BPL_TEST2_Batch_calibration script with FMPy

The key library FMPy and scipy and more are installed.

After the installation a small application BPL_TEST2_Batch_calibration is loaded and run. You can continue with this example if you like.

```
!lsb_release -a # Actual VM Ubuntu version used by Google
```

```
No LSB modules are available. Distributor ID: Ubuntu
```

Description: Ubuntu 22.04.3 LTS

Release: 22.04 Codename: jammy

%env PYTH0NPATH=

```
→ env: PYTHONPATH=
```

```
!wget https://repo.anaconda.com/miniconda/Miniconda3-py312_24.3.0-0-Linux-x86_64.sh
!chmod +x Miniconda3-py312_24.3.0-0-Linux-x86_64.sh
!bash ./Miniconda3-py312_24.3.0-0-Linux-x86_64.sh -b -f -p /usr/local
import sys
sys.path.append('/usr/local/lib/python3.12/site-packages/')
```

2024-05-16 09:56:27 (152 MB/s) - 'Miniconda3-py312_24.3.0-0-Linux-x86_64.sh' saved [143351488/143351488]

PREFIX=/usr/local Unpacking payload ...

Installing base environment...

Preparing transaction: ...working... done Executing transaction: ...working... done installation finished.

!conda update -n base -c defaults conda --yes

Channels:
- defaults
Platform: linux-64
Collecting package metadata (repodata.json): done
Solving environment: done

Package Plan

environment location: /usr/local

added / updated specs:
 - conda

The following packages will be downloaded:

package	build		
conda-24.5.0 frozendict-2.4.2 openssl-3.0.13	py312h06a4308_0 py312h06a4308_0 h7f8727e_1	1.2 36 5.2	KB
	Total:	6.5	MR

The following NEW packages will be INSTALLED:

```
frozendict pkgs/main/linux-64::frozendict-2.4.2-py312h06a4308_0
```

The following packages will be UPDATED:

```
onda 24.3.0-py312h06a4308_0 --> 24.5.0-py312h06a4308_0
```

```
Downloading and Extracting Packages:
     openssl-3.0.13
                             | 5.2 MB
                                           |:
                                                 0% 0/1 [00:00<?, ?it/s]
     conda-24.5.0
                             1.2 MB
                                                 0% 0/1 [00:00<?, ?it/s]
     frozendict-2.4.2
                             | 36 KB
                                                 0% 0/1 [00:00<?, ?it/s]
                                           |:
     openssl-3.0.13
                             | 5.2 MB
                                                 0% 0.002997347135570501/1 [00:00<01:08, 69.09s/it]
                                           1:
                                          | : 100% 1.0/1 [00:00<00:00, 2.41it/s]
| : 100% 1.0/1 [00:00<00:00, 1.41it/s]
| : 100% 1.0/1 [00:00<00:00, 1.41it/s]
     frozendict-2.4.2
                             | 36 KB
     openssl-3.0.13
                             | 5.2 MB
     conda-24.5.0
                             i 1.2 MB
    Preparing transaction: done
    Verifying transaction: done
    Executing transaction: done
!conda --version
!python --version
     conda 24.5.0
     Python 3.12.2
!conda install -c conda-forge fmpy --yes # Install the key package
→ Channels:
      conda-forgedefaults
     Platform: linux-64
     Collecting package metadata (repodata.json): done Solving environment: done
     ## Package Plan ##
       environment location: /usr/local
       added / updated specs:
         - fmpy
```

The following packages will be downloaded:

package	build			
_libgcc_mutex-0.1	conda_forge	3	KB	conda-forge
_openmp_mutex-4.5	2_gnu	23	ΚB	conda-forge
abseil-cpp-20211102.0	h27087fc_1	1.1	MB	conda-forge
anyio-4.3.0	pyhd8ed1ab_0	100	ΚB	conda-forge
argon2-cffi-23.1.0	pyhd8ed1ab_0	18	ΚB	conda-forge
argon2-cffi-bindings-21.2.0	py312h98912ed_4	34	KΒ	conda-forge
arrow-1.3.0	pyhd8ed1ab_0	98	ΚB	conda-forge
arrow-cpp-14.0.2	h374c478_1	11.7	MB	
asttokens-2.4.1	pyhd8ed1ab_0	28	KΒ	conda-forge
async-lru-2.0.4	pyhd8ed1ab_0	15	KΒ	conda-forge
attrs-23.2.0	pyh71513ae_0	53	ΚB	conda-forge
aws-c-auth-0.6.19	h5eee18b_0	99	ΚB	
aws-c-cal-0.5.20	hff2c3d7_3	43	KΒ	conda-forge
aws-c-common-0.8.5	h166bdaf_0	198	ΚB	conda-forge
aws-c-compression-0.2.16	hf5f93bc_0	18	KΒ	conda-forge
aws-c-event-stream-0.2.15	h6a678d5_0	50	KΒ	
aws-c-http-0.6.25	h5eee18b_0	200	KΒ	
aws-c-io-0.13.10	h2666983_0	140	ΚB	conda-forge
aws-c-mqtt-0.7.13	h5eee18b_0	67		
aws-c-s3-0.1.51	hdbd6064_0	71		
aws-c-sdkutils-0.1.6	hf5f93bc_1	52	ΚB	conda-forge
aws-checksums-0.1.13	hf5f93bc_5	51		conda-forge
aws-crt-cpp-0.18.16	h6a678d5_0	213	KΒ	
aws-sdk-cpp-1.10.55	h721c034_0	2.5		
babel-2.14.0	pyhd8ed1ab_0	7.3		conda-forge
beautifulsoup4-4.12.3	pyha770c72_0	115		conda-forge
blas-1.1	openblas		KB	conda-forge
bleach-6.1.0	pyhd8ed1ab_0	128		conda-forge
blinker-1.8.2	pyhd8ed1ab_0	14		conda-forge
bokeh-3.4.1	pyhd8ed1ab_0	4.5		conda-forge
boost-cpp-1.82.0	hdb19cb5_2	11		
bottleneck-1.3.8	py312hc7c0aa3_0	137		conda-forge
brotli-1.0.9	h166bdaf_9	20	KB	conda-forge

```
h166bdaf_9
                                                   20 KB conda-forge
brotli-bin-1.0.9
cached-property-1.5.2
                                 hd8ed1ab_1
                                                    4 KB conda-forge
cached_property-1.5.2
                               pyha770c72_1
                                                    11 KB conda-forge
                                                   157 KB conda-forge
certifi-2024.2.2
                               pyhd8ed1ab_0
                          |unix_pyh707e725_0
                                                   82 KB conda-forge
click-8.1.7
```

#!conda install matplotlib --yes

→ Channels:

defaultsconda-forge

Platform: linux-64

Collecting package metadata (repodata.json): done

Solving environment: done

Package Plan

environment location: /usr/local

added / updated specs:

matplotlib

The following packages will be downloaded:

package	build	
matplotlib-3.8.4	 py312h06a4308_0	8 KB
	 Total:	8 KB

The following NEW packages will be INSTALLED:

pkgs/main/linux-64::matplotlib-3.8.4-py312h06a4308_0 matplotlib

The following packages will be SUPERSEDED by a higher-priority channel:

conda-forge/noarch::certifi-2024.2.2-~ --> pkgs/main/linux-64::certifi-2024.2.2-py312h06a430% conda conda-forge::conda-24.5.0-py312h7900f~ --> pkgs/main::conda-24.5.0-py312h06a4308_0

Downloading and Extracting Packages:

Preparing transaction: done Verifying transaction: done Executing transaction: done

#!conda install scipy --yes

→ Channels:

- defaults

- conda-forge

Platform: linux-64

Collecting package metadata (repodata.json): done

Solving environment: done

Package Plan

environment location: /usr/local

added / updated specs:

scipy

The following packages will be downloaded:

package	build		
libmamba-1.5.8 libmambapy-1.5.8 pybind11-abi-5 scipy-1.13.0		1.9 327 14 23.7	KB KB
	Total:	25 . 9	

The following packages will be UPDATED:

libmamba 1.5.8-hfe524e5_1 --> 1.5.8-hfe524e5_2 libmambapy 1.5.8-py312h2dafd23_1 --> 1.5.8-py312h2dafd23_2 4-hd3eb1b0_1 --> 5-hd3eb1b0_0 pybind11-abi 1.12.0-py312h2809609_0 --> 1.13.0-py312h2809609_0 scipy

```
Downloading and Extracting Packages:
    scipy-1.13.0
                         | 23.7 MB
                                           0% 0/1 [00:00<?, ?it/s]
                                     | :
                         1.9 MB
    libmamba-1.5.8
                                     1:
                                           0% 0/1 [00:00<?, ?it/s]
    libmambapy-1.5.8
                         | 327 KB
                                           0% 0/1 [00:00<?, ?it/s]
                                     |: 0% 0.0006595458738429316/1 [00:00<03:07, 187.22s/it]
    scipy-1.13.0
                         | 23.7 MB
                         | 14 KB
    pybind11-abi-5
                                     | : 100% 1.0/1 [00:00<00:00, 8.28it/s]
    libmambapy-1.5.8
                         | 327 KB
                                           5% 0.048856710044491096/1 [00:00<00:02, 2.62s/it]
    libmamba-1.5.8
                                           1% 0.008399983593782044/1 [00:00<00:15, 15.94s/it]
                         1.9 MB
    scipy-1.13.0
                         | 23.7 MB
                                     | : 21% 0.2090760420082093/1 [00:00<00:00, 1.12it/s]
    libmambapy-1.5.8
                         I 327 KB
                                     | : 100% 1.0/1 [00:00<00:00, 5.18it/s]
    scipy-1.13.0
                         | 23.7 MB
                                     | : 56% 0.5619330845141777/1 [00:00<00:00, 2.16it/s]
    libmamba-1.5.8
                         1.9 MB
                                     : 100% 1.0/1 [00:00<00:00, 2.77it/s]
!conda install xlrd --yes
→ Channels:
     - defaults
     - conda-forge
    Platform: linux-64
    Collecting package metadata (repodata.json): done
    Solving environment: done
    ## Package Plan ##
      environment location: /usr/local
      added / updated specs:
        - xlrd
    The following packages will be downloaded:
                                                build
        package
        xlrd-2.0.1
                                         pyhd3eb1b0_1
                                                               97 KB
                                                               97 KB
                                               Total:
    The following NEW packages will be INSTALLED:
      xlrd
                         pkgs/main/noarch::xlrd-2.0.1-pyhd3eb1b0_1
    Downloading and Extracting Packages:
    Preparing transaction: done
    Verifying transaction: done
    Executing transaction: done
!conda install openpyxl --yes
→ Channels:
     - defaults
     conda-forge
    Platform: linux-64
    Collecting package metadata (repodata.json): done
    Solving environment: done
    ## Package Plan ##
      environment location: /usr/local
      added / updated specs:
        - openpyxl
    The following packages will be downloaded:
        package
```

py312h06a4308_1

12 KB

et_xmlfile-1.1.0

The following NEW packages will be INSTALLED:

Downloading and Extracting Packages:

openpyxl-3.1.2 | 710 KB | : 0% 0/1 [00:00<?, ?it/s]

openpyxl-3.1.2 | 710 KB | : 2% 0.02253139942488823/1 [00:00<00:05, 5.73s/it]

et_xmlfile-1.1.0 | 12 KB | : 100% 1.0/1 [00:00<00:00, 6.72it/s]

Preparing transaction: done Verifying transaction: done Executing transaction: done

Now specific installation and the run simulations. Start with connecting to Github. Then upload the four files:

- FMU BPL_TEST2_Batch_linux_om_me.fmu
- Setup-file BPL_TEST2_Batch_fmpy_explore.py

%%bash

git clone https://github.com/janpeter19/BPL_TEST2_Batch_calibration

Transport Cloning into 'BPL_TEST2_Batch_calibration'...

%cd BPL_TEST2_Batch_calibration

/content/BPL_TEST2_Batch_calibration

BPL TEST2 Batch calibration - demo

Author: Jan Peter Axelsson

This notebook shows the possibilities for calibration of the model BPL_TEST2_Batch using scipy.optimize.minimize() routine. There are several different methods to choose between. In this notebook we work with simulated data.

The text-book model of batch cultivation we simulate is the following where S is substrate, X is cell concentration, and V is volume of the broth

$$\frac{d(VS)}{dt} = -q_S(S) \cdot VX$$

$$\frac{d(VX)}{dt} = \mu(S) \cdot VX$$

and where specific cell growth rate μ and substrate uptake rate q_S are

$$\mu(S) = Y \cdot q_S(S)$$

$$q_S(S) = q_S^{max} \frac{S}{K_s + S}$$

where Y is the yield, q_S^{max} is the maximal specific substrate uptake rate and K_S is the corresponding saturation constant.

The parameter estimation is done with optimization methods that only require evaluation of the missmatch between simulation with given parameters and data. At start the allowed range for each parameter is given. The method used for optimization is SLSQP but can easily be changed [1].

In the near future the FMU may provide first derivative gradient information, that will make it possible to choose corresponding method of minimize() for improved performance. This possibility is related to the upgrade to the FMI-standard ver 3.0 for the Modelica compiler.

The Python package PyFMI [2] that is the base for FMU-explore has a simplified built-in functionality for parameter estimation that also use scipy.optimize.minimize(). However, there is estimatation functionally but the purpose seems to only address smaller examples. There is for instance no support to handle models that takes sub-models from libraries and necessary changes of default parameters not to be estimated. Therefore we here define a Python function evaluate() that facilitate the formulation of the parameter estimation and also bring flexibility to choice of optimization method, default Nelder-Mead.

run -i BPL_TEST2_Batch_fmpy_explore.py

Linux - run FMU pre-compiled OpenModelica 1.21.0

```
Model for bioreactor has been setup. Key commands:
- par() - change of parameters and initial values
- init() - change initial values only
- simu() - simulate and plot
- newplot() - make a new plot
- show() - show plot from previous simulation
- disp() - display parameters and initial values from the last simulation
- describe() - describe culture, broth, parameters, variables with values/units
```

Note that both disp() and describe() takes values from the last simulation and the command process_diagram() brings up the main configuration ${\bf r}$

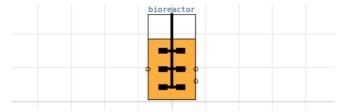
Brief information about a command by help(), eg help(simu) Key system information is listed with the command system_info()

```
# Adjust the size of diagrams
plt.rcParams['figure.figsize'] = [15/2.54, 12/2.54]
```

process_diagram()

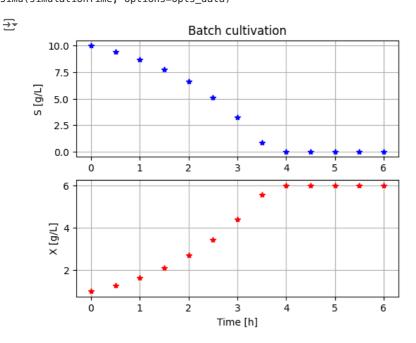
import pandas as pd

No processDiagram.png file in the FMU, but try the file on disk.



1 Generate data later used for parameter estimation

```
# Data generated
simulationTime = 6.0
par(Y=0.50, qSmax=1.00, Ks=0.1)
init(V_start=1.0, VS_start=10, VX_start=1.0)
newplot(plotType='Demo_2')
simu(simulationTime, options=opts data)
```



Store data in a DataFrame for later use
data = pd.DataFrame(data={'time':sim_res['time'], 'X':sim_res['bioreactor.c[1]'], 'S':sim_res['bioreactor.c[2]']})
data

→		time	Х	S
	0	0.0	1.000000	1.000000e+01
	1	0.5	1.280777	9.438447e+00
	2	1.0	1.640089	8.719823e+00
	3	1.5	2.099634	7.800732e+00
	4	2.0	2.686794	6.626412e+00
	5	2.5	3.435509	5.128981e+00
	6	3.0	4.385357	3.229286e+00
	7	3.5	5.559274	8.814516e-01
	8	4.0	6.000000	4.618858e-07
	9	4.5	6.000000	-7.022022e-11
	10	5.0	6.000000	-2.610415e-12
	11	5.5	6.000000	1.020722e-14
	12	6.0	6.000000	-1.037244e-17

2 Simulation with initial guess of parameters compared with data

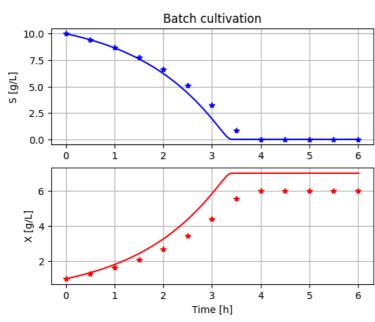
Here we define the parameters that should be estimated and specify allowed ranges. Nominal parameters are chosen as the mid-point of the allowed parameter range.

Simulation with these nominal parameter set and compare with data give an idea of who well the model fit data.

```
# Parameters to be estimated using parDict names and their bounds
parEstim = ['Y', 'qSmax', 'Ks']
parBounds = [(0.4, 0.8), (0.7, 1.3), (0.05, 0.20)]
parEstim_0 = [np.mean(parBounds[k]) for k in range(len(parBounds))]

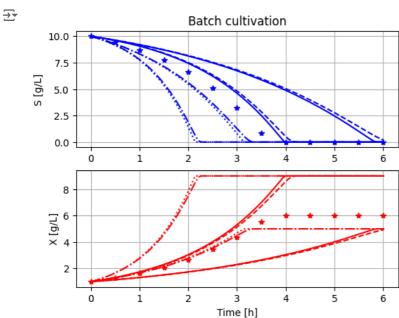
# Simulation with nominal parameters
newplot(plotType='Demo_1')
par(Y=parEstim_0[0], qSmax=parEstim_0[1], Ks=parEstim_0[2])
simu(simulationTime)

# Show data
ax1.plot(data['time'], data['S'],'b*')
ax2.plot(data['time'], data['X'],'r*')
plt.show()
Patch cultivation
```



```
# Simulation over the parameter ranges given
newplot(plotType='Demo_1')
for Y_value in parBounds [0]:
    for qSmax_value in parBounds[1]:
        for Ks_value in parBounds[2]:
            par(Y=Y_value, qSmax=qSmax_value, Ks=Ks_value)
            simu(simulationTime)

# Show data
ax1.plot(data['time'], data['S'],'b*')
ax2.plot(data['time'], data['X'],'r*')
plt.show()
```



Simulation over the different parameter combinations of the parameter bounds shows that data is "covered" and we have good hope to find a parameter combination that fits data well.

3 Parameter estimation

Here we use the scipy.optimize.minimize() procedure which contain a family of different methods [1]. The default method is Nelder-Mead and is robust for fitting a model to data. Further we have chosen to work with bounds for the parameters to be estimated and the initial guess is chosen as the middle point in parameter space.

```
# Optimization routine import
import scipy.optimize
# Parameters to be estimated using parDict names and their bounds
extra_args = (parEstim, data, fmu_model, simulationTime, parDict, parLocation)
# Modified evaluation function tailored for Python optimization algorithms
def objective(x, parEstim, data=data, fmu_model=fmu_model, simulationTime=simulationTime,
             parDict=parDict, parLocation=parLocation):
    """The parameter list is tailored for scipy optimization algorithms interface,
       where the first parameter x is an array with parameters that are tuned
       and evalauted and parEstim is a list of the names of these parameters.
       The code can be made 20-30% faster, but loner, using pyfmi-commands directly."""
    # Update parameters and simulate
    for i, p in enumerate(parEstim): par(**{p:x[i]})
    simu(simulationTime, options=opts_data)
    # Calculate loss function V
    V={}
    V['X'] = np.linalg.norm(data['X'] - np.interp(data['time'], sim_res['time'], sim_res['bioreactor.c[1]']))
     V['S'] = np.linalg.norm(data['S'] - np.interp(data['time'], sim_res['time'], sim_res['bioreactor.c[2]'])) \\
    return V['X'] + V['S']
```

```
import time
```

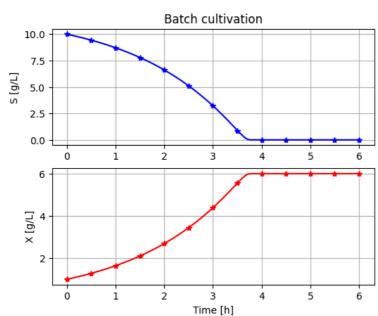
```
# Run minimize()
start_time = time.time()
result = scipy.optimize.minimize(objective, x0=parEstim_0, args=extra_args,
                              method='Nelder-Mead', bounds=parBounds, options={"disp":True})
print('CPU-time =', time.time()-start_time)
Optimization terminated successfully.
            Current function value: 0.045511
            Iterations: 39
            Function evaluations: 75
    CPU-time = 1.915511131286621
result
\overline{2}
          message: Optimization terminated successfully.
          success: True
           status: 0
              fun: 0.045510651189744136
                x: [ 5.001e-01 1.007e+00 1.405e-01]
              nit: 39
             nfev: 75
     5.001e-01, 1.007e+00,
                                                 1.405e-01],
                                                 1.405e-01]]), array([ 4.551e-02, 4.552e-02, 4.556e-02,
                          [ 5.001e-01, 1.007e+00,
    4.559e-02]))
```

The estimated parameters result.x are very close to the original values and no surprise.

4 Simulation with estimated parameters compared with data

```
newplot(plotType='Demo_1')
par(Y=result.x[0], qSmax=result.x[1], Ks=result.x[2])
simu(simulationTime)

# Show data
ax1.plot(data['time'], data['S'],'b*')
ax2.plot(data['time'], data['X'],'r*')
plt.show()
Patch cultivation
```



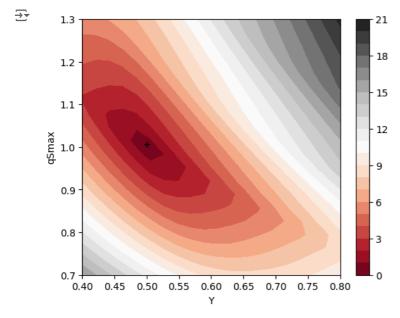
```
# The estimated parameters are for i in range(len(parEstim)): print(parEstim[i],':', result.x[i])

Y: 0.5000549816703198
qSmax: 1.0066481313036082
Ks: 0.14048278753421406
```

5 Analysis of the loss function

The problem is small and analysis of the loss function brings some insight. From the diagram above showing parameter sweep over combinations min- and max-parameters we see that the parameter K_s has little influence. Let use set that a fixed value and then plot the loss function in the parameters Y and qSmax. We do this by go through all the parametera combinations and evaluate each of them.

```
# Sweep through Y and qSmax variation and store the value of the loss-function for each
nY = 20
nqSmax = 20
V = np.zeros((nY, nqSmax))
Y = np.linspace(parBounds[0][0],parBounds[0][1],nY)
qSmax = np.linspace(parBounds[1][0],parBounds[1][1],nqSmax)
for j in range(nY):
    for k in range(nqSmax):
        V[k,j] = objective([Y[j], qSmax[k], 0.1], parEstim)
# Contour plot
plt.figure()
plt.clf
plt.subplot(1,1,1)
plt.contourf(Y, qSmax, V, 20, cmap='RdGy')
plt.plot(result.x[0], result.x[1],'k+')
plt.colorbar()
plt.ylabel('qSmax')
plt.xlabel('Y')
plt.show()
```



We see the following in the contour diagram of the loss function simplified:

- The minima is unique in the range of parmaters we study. This is good news.
- The contour plot is ellipsoid and rather narrow. The more narrow the ellipsoid the more difficult and more time it takes to converge to the minima.
- The direction of the ellipsoid axis indicate the correlation you may get between the two parameters during the minimization process.

Note that the form of the contour plot change with the parameters (and initial values) of the actual proces. You can see the impact by changing the parameters in "cell # 4" where data is generated and then just choose to run that cell and the cells below. No need to restart the notebook.

6 Summary

A choice was made to work with allowed ranges of parameters to be estimated and a start value was defined as the center point in this parameter space. There are only three methods available in optimize.minimize() that can handle bounds on parameters.

An evaluate() function was created that define how the difference between simulation and data is measured. The function is rather transparent and easy to modify and you may want to change weight on the loss in S and X, for instance. Here they have so far equal weight.

The FMU-explore workspace dictionaries partDict[] and parLocation[] are useful also here and simplify the code for the evaluation() function. But we also use the detailed PyFMI-functions to administrate and set parameters of the actual simulation.

The call optimize.minimize() has several parameters and can easily be modified, for instance change of method. For fitting a model to data Nelder-Mead is ao a robust and good choice, but can be somewhat slow.

The estimated parameters were close to perfect!

The contour plot of the simplified loss function shows that the minima is unique and should not be difficult too difficult to obtain. More narrow elliptical contour plots would indicate difficulties. Multiple local minima would also be a problem.

7 References

[1] Scipy Reference guide on optimize.minimize() here

[2] Andersson, C., Åkesson, J., Fuhrer C.: "PyFMI: A Python package for simulation of coupled dynamic models with the functional mock-up interface", Centre for Mathematical Sciences, Lund University, Report LUTFNA-5008-2016, 2016.

Appendix

```
describe('parts')
['bioreactor', 'bioreactor.culture']
describe('MSL')
→ MSL: 3.2.3 – used components: none
system_info()
    System information
     -OS: Linux
     -Python: 3.10.12
     -Scipy: 1.11.4
     -FMPy: 0.3.20
     -FMU by: OpenModelica Compiler OpenModelica 1.21.0
     -FMI: 2.0
     -Type: ME
     -Name: BPL_TEST2.Batch
     -Generated: 2024-03-05T08:05:44Z
     -MSL: 3.2.3
     -Description: Bioprocess Library version 2.2.0
     -Interaction: FMU-explore for FMPy version 1.0.0
```