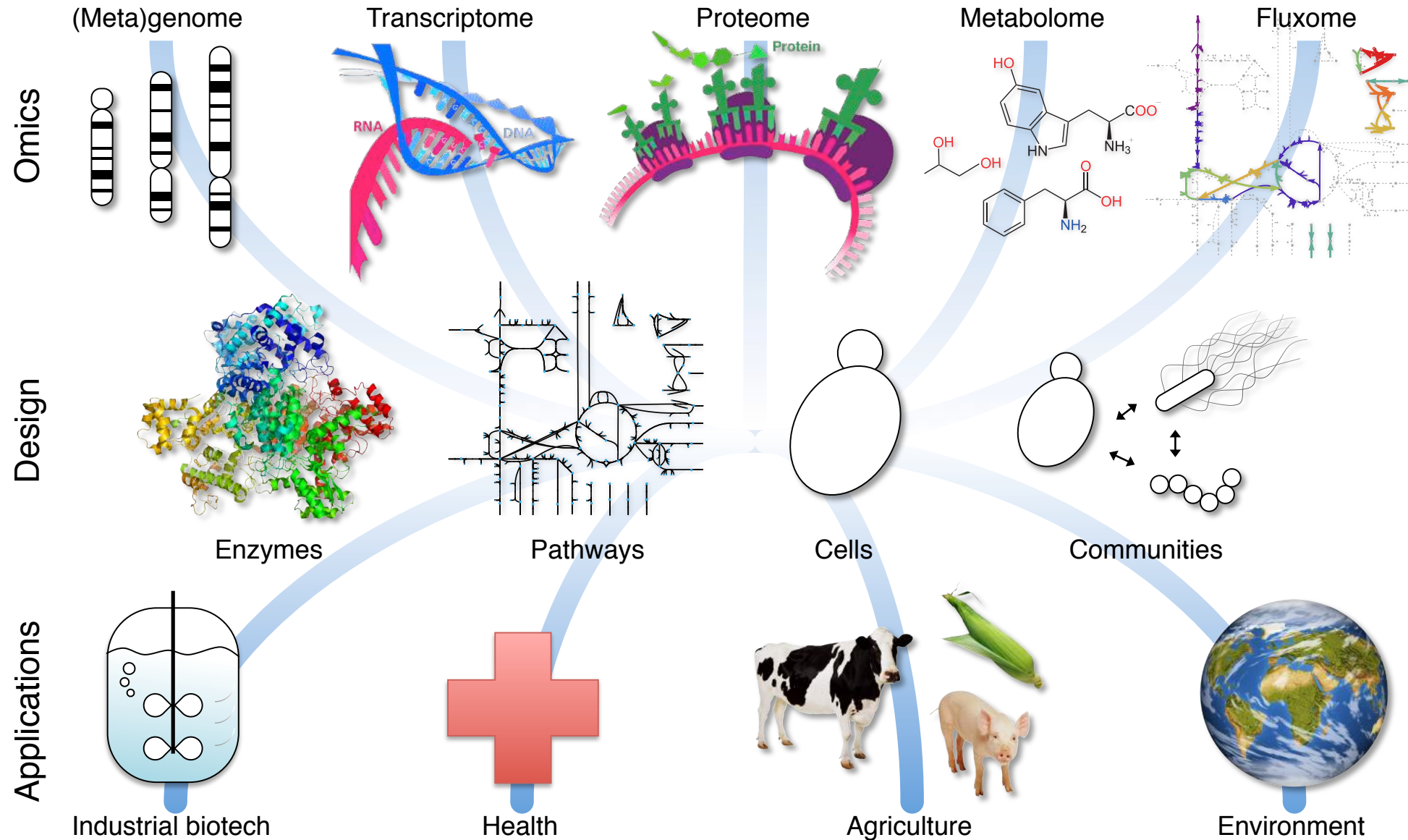


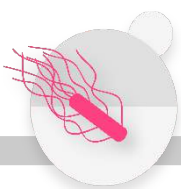
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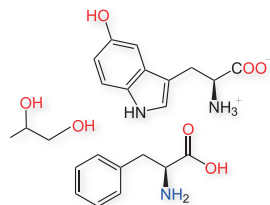
# Horizon 2020: Data-Driven Design of Cell Factories and Communities





# Consortium

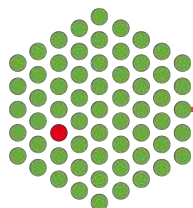
Metabolomics



ÉCOLE POLYTECHNIQUE  
FÉDÉRALE DE LAUSANNE

Vassily Hatzimanikatis

EMBL



Peer Bork & Kiran Patil



Science

Jens Nielsen

CHALMERS

Isabel  
Rocha



Universidade do Minho  
Escola de Engenharia

DTU



Coordinator



Markus Herrgård  
& Niko Sonnenschein

Bioinformatics  
SMEs



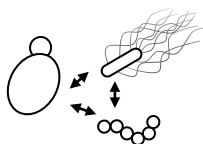
Genialis

Biosyntia

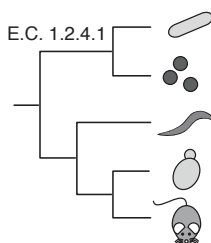
End users



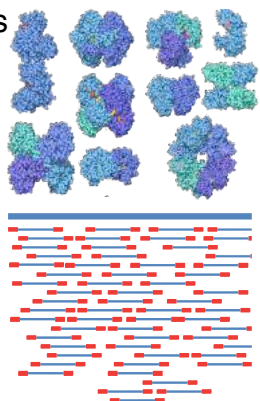
Communities



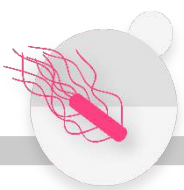
Enzymes



Transcriptomics/  
Proteomics







# Platform demo



Genialis



Svetlana



Henning



Danny



Moritz



Nace



Matyas

DD-DeCaF

<

Home

🔍

⋮

Projects

📁 Demo

📁 Test

📁 Biosyntia

📁 DSM

📁 pabnik

📁 kosc

📁 Media

📁 Upload data

📁 Pathways

📁 Theoretical Yield

📁 Interactive Map

Welcome to DD-DeCaF

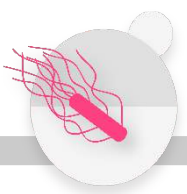
Get started by selecting a project or one of the tools.



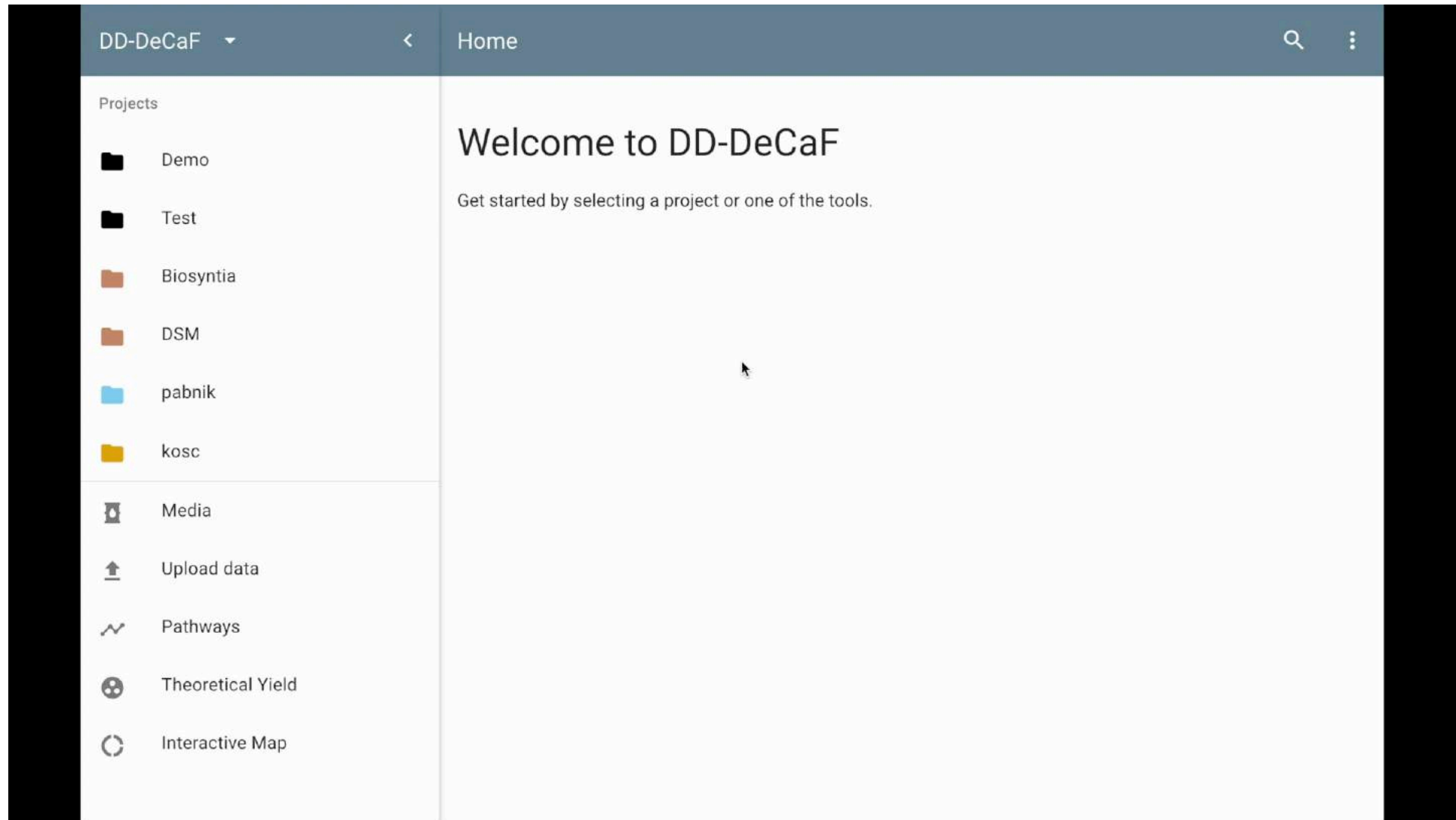
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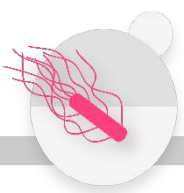
# Interactive pathway visualizations + predictions



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# Uploading data

DD-DeCaF

<

Upload data

🔍

⋮

Projects

📁 Demo

📁 Test

📁 Biosyntia

📁 DSM

📁 pabnik

📁 kosc

📁 LLU ITF

📁 Media

📁 Upload data

📁 Pathways

📁 Theoretical Yield

📁 Interactive Map

Choose a project, then one or more csv files containing the data you wish to upload.

Project  
Test

Data type  
fluxes

Make sure that you have uploaded media and strain definitions first as you have to refer to these as indicated in the file schema.

📎

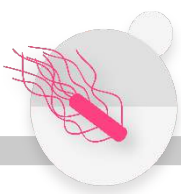
CHOOSE FLUXES FILE

FILE SCHEMA..

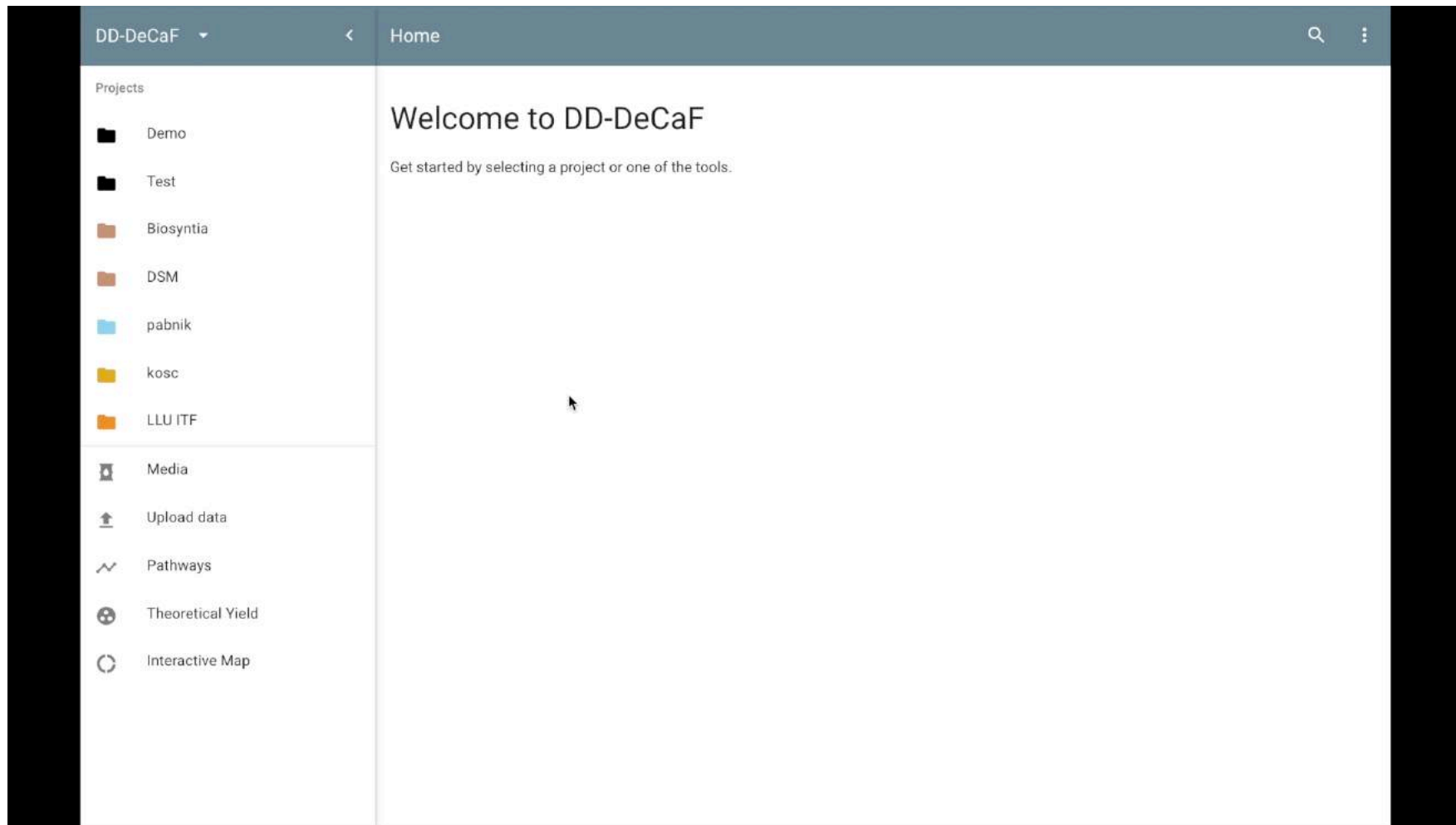
SUBMIT

CLEAR

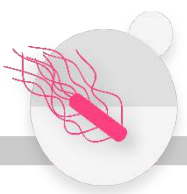




# Gecko/ecYeast7 model demo (from WP5)

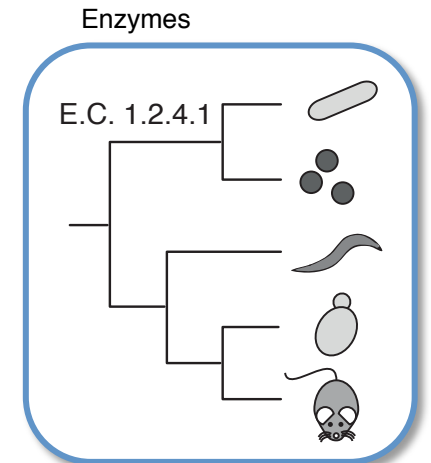
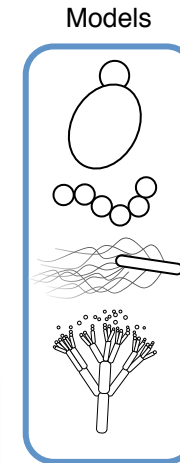
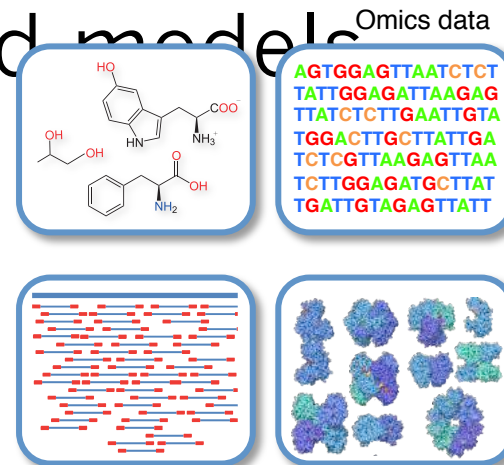
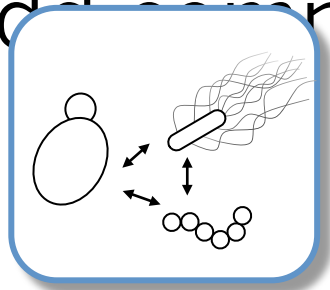
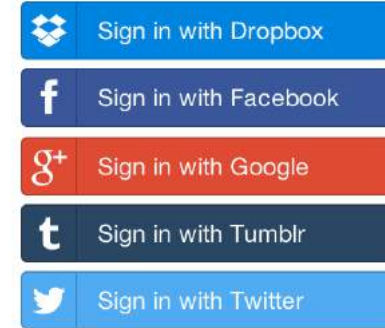


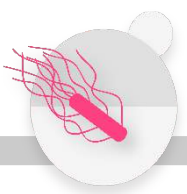




# Next steps

- Registration via Google, Twitter, Github, Facebook, ORCID, ...
- Bring your own models
- Mine (meta)genomic data for enzymes
- More types of omics data and models
- Add community modeling

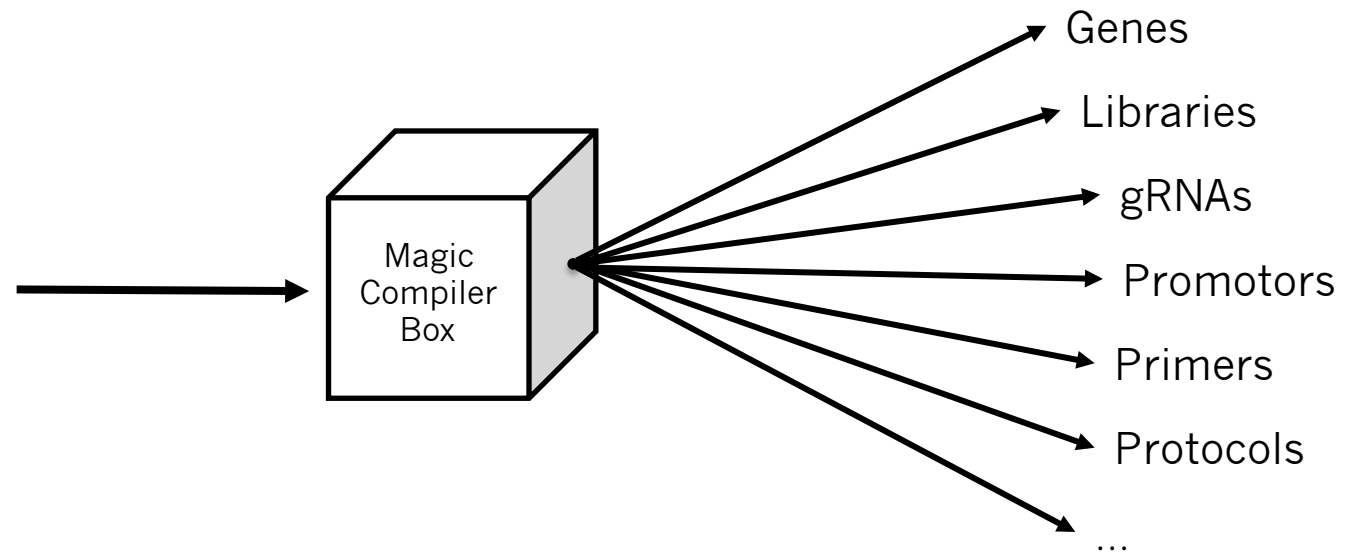


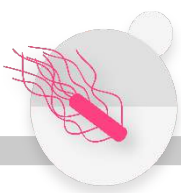


# The future ...

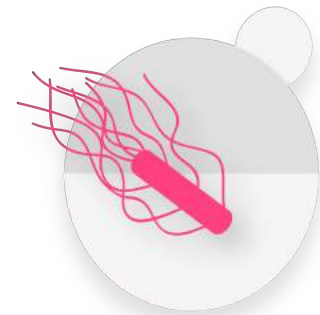
## High-level strain design

*“Delete native genes A, B, C, and D. Add foreign genes X, Y, Z. Increase flux through reaction F by twofold while reducing flux through reaction G by threefold. Remove product inhibition in pathway Q ...”*





# Import into Genetic Constructor (by Autodesk)



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GENETIC CONSTRUCTOR

CRISPRainbow Multiplex Labeling Kit

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    - pCRISPRrainbow-DONOR1
    - pLH-sgRNA1-boxB-MS2-PP7
    - pLH-sgRNA1-boxB-MS2
    - pLH-sgRNA1-PP7-boxB
    - pLH-sgRNA1-MS2-PP7
    - pLH-sgRNA1-2XboxB
    - pLH-sgRNA1-2XPP7
    - pLH-sgRNA1-2XMS2
    - pLH-sgRNA1
    - pHAGE-EFS-N22b-3XRFPhs
    - pHAGE-EFS-PCP-3XGFPPhs
    - pHAGE-EFS-MCP-3XBFPPhs
    - pHAGE-TO-MCP-3XBFPPhs
    - pHAGE-TO-dCas9
  - Bacterial expression plasmids
  - Lentiviral plasmids
  - EMMA Templates

Block Information

Name

Multiple blocks selected

Description

Multiple blocks selected

Not Protected

Source

Multiple Sources

Sequence Length

2479 bp

Color & Symbol

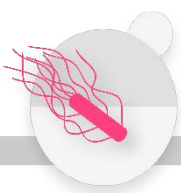
Strain designs



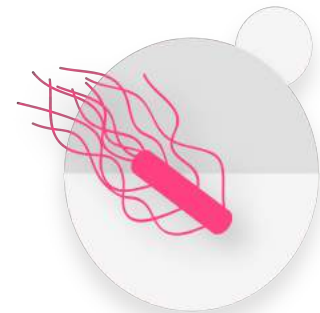
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# Export Genotype Specification Language (GSL)



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  - pCRISPRrainbow-DONOR1
  - pLH-sgRNA1-box8-MS2-PP7
  - pLH-sgRNA1-box8-MS2
  - pLH-sgRNA1-PP7-box8
  - pLH-sgRNA1-MS2-PP7
  - pLH-sgRNA1-2Xbox3
  - pLH-sgRNA1-2XPP7
  - pLH-sgRNA1-2XMS2
  - pLH-sgRNA1
  - pHAGE-EFS-N22p-3XRFPhis
  - pHAGE-EFS-PCP-3XGFPhis
  - pHAGE-EFS-MCP-3XBFPhis
  - pHAGE-TO-MCP-3XBFPhis
  - pHAGE-TO-dCas9
- Bacterial expression plasmids
- Lentiviral plasmids
- EMMA Templates

Block Information

Name

Multiple blocks selected

Description

Multiple blocks selected

Not Protected

Source

Multiple Sources

Sequence Length

2479 bp

Color & Symbol

SEQUENCE

GSL EDITOR

```
1 // First construct derives all elements from BY4741 genome
2 #refgenome BY4741
3 #name BY4741_construct
4 uMO ; pADH1 ; gERG10 ; ### ; dHO
5
6 // Second construct only derives ERG10 from S288C while the rest
7 // come from BY4741
8 #name BY4741_construct_with_288C_erg10
9 uMO ; pADH1 ; gERG10 [#refgenome S288C] ; ### ; dHO
```

AMYRIS

Genotype Specification Language (GSL)

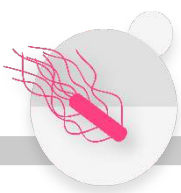


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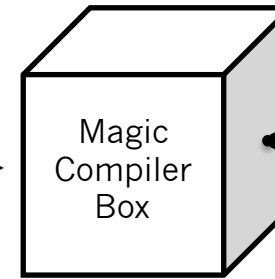




# Automate all the things

## High-level strain design

*“Delete native genes A, B, C, and D. Add foreign genes X, Y, Z. Increase flux through reaction F by twofold while reducing flux through reaction G by threefold. Remove product inhibition in pathway Q ...”*



Genes

Libraries

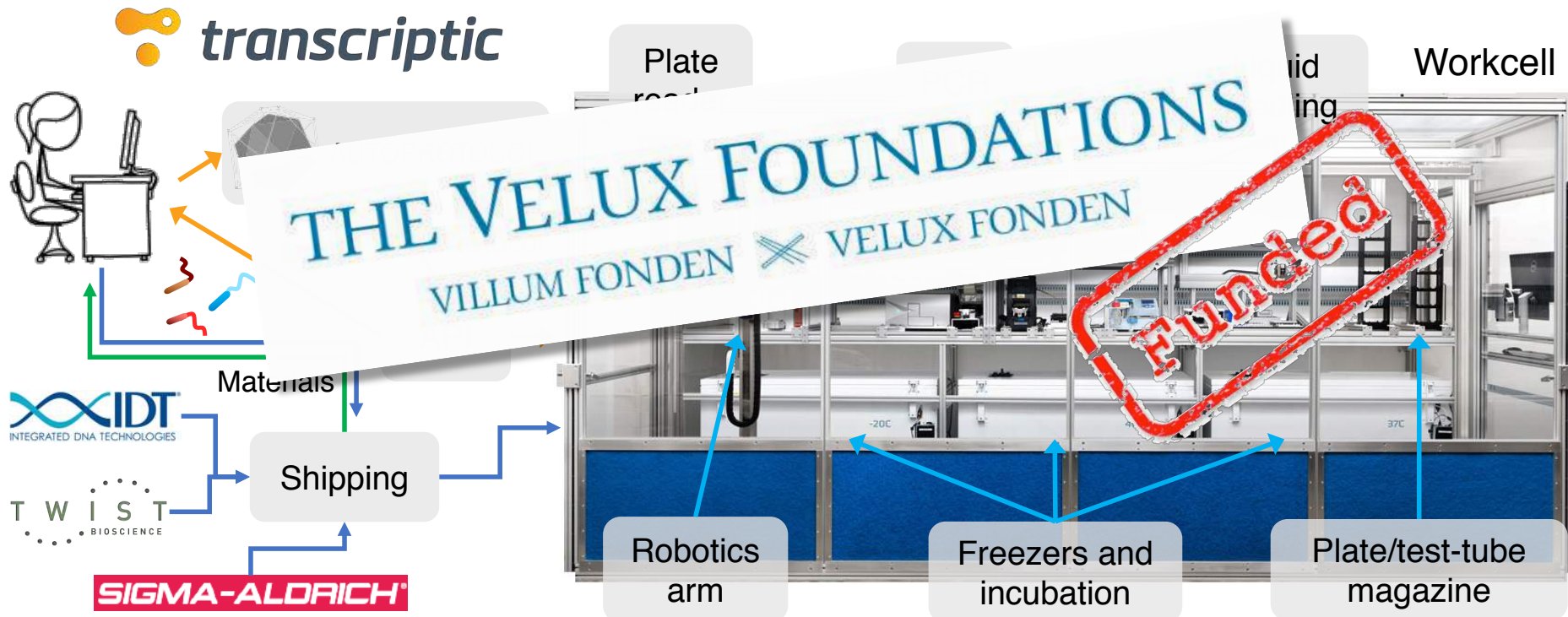
gRNAs

Promoters

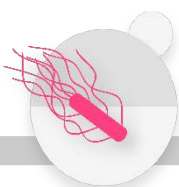
Primers

Protocols

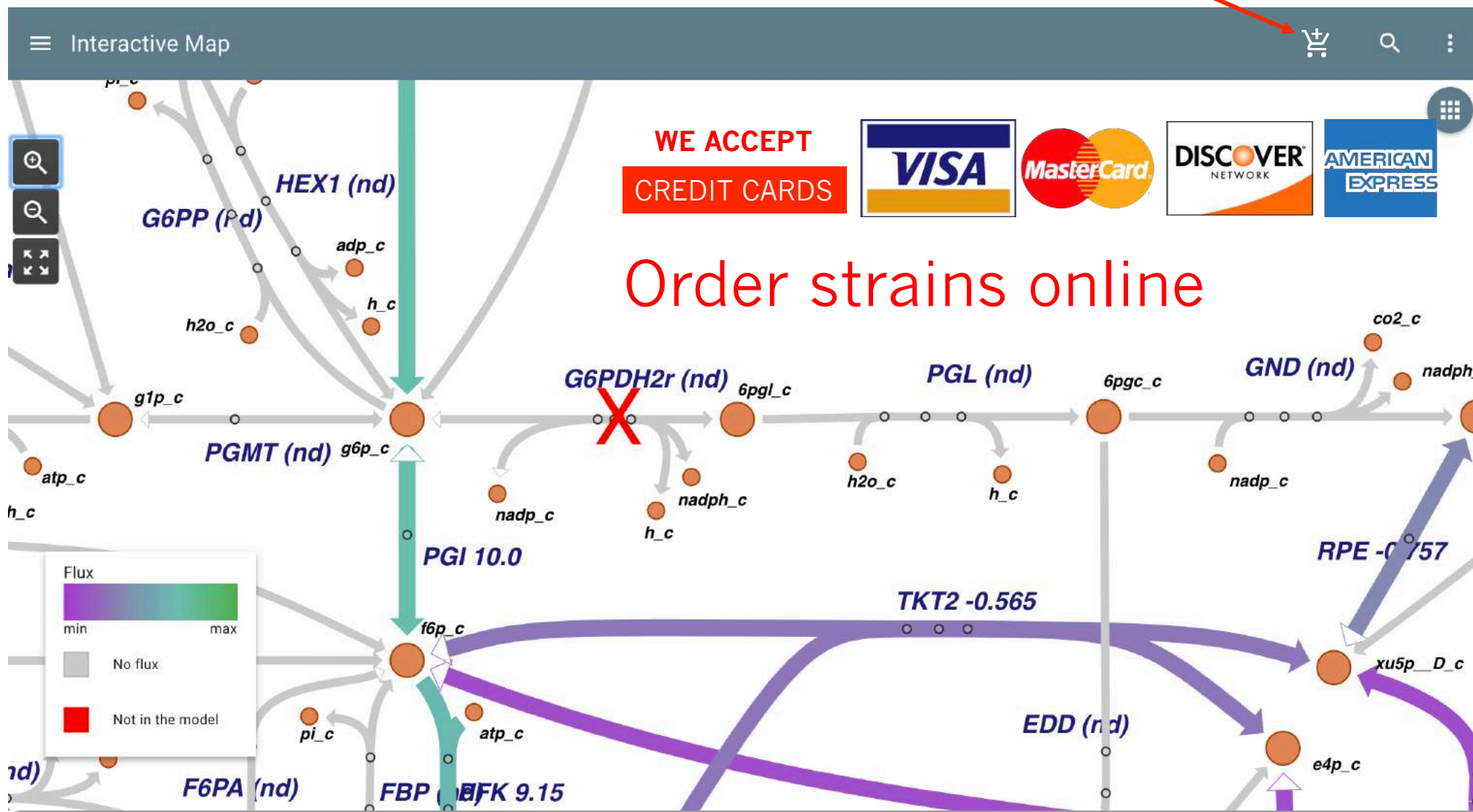
...

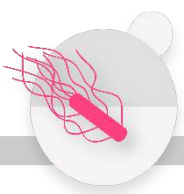


This project  
research



# Order button





# So many tools ...

- Programing skills required
- Detailed understanding of models required

cbrapy

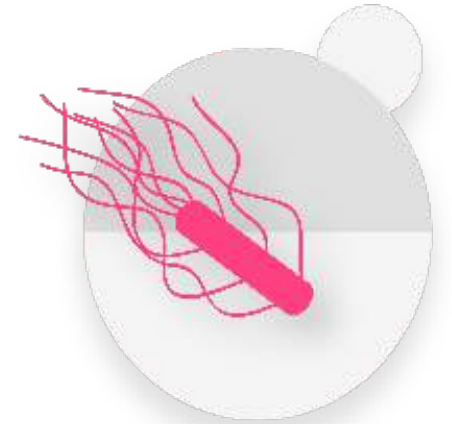
cameo

- No programming skills required
- Detailed understanding of models required

optflux  
Metabolic engineering workbench

To be covered in Session 5

- No programming skills required
- No in-depth understanding of models required



[app.dd-decaf.eu](http://app.dd-decaf.eu)

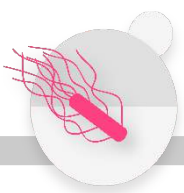
Poweruser capabilities & learning barrier



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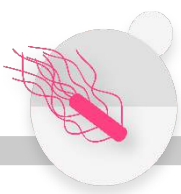
<https://workshop.dd-decaf.eu/hub/home>



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account if you don't  
have one yet (~5 min)

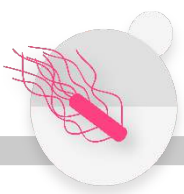


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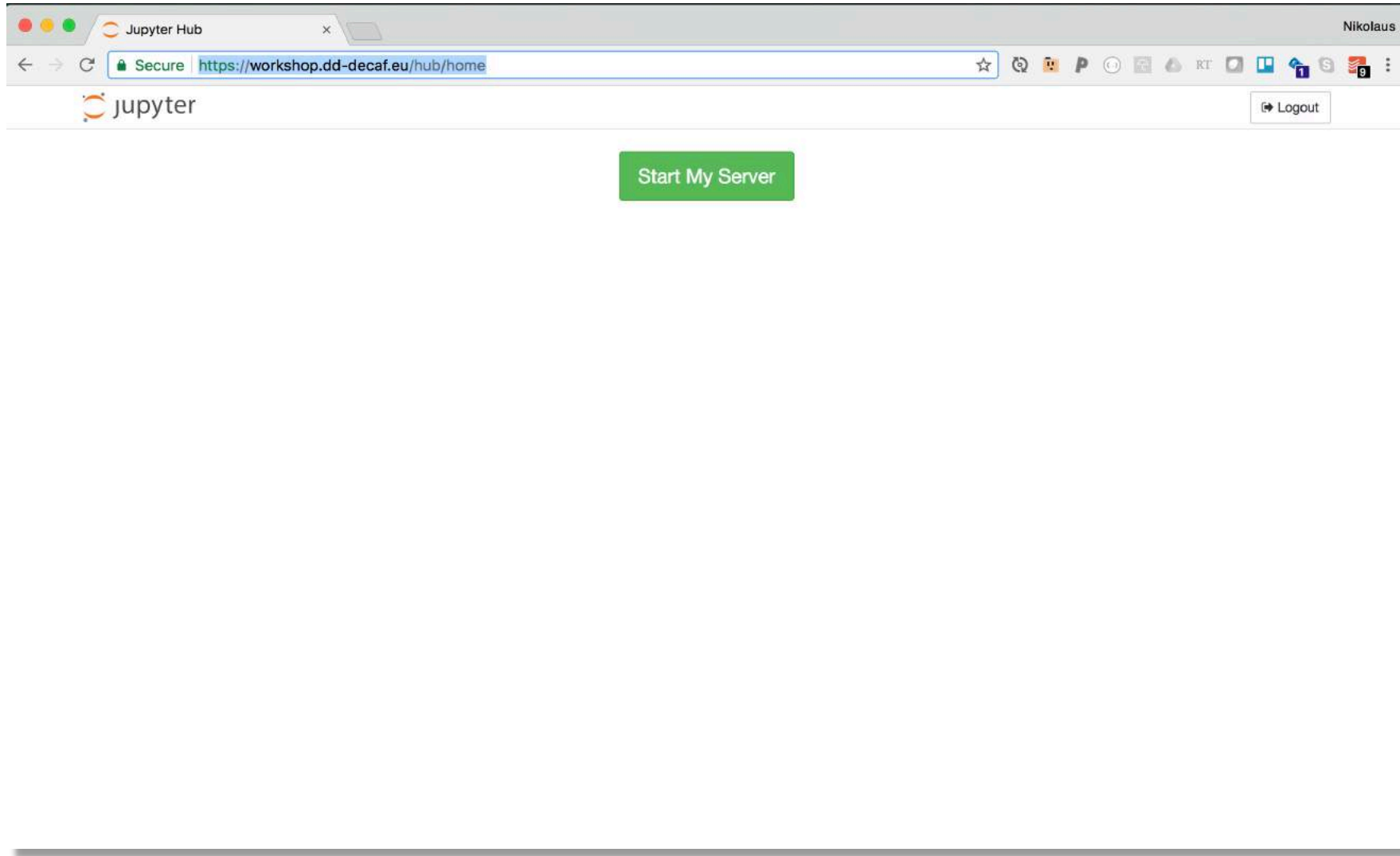
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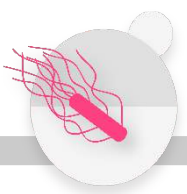
# <https://workshop.dd-decaf.eu/hub/home>



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*DD-DeCaF: Bioinformatics Services for Data-Driven Design of Cell Factories and Communities*

DEMO 11-Sep-2017



# Practical part

- Gentle introduction to Python + Jupyter notebooks (5 min)
- Cobrapy
  - <https://github.com/DD-DeCaF/tutorials/blob/master/cobrapy-01-getting-started.ipynb> (5 min)
  - <https://github.com/DD-DeCaF/tutorials/blob/master/cobrapy-02-genome-scale-metabolic-models.ipynb> (10 min)
  - <https://biosustain.github.io/cell-factory-design-course/08-Theoretical-maximum-yields/> (15 min)
- Cameo
  - <https://github.com/DD-DeCaF/tutorials/blob/master/cameo-01-predict-heterologous-pathways.ipynb> (15 min)
  - <https://github.com/DD-DeCaF/tutorials/blob/master/cameo-02-generating-gene-knockout-strategies.ipynb> (15 min OptGene example)
- DD-DeCaF
  - Download workshop.zip from JupyterHub
  - <https://app.dd-decaf.eu> (User: [workshop@dsm.nl](mailto:workshop@dsm.nl), Password: DSMNL2017)
  - Manipulate the data to your liking
  - Upload data in the following order: medium, strain, (samples, physiology), fluxes





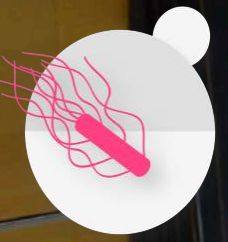
# Acknowledgements



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Get in touch with us via:

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