BPL_YEAST_AIR_Fedbatch script with PyFMI ver 2.7.4

The key library PyFMI v2.7.4 is installed and downgrading is done Numpy v1.19.1. To simplify this we first install conda.

After the installation a small application BPL_YEAST_AIR_Fedbatch 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 18.04.6 LTS
Release:        18.04
Codename:       bionic
```

```
%env PYTHONPATH=
```

```
env: PYTHONPATH=
```

```
!wget https://repo.anaconda.com/miniconda/Miniconda3-py37_4.12.0-Linux-x86_64.sh
!chmod +x Miniconda3-py37_4.12.0-Linux-x86_64.sh
!bash ./Miniconda3-py37_4.12.0-Linux-x86_64.sh -b -f -p /usr/local
import sys
sys.path.append('/usr/local/lib/python3.7/site-packages/')
```

```
    - ruamel_yaml==0.15.100=py37h27cfd23_0
    - setuptools==61.2.0=py37h06a4308_0
    - six==1.16.0=pyhd3eb1b0_1
    - sqlite==3.38.2=hc218d9a_0
    - tk==8.6.11=h1ccaba5_0
    - tqdm==4.63.0=pyhd3eb1b0_0
    - urllib3==1.26.8=pyhd3eb1b0_0
    - wheel==0.37.1=pyhd3eb1b0_0
    - xz==5.2.5=h7b6447c_0
    - yaml==0.2.5=h7b6447c_0
    - zlib==1.2.12=h7f8727e_1


The following NEW packages will be INSTALLED:

  _libgcc_mutex      pkgs/main/linux-64::_libgcc_mutex-0.1-main
  _openmp_mutex      pkgs/main/linux-64::_openmp_mutex-4.5-1_gnu
  brotlipy           pkgs/main/linux-64::brotlipy-0.7.0-py37h27cfd23_1003
  ca-certificates    pkgs/main/linux-64::ca-certificates-2022.3.29-h06a4308_1
  certifi            pkgs/main/linux-64::certifi-2021.10.8-py37h06a4308_2
  cffi               pkgs/main/linux-64::cffi-1.15.0-py37hd667e15_1
  charset-normalizer pkgs/main/noarch::charset-normalizer-2.0.4-pyhd3eb1b0_0
  colorama           pkgs/main/noarch::colorama-0.4.4-pyhd3eb1b0_0
  conda              pkgs/main/linux-64::conda-4.12.0-py37h06a4308_0
  conda-content-tru~ pkgs/main/noarch::conda-content-trust-0.1.1-pyhd3eb1b0_0
  conda-package-han~ pkgs/main/linux-64::conda-package-handling-1.8.1-py37h7f8
  cryptography       pkgs/main/linux-64::cryptography-36.0.0-py37h9ce1e76_0
```

```
      idna               pkgs/main/noarch::idna-3.3-pyhd3eb1b0_0
      ld_impl_linux-64   pkgs/main/linux-64::ld_impl_linux-64-2.35.1-h7274673_9
      libffi             pkgs/main/linux-64::libffi-3.3-he6710b0_2
      libgcc-ng          pkgs/main/linux-64::libgcc-ng-9.3.0-h5101ec6_17
      libgomp            pkgs/main/linux-64::libgomp-9.3.0-h5101ec6_17
      libstdcxx-ng       pkgs/main/linux-64::libstdcxx-ng-9.3.0-hd4cf53a_17
      ncurses            pkgs/main/linux-64::ncurses-6.3-h7f8727e_2
      openssl            pkgs/main/linux-64::openssl-1.1.1n-h7f8727e_0
      pip                pkgs/main/linux-64::pip-21.2.2-py37h06a4308_0
      pycosat            pkgs/main/linux-64::pycosat-0.6.3-py37h27cfd23_0
      pycparser          pkgs/main/noarch::pycparser-2.21-pyhd3eb1b0_0
      pyopenssl          pkgs/main/noarch::pyopenssl-22.0.0-pyhd3eb1b0_0
      pysocks            pkgs/main/linux-64::pysocks-1.7.1-py37_1
      python             pkgs/main/linux-64::python-3.7.13-h12debd9_0
      readline           pkgs/main/linux-64::readline-8.1.2-h7f8727e_1
      requests           pkgs/main/noarch::requests-2.27.1-pyhd3eb1b0_0
      ruamel_yaml        pkgs/main/linux-64::ruamel_yaml-0.15.100-py37h27cfd23_0
      setuptools         pkgs/main/linux-64::setuptools-61.2.0-py37h06a4308_0
      six                pkgs/main/noarch::six-1.16.0-pyhd3eb1b0_1
      sqlite             pkgs/main/linux-64::sqlite-3.38.2-hc218d9a_0
      tk                 pkgs/main/linux-64::tk-8.6.11-h1ccaba5_0
      tqdm               pkgs/main/noarch::tqdm-4.63.0-pyhd3eb1b0_0
      urllib3            pkgs/main/noarch::urllib3-1.26.8-pyhd3eb1b0_0
      wheel              pkgs/main/noarch::wheel-0.37.1-pyhd3eb1b0_0
      xz                 pkgs/main/linux-64::xz-5.2.5-h7b6447c_0
      yaml               pkgs/main/linux-64::yaml-0.2.5-h7b6447c_0
      zlib               pkgs/main/linux-64::zlib-1.2.12-h7f8727e_1


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

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

```
    The following packages will be REMOVED:

      colorama-0.4.4-pyhd3eb1b0_0
      conda-content-trust-0.1.1-pyhd3eb1b0_0
      six-1.16.0-pyhd3eb1b0_1

    The following packages will be UPDATED:

      _openmp_mutex                                     4.5-1_gnu --> 5.1-1_gnu
      ca-certificates                        2022.3.29-h06a4308_1 --> 2022.07.19-h06
      certifi                           2021.10.8-py37h06a4308_2 --> 2022.6.15-py37
      cffi                                1.15.0-py37hd667e15_1 --> 1.15.1-py37h74
      conda                               4.12.0-py37h06a4308_0 --> 4.14.0-py37h06
      cryptography                        36.0.0-py37h9ce1e76_0 --> 37.0.1-py37h9c
      ld_impl_linux-64                        2.35.1-h7274673_9 --> 2.38-h1181459_
      libgcc-ng                               9.3.0-h5101ec6_17 --> 11.2.0-h123456
      libgomp                                 9.3.0-h5101ec6_17 --> 11.2.0-h123456
      libstdcxx-ng                            9.3.0-hd4cf53a_17 --> 11.2.0-h123456
      ncurses                                    6.3-h7f8727e_2 --> 6.3-h5eee18b_3
      openssl                                 1.1.1n-h7f8727e_0 --> 1.1.1q-h7f8727
      pip                                 21.2.2-py37h06a4308_0 --> 22.1.2-py37h06
      requests           pkgs/main/noarch::requests-2.27.1-pyh~ --> pkgs/main/linu
      setuptools                          61.2.0-py37h06a4308_0 --> 63.4.1-py37h06
      sqlite                                  3.38.2-hc218d9a_0 --> 3.39.2-h508229
      tk                                      8.6.11-h1ccaba5_0 --> 8.6.12-h1ccaba
      tqdm               pkgs/main/noarch::tqdm-4.63.0-pyhd3eb~ --> pkgs/main/linu
      urllib3            pkgs/main/noarch::urllib3-1.26.8-pyhd~ --> pkgs/main/linu
```

```
  urllib3            pkgs/main/noarch::urllib3-1.26.8-pyhd~ --> pkgs/main/linu
  xz                                     5.2.5-h7b6447c_0 --> 5.2.5-h7f8727e
  zlib                                  1.2.12-h7f8727e_1 --> 1.2.12-h7f8727



Downloading and Extracting Packages
ncurses-6.3          | 781 KB    | : 100% 1.0/1 [00:00<00:00,  3.06it/s]
cffi-1.15.1          | 227 KB    | : 100% 1.0/1 [00:00<00:00, 12.71it/s]
xz-5.2.5             | 339 KB    | : 100% 1.0/1 [00:00<00:00, 12.84it/s]
pip-22.1.2           | 2.4 MB    | : 100% 1.0/1 [00:00<00:00,  3.53it/s]
libgomp-11.2.0       | 474 KB    | : 100% 1.0/1 [00:00<00:00, 14.74it/s]
zlib-1.2.12          | 106 KB    | : 100% 1.0/1 [00:00<00:00, 12.46it/s]
ca-certificates-2022 | 124 KB    | : 100% 1.0/1 [00:00<00:00, 17.64it/s]
libgcc-ng-11.2.0     | 5.3 MB    | : 100% 1.0/1 [00:00<00:00,  4.62it/s]
tqdm-4.64.0          | 126 KB    | : 100% 1.0/1 [00:00<00:00, 14.61it/s]
conda-4.14.0         | 909 KB    | : 100% 1.0/1 [00:00<00:00,  8.19it/s]
cytoolz-0.11.0       | 328 KB    | : 100% 1.0/1 [00:00<00:00, 13.11it/s]
sqlite-3.39.2        | 1.1 MB    | : 100% 1.0/1 [00:00<00:00, 12.11it/s]
ld_impl_linux-64-2.3 | 654 KB    | : 100% 1.0/1 [00:00<00:00, 13.14it/s]
_openmp_mutex-5.1    | 21 KB     | : 100% 1.0/1 [00:00<00:00, 13.16it/s]
cryptography-37.0.1  | 1.3 MB    | : 100% 1.0/1 [00:00<00:00,  8.21it/s]
setuptools-63.4.1    | 1.1 MB    | : 100% 1.0/1 [00:00<00:00,  6.16it/s]
urllib3-1.26.11      | 181 KB    | : 100% 1.0/1 [00:00<00:00, 10.67it/s]
requests-2.28.1      | 92 KB     | : 100% 1.0/1 [00:00<00:00, 13.94it/s]
toolz-0.11.2         | 49 KB     | : 100% 1.0/1 [00:00<00:00, 15.76it/s]
libstdcxx-ng-11.2.0  | 4.7 MB    | : 100% 1.0/1 [00:00<00:00,  4.90it/s]
tk-8.6.12            | 3.0 MB    | : 100% 1.0/1 [00:00<00:00,  2.68it/s]
certifi-2022.6.15    | 153 KB    | : 100% 1.0/1 [00:00<00:00, 17.50it/s]
openssl-1.1.1q       | 2.5 MB    | : 100% 1.0/1 [00:00<00:00,  7.07it/s]
Preparing transaction: done
Verifying transaction: done
Executing transaction: done
```

```
!conda --version
!python --version
```

```
conda 4.14.0
Python 3.7.13
```

```
!conda install -c conda-forge pyfmi==2.7.4 --yes # Install the key package
```

```
  liblapack          conda-forge/linux-64::liblapack-3.9.0-15_linux64_openblas
  libopenblas        conda-forge/linux-64::libopenblas-0.3.20-pthreads_h78a641
  libxml2            conda-forge/linux-64::libxml2-2.9.12-h72842e0_0
  libxslt            conda-forge/linux-64::libxslt-1.1.33-h15afd5d_2
  lxml               conda-forge/linux-64::lxml-4.8.0-py37h540881e_2
  metis              conda-forge/linux-64::metis-5.1.0-h58526e2_1006
  mpfr               conda-forge/linux-64::mpfr-4.1.0-h9202a9a_1
  numpy              conda-forge/linux-64::numpy-1.21.6-py37h976b520_0
  pyfmi              conda-forge/linux-64::pyfmi-2.7.4-py37h161383b_0
  python_abi         conda-forge/linux-64::python_abi-3.7-2_cp37m
  scipy              conda-forge/linux-64::scipy-1.7.3-py37hf2a6cf1_0
  suitesparse        conda-forge/linux-64::suitesparse-5.10.1-h9e50725_1
  sundials           conda-forge/linux-64::sundials-5.8.0-h558c624_0
  tbb                conda-forge/linux-64::tbb-2021.5.0-h924138e_1

The following packages will be UPDATED:

  certifi            pkgs/main/linux-64::certifi-2022.6.15~ --> conda-forge/nc
```

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

  ca-certificates    pkgs/main::ca-certificates-2022.07.19~ --> conda-forge::c
  conda              pkgs/main::conda-4.14.0-py37h06a4308_0 --> conda-forge::c
  openssl              pkgs/main::openssl-1.1.1q-h7f8727e_0 --> conda-forge::c



Downloading and Extracting Packages
metis-5.1.0          | 4.1 MB    | : 100% 1.0/1 [00:01<00:00,  1.08s/it]
libgfortran-ng-12.1. | 23 KB     | : 100% 1.0/1 [00:00<00:00, 20.00it/s]
libblas-3.9.0        | 12 KB     | : 100% 1.0/1 [00:00<00:00, 19.68it/s]
libiconv-1.16        | 1.4 MB    | : 100% 1.0/1 [00:00<00:00,  3.83it/s]
pyfmi-2.7.4          | 12.4 MB   | : 100% 1.0/1 [00:08<00:00,  8.27s/it]
python_abi-3.7       | 4 KB      | : 100% 1.0/1 [00:00<00:00, 25.96it/s]
openssl-1.1.1o       | 2.1 MB    | : 100% 1.0/1 [00:00<00:00,  2.17it/s]
libcblas-3.9.0       | 12 KB     | : 100% 1.0/1 [00:00<00:00, 18.09it/s]
libxml2-2.9.12       | 772 KB    | : 100% 1.0/1 [00:00<00:00,  3.77it/s]
sundials-5.8.0       | 1.0 MB    | : 100% 1.0/1 [00:00<00:00,  2.25it/s]
tbb-2021.5.0         | 1.9 MB    | : 100% 1.0/1 [00:00<00:00,  2.31it/s]
lxml-4.8.0           | 1.4 MB    | : 100% 1.0/1 [00:00<00:00,  2.59it/s]
conda-4.14.0         | 1010 KB   | : 100% 1.0/1 [00:00<00:00,  2.57it/s]
assimulo-3.2.9       | 2.6 MB    | : 100% 1.0/1 [00:00<00:00,  1.29it/s]
libxslt-1.1.33       | 522 KB    | : 100% 1.0/1 [00:00<00:00,  4.49it/s]
fmilib-2.2.3         | 532 KB    | : 100% 1.0/1 [00:00<00:00,  1.15it/s]
libopenblas-0.3.20   | 10.1 MB   | : 100% 1.0/1 [00:02<00:00,  2.25s/it]
libgfortran5-12.1.0  | 1.8 MB    | : 100% 1.0/1 [00:00<00:00,  2.51it/s]
icu-68.2             | 13.1 MB   | : 100% 1.0/1 [00:02<00:00,  2.48s/it]
mpfr-4.1.0           | 2.6 MB    | : 100% 1.0/1 [00:00<00:00,  1.95it/s]
liblapack-3.9.0      | 12 KB     | : 100% 1.0/1 [00:00<00:00, 28.58it/s]
certifi-2022.6.15    | 154 KB    | : 100% 1.0/1 [00:00<00:00, 16.60it/s]
ca-certificates-2022 | 149 KB    | : 100% 1.0/1 [00:00<00:00, 18.51it/s]
numpy-1.21.6         | 6.1 MB    | : 100% 1.0/1 [00:01<00:00,  1.76s/it]
gmp-6.2.1            | 806 KB    | : 100% 1.0/1 [00:00<00:00,  4.33it/s]
scipy-1.7.3          | 21.8 MB   | : 100% 1.0/1 [00:04<00:00,  4.71s/it]
suitesparse-5.10.1   | 2.4 MB    | : 100% 1.0/1 [00:00<00:00,  1.60it/s]
Preparing transaction: done
Verifying transaction: done
Executing transaction: done
Retrieving notices: ...working... done
```

```
!conda install numpy=1.19.1 --yes # Need to downgrade numpy
```

```
Collecting package metadata (current_repodata.json): done
Solving environment: failed with initial frozen solve. Retrying with flexible
Collecting package metadata (repodata.json): done
Solving environment: done

## Package Plan ##

  environment location: /usr/local

  added / updated specs:
    - numpy=1.19.1


The following packages will be downloaded:

    package                    |            build
    ---------------------------|-----------------
    blas-1.0                   |        openblas          46 KB
    numpy-1.19.1               |   py37h30dfecb_0          21 KB
    numpy-base-1.19.1          |   py37h75fe3a5_0         4.1 MB
    ------------------------------------------------------------
                                           Total:         4.2 MB

The following NEW packages will be INSTALLED:

  blas               pkgs/main/linux-64::blas-1.0-openblas
  numpy-base         pkgs/main/linux-64::numpy-base-1.19.1-py37h75fe3a5_0

The following packages will be UPDATED:

  ca-certificates    conda-forge::ca-certificates-2022.6.1~ --> pkgs/main::ca-
  openssl            conda-forge::openssl-1.1.1o-h166bdaf_0 --> pkgs/main::ope

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

  certifi            conda-forge/noarch::certifi-2022.6.15~ --> pkgs/main/linu
  conda              conda-forge::conda-4.14.0-py37h89c186~ --> pkgs/main::con
  numpy              conda-forge::numpy-1.21.6-py37h976b52~ --> pkgs/main::num



Downloading and Extracting Packages
numpy-1.19.1         | 21 KB     | : 100% 1.0/1 [00:00<00:00,  5.67it/s]
blas-1.0             | 46 KB     | : 100% 1.0/1 [00:00<00:00, 17.05it/s]
numpy-base-1.19.1    | 4.1 MB    | : 100% 1.0/1 [00:01<00:00,  1.34s/it]
Preparing transaction: done
Verifying transaction: done
Executing transaction: done
Retrieving notices: ...working... done
```

Notes of BPL_YEAST_AIR_Fedbatch

This notebook demonstrate yeast fedbatch cultivation. We look at impact of changes in the glucose feeding. We also take a look at tuning of the DO-control system. Both liquid- and gasphase are included in the model.

Interaction with the compiled model as FMU is mainly through the simplified commands: par(), init(), newplot(), simu() etc. The last simulation is always available in the workspace and called 'sim_res'. The command describe() brings mainly up description infomration from the actual Modelica code from the FMU but is complemented with information given in the dedicated Python setup-file.

The idea is to demonstrate how simulations and varyiing conditions can provide some process insight that can support the experimetnal work. I hope that at the end of this session you are ready to formulate your own questions you want to address with simulations - and you can just go on in this notebook! Just press the field "+Code" in the upper left part of notebook interface and you get a new "cell" where you write your own code. You can copy and paste from cells above using ctrol-c and ctrl-p as usual and edit the cell. When your are ready to execute the cell just press the "play button" to the left in the cell or press shift-enter as in "ordinary" Jupyter notebooks.

After a session you may want to save your own notebook. That you can do on your Google Drive account and I refer to Colab instructions for how to do this. It is easy.

Enjoy!

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

- FMU - BPL_YEAST_AIR_Fedbatch_linux_jm_cs.fmu
- Setup-file - BPL_YEAST_AIR_Fedbatch_explore

```
# Filter out DepracationWarnings for 'np.float as alias' is needed - wish I could m
import warnings
warnings.filterwarnings("ignore")
```

```
%%bash
git clone https://github.com/janpeter19/BPL_YEAST_AIR_Fedbatch
```

```
     Cloning into 'BPL_YEAST_AIR_Fedbatch'...
```

```
%cd BPL_YEAST_AIR_Fedbatch
```

```
     /content/BPL_YEAST_AIR_Fedbatch
```

BPL_YEAST_AIR_Fedbatch - demo

This notebook demonstrate yeast fedbatch cultivation. We look at impact of changes in the glucose feeding. We also take a look at tuning of the DO-control system. Both liquid- and gasphase are included in the model. The culture growth and metabolism are formulated in relation to to the respiratory capacity [1] and the model is exapanded to describe also the gas phase as well as the culture heat production.

Interaction with the compiled model as FMU is mainly through the simplified commands: par(), init(), newplot(), simu() etc. The last simulation is always available in the workspace and called 'sim_res'. The command describe() brings mainly up description infomration from the actual Modelica code from the FMU but is complemented with information given in the dedicated Python setup-file.

The idea is to demonstrate how simulations and varyiing conditions can provide some process insight that can support the experimetnal work. I hope that at the end of this session you are ready to formulate your own questions you want to address with simulations - and you can just go on in this notebook! Just press the field "+Code" in the upper left part of notebook interface and you get a new "cell" where you write your own code. You can copy and paste from cells above using ctrol-c and ctrl-p as usual and edit the cell. When your are ready to execute the cell just press the "play button" to the left in the cell or press shift-enter as in "ordinary" Jupyter notebooks.

After a session you may want to save your own notebook. That you can do on your Google Drive account and I refer to Colab instructions for how to do this. It is easy.

Enjoy!

```
run -i BPL_YEAST_AIR_Fedbatch_DOcontrol_explore.py
```

```
    Linux - run FMU pre-comiled JModelica 2.4

    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 simulatic
     - describe()  - describe culture, broth, parameters, variables with values /

    Note that both disp() and describe() takes values from the last simulation

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

```
%matplotlib inline
plt.rcParams['figure.figsize'] = [36/2.54, 30/2.54]
```

About the process model

We can get information about the process, liquid- and gas-phase by the command describe(). This command can also be used to bring up information about a specific variable or parameter. However, you should use describe() after a simulation to get the valued used during the simulation.

```
describe('culture'); print(); describe('liquidphase'); print(); describe('gasphase'
```

```
    Saccharomyces cerevisae - default parameters for strain H1022

    Reactor broth substances included in the model

    Cells   index       =  1 - molecular weight =  24.6 Da
    Glucose index       =  2 - molecular weight =  180.0 Da
    Ethanol index       =  3 - molecular weight =  46.0 Da
    Dissolved O2 index  =  4 - molecular weight =  32.0 Da
    Dissolved CO2 index =  5 - molecular weight =  44.0 Da
```

```
Reactor gasphase substances included in the model

N2 etc index  =  1 - molecular weight =  28.0 Da
O2 index      =  2 - molecular weight =  32.0 Da
CO2 index     =  3 - molecular weight =  44.0 Da
Ethanol index =  4 - molecular weight =  46.0 Da
```

The model of the process has parameters both for culture, gas_liquid_transfer, as well as feeding procedure. The paramters that are available for changes you find by the command disp() and you get a long list and you change by them by command par(). The model has even more parameters in the background but not made available for interaction.

First simulations - adjusting start of substrate feeding

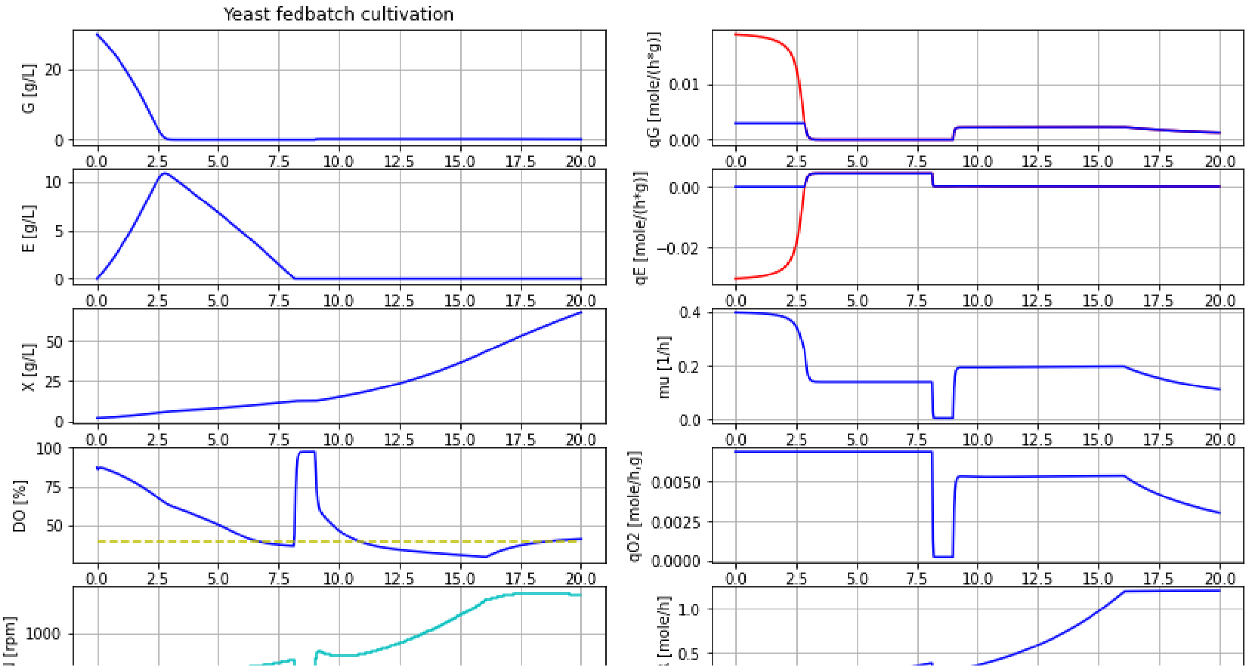
```
# Culture parameters and others at default values
par(qO2lim=0.0069)

# Process initial conditions
init(V_0=4.5, VG_0=4.5*30, VX_0=4.5*2, VE_0=4.5*0)

# Feed profile
par(t_start=9, F_start=0.044, mu_feed=0.20, F_max=0.18)

# DO-control parameters
par(samplePeriod=1/60, K=10, Ti=0.5, I_0=500)

# Simulate and plot
newplot(title='Yeast fedbatch cultivation', plotType='Overview')
simu(20)
```



Now we can get value of broth volume as well as the headspace and values are the last ones in the simulation

```
describe('bioreactor.V')
```

```
    Reactor broth volume : 5.892 [ L ]
```

```
describe('bioreactor.V_gasphase')
```

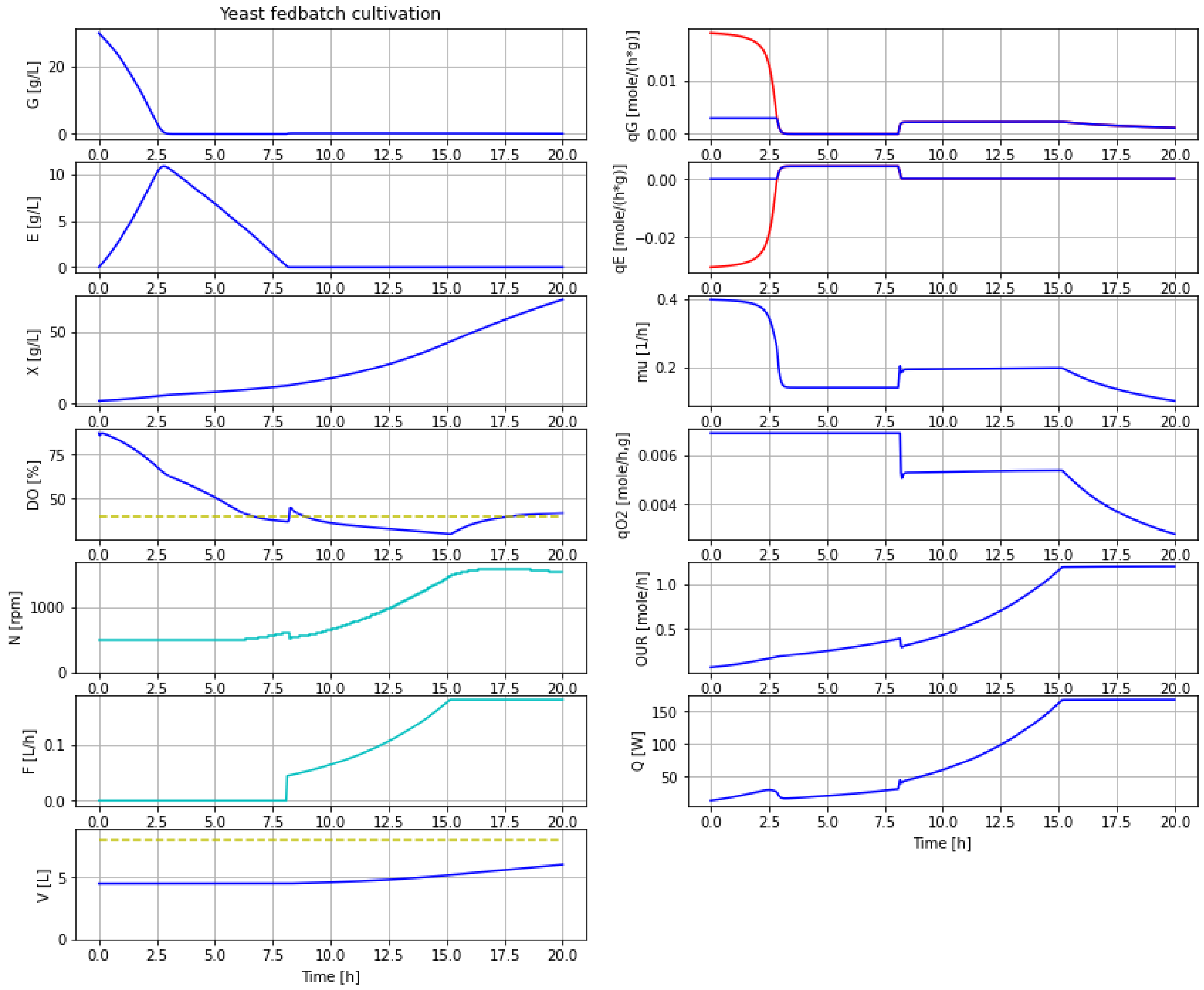
```
    Volume of the gas phase : 2.108 [ L ]
```

```
# Take a look at the parameters available to adjust the dosage scheme
disp('dosage', decimals=4)
```

```
    mu_feed : 0.2
    F_0 : 0.0
    t_start : 9.0
    F_start : 0.044
    F_max : 0.18
```

```
# Let us start the feeding just after the batch phase has ended and keep other para
par(t_start=8.1)

# Simulate and plot
newplot(title='Yeast fedbatch cultivation', plotType='Overview')
simu(20)
```



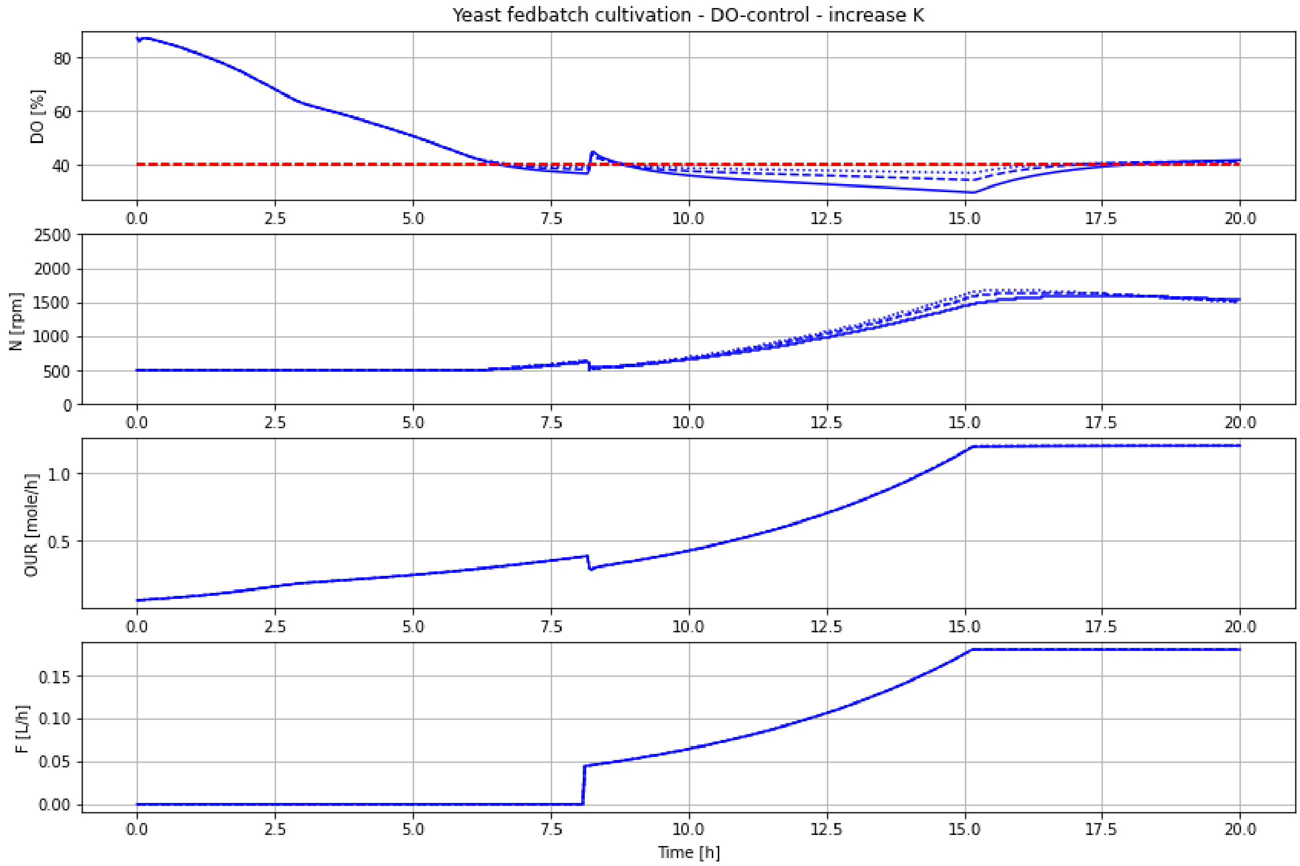
The increase of DO to about 50 % at end of batch phase should be possible to detect easily. This simulation is more realistic and we use these settings from now on.

DO-control - tuning of PI-regulator parameters

Let us focus on the DO-control system and choose a more limited plotType. We study the impact of PI control parameters and see if we can decrease the control error without looing stability.

```
# Let us take a closer look at the DO-control system and try to make control error
newplot(title='Yeast fedbatch cultivation - DO-control - increase K', plotType='Foc
for value in [10, 20, 40]: par(K=value); simu(20)

# Reset K to the original value
par(K=10)
```



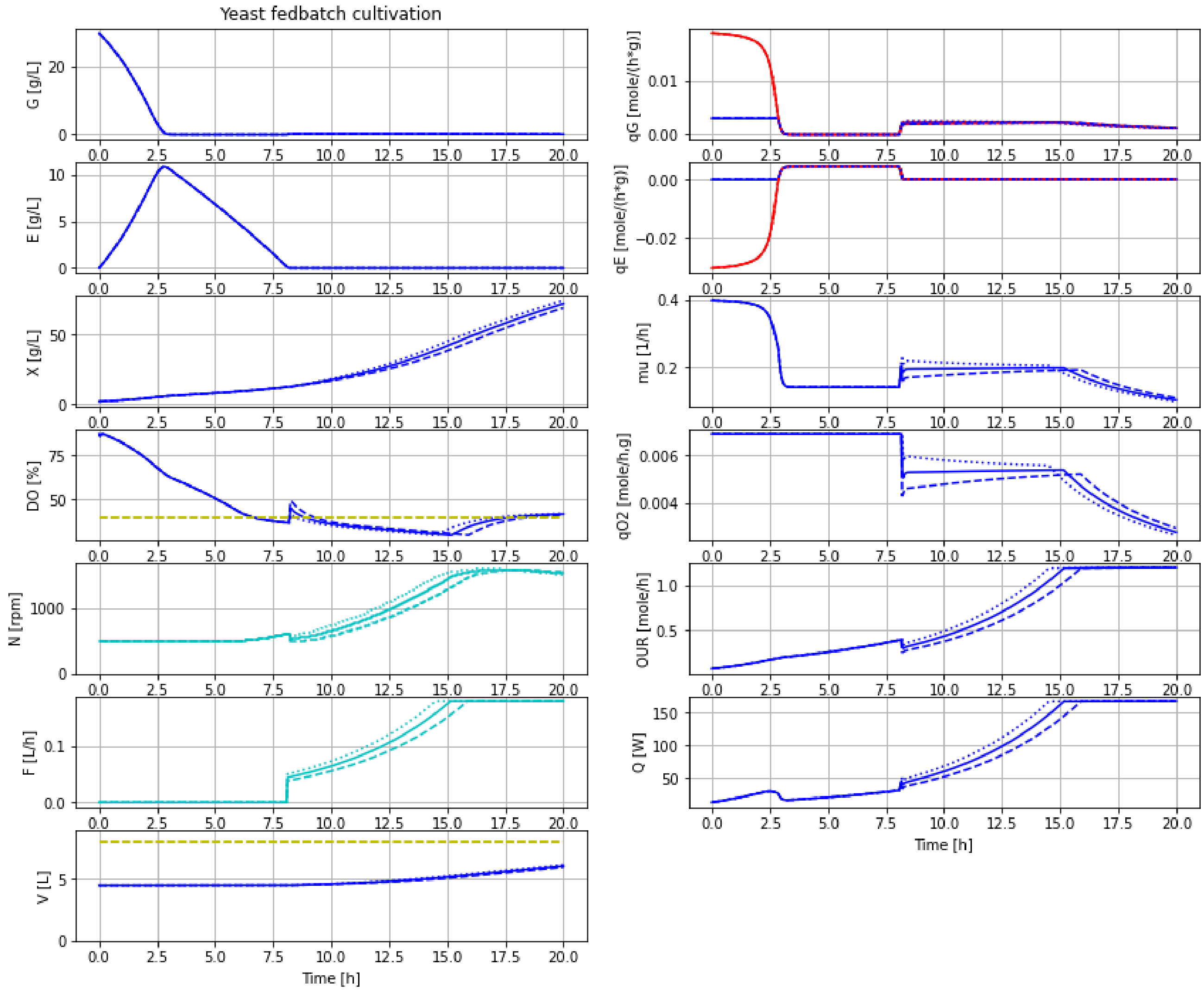
We see that by a higher control gain K the DO-control error get smaller and the stability of the control system is maintained.

Exercise I leave for you to study the impact variation of the Ti-parameter. Just make a new cell below. Then copy and paste the cell above and change parameter to Ti.

Sensitivity to changes in feed-profile

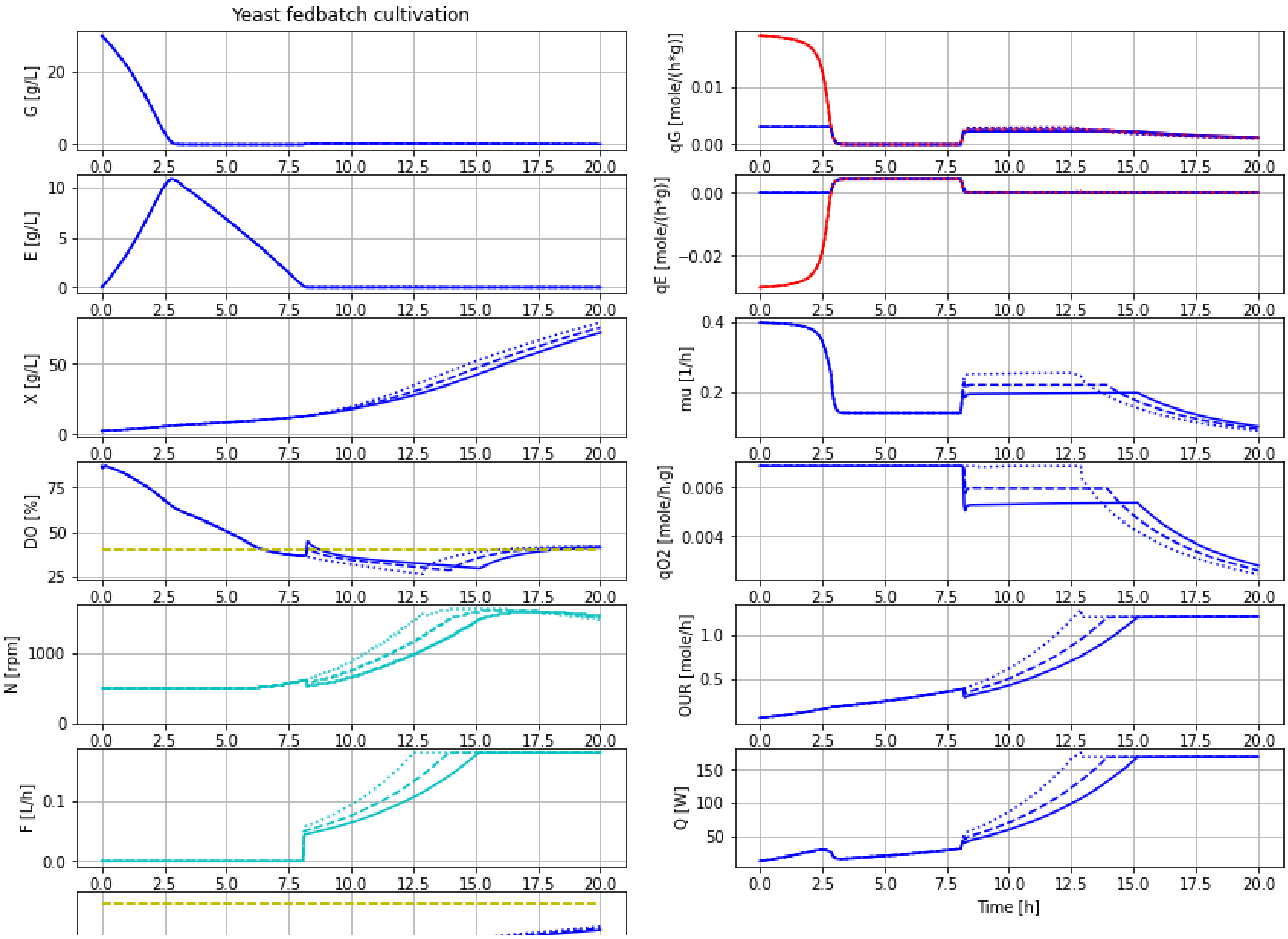
Now, let us focus on investigating impact of changes in the feed-profile. The goal is to increase the produced cell mass without accumulation of by-product ethanol. Simulation can bring some insight into how behaviour of the differen variables change when by-product is formed. This insight can help to interpret experimental results.

```
# Let us check the sensitivity to changes in the feed profile design
newplot(title='Yeast fedbatch cultivation', plotType='Overview')
for value in [0.044, 0.038, 0.050]: par(F_start=value); simu(20)
```

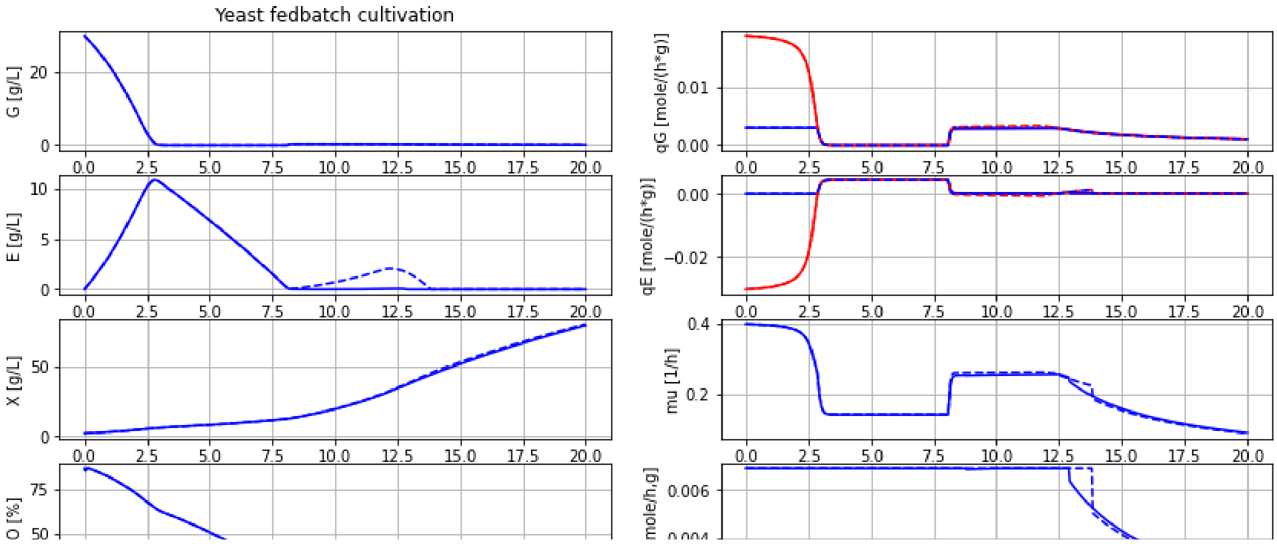


The variation in F_start has an impact and we see that the actual growth rate during fedbatch phase do converge to the set growth rate of the feed, but i takes more than 5 hours.

```
# Let us investigate a feedprofile that is closer to the maximal capacity
newplot(title='Yeast fedbatch cultivation', plotType='Overview')
par(F_start=0.044, mu_feed=0.20); simu(20)
par(F_start=0.050, mu_feed=0.22); simu(20)
par(F_start=0.057, mu_feed=0.26); simu(20)
```



```
# And let us see what happens if the feedprofile exceed the culture capacity
newplot(title='Yeast fedbatch cultivation', plotType='Overview')
par(F_start=0.057, mu_feed=0.26); simu(20)
par(F_start=0.063, mu_feed=0.28); simu(20)
par(F_start=0.044, mu_feed=0.20)
```



Note that with the feedprofile that exceed culture respiratory capacity, ethanol is accumulated during time 8-12.5 hours. When the feedprofile then is constant from time 12.5 hours and on, then the accumulated ethanol is consumed over about an hour. This leads to a higher oxygen demand and heat production during this time. The specific cell growth rate is also slightly higher during this period.

Exercise You can investiate the impact of changing the maximal feedrate F_max. Make sure that the DO level do not get too low.

Make your own diagrams

There are a couple of pre-defined plotType for the application that you make by the command newplot(). The command result in a list "diagrams" that desccrige the commands that make the plot when you call simu() or you just want to look at the last simulation again with a changed plotType using show().

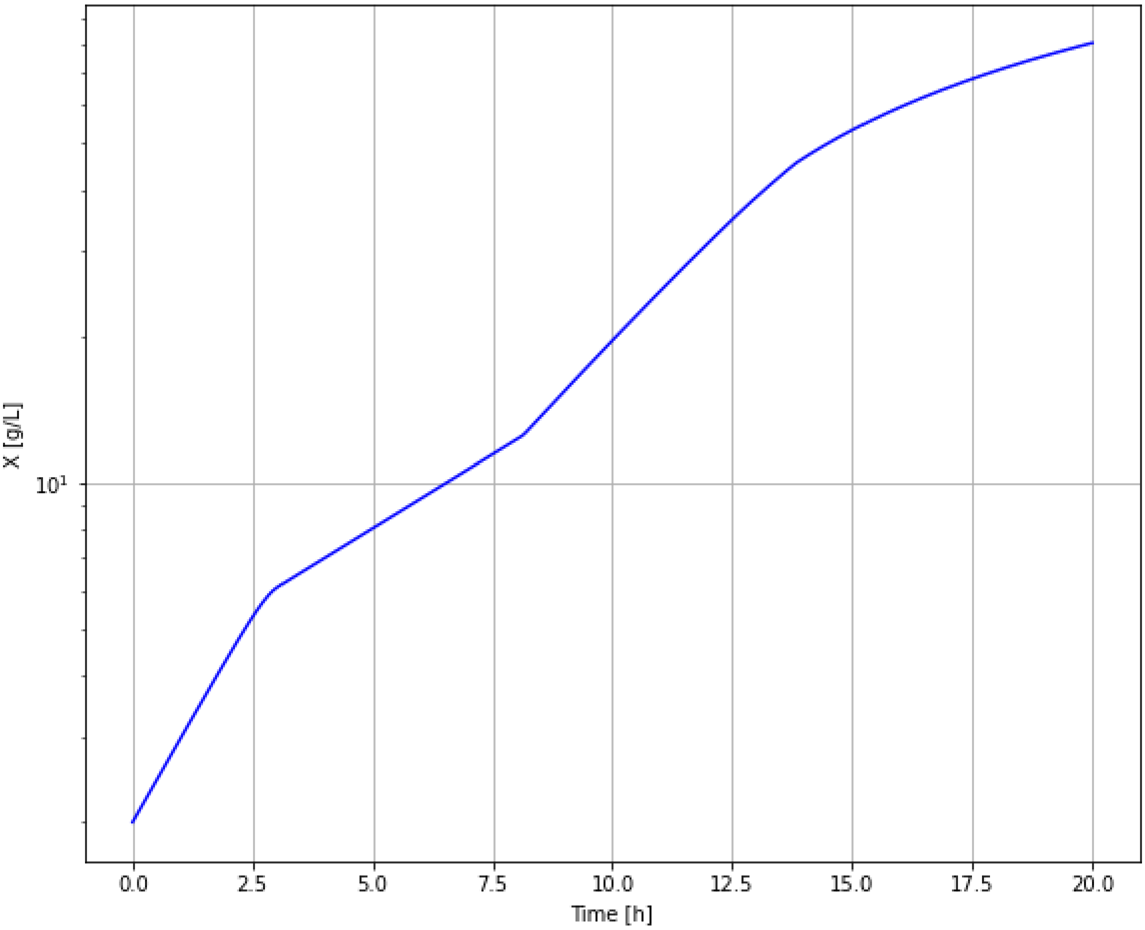
You can also in Jupyter notebook directly define the list "diagrams" and then that will be used for subsequent calls of simu() or show(). When you have made a diagram that you want to reuse many times you can bring it into the python-setup file and edit the newplot() commmand and add a new plotType.

Below a few simple examples that show how to do a diagram directly i the notebook

```
# First decrease the diagram size
plt.rcParams['figure.figsize'] = [24/2.54, 20/2.54]
```

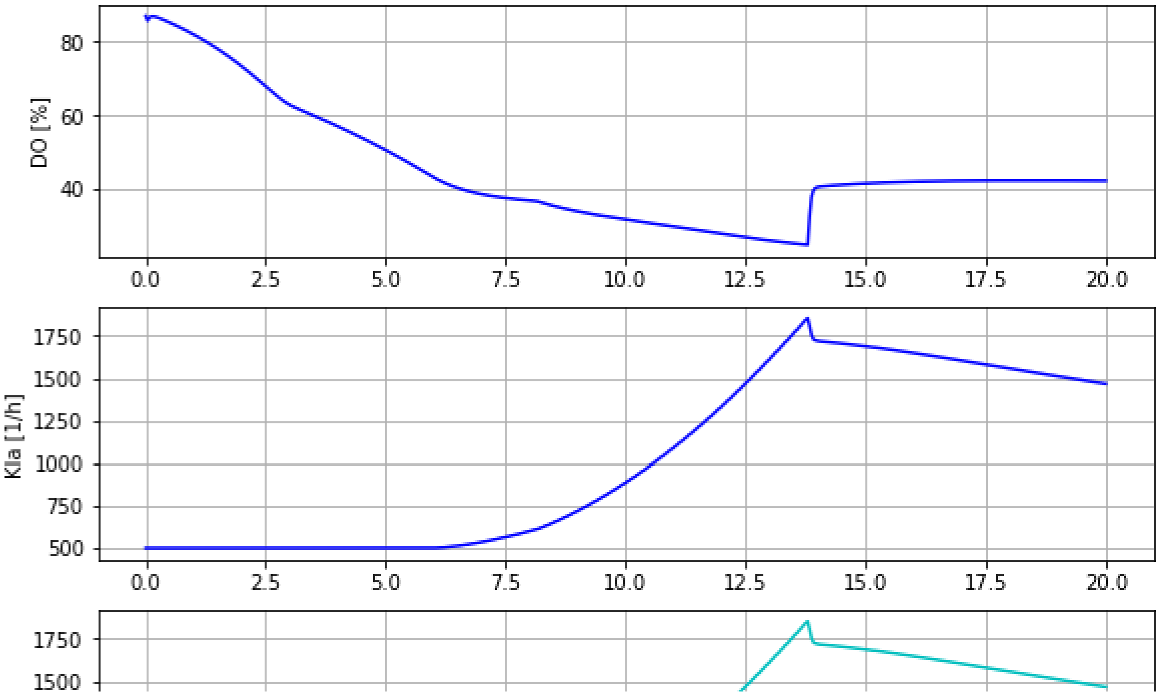
```
# Improvise and make your own diagram - cell concentration in a logaritmic plot
plt.figure()
ax1 = plt.subplot(1,1,1)
ax1.set_ylabel('X [g/L]')
ax1.set_xlabel('Time [h]')
ax1.grid()
```

```
setLines()
diagrams.clear()
diagrams.append("ax1.semilogy(sim_res['time'], sim_res['bioreactor.c[1]'], color='b
show()
```



```
# - study the variation of Kla together with DO and N during cultivation
plt.figure()
ax1 = plt.subplot(3,1,1); ax2 = plt.subplot(3,1,2); ax3 = plt.subplot(3,1,3)
ax1.set_ylabel('DO [%]'); ax1.grid()
ax2.set_ylabel('Kla [1/h]'); ax2.grid()
ax3.set_ylabel('N [rpm]'); ax3.grid()
ax3.set_xlabel('Time [h]')

setLines()
diagrams.clear()
diagrams.append("ax1.plot(sim_res['time'], sim_res['DOsensor.out'], color='b', line
diagrams.append("ax2.plot(sim_res['time'], sim_res['bioreactor.gas_liquid_transfer.
diagrams.append("ax3.plot(sim_res['time'], sim_res['bioreactor.N'], color='c', line
show()
```



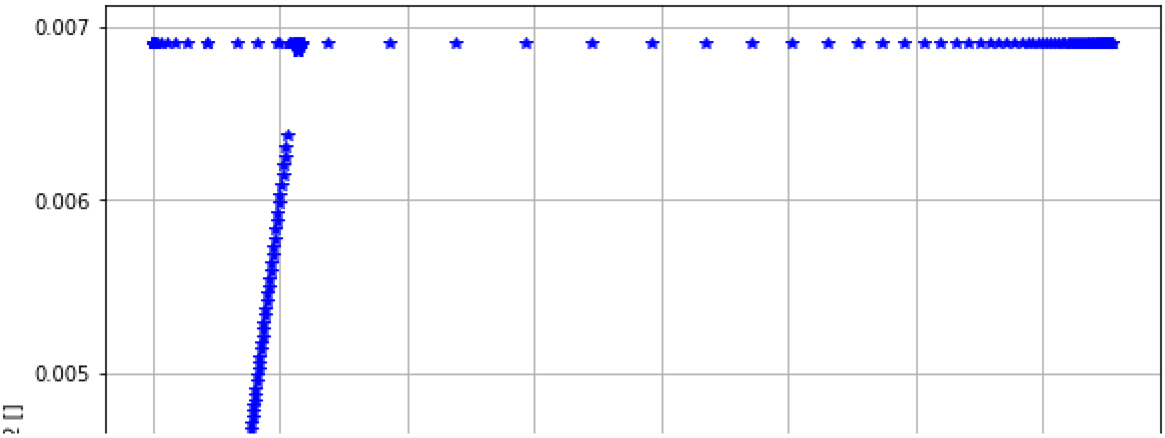
The relation is Kla = alpha_O2*N and we see the value of the parameter should be around 1.0, and we check below

```
disp('bioreactor.gas_liquid_transfer.alpha_O2')

    alpha_O2 : 1.0


# - study the relation qO2 vs qG(G)
plt.figure()
ax1 = plt.subplot(1,1,1)
ax1.set_ylabel('qO2 []')
ax1.set_xlabel('qG []')
ax1.grid()

setLines()
diagrams.clear()
diagrams.append("ax1.plot(sim_res['bioreactor.culture.qGm'], sim_res['bioreactor.cu
par(F_start=0.057, mu_feed=0.26)
simu(20)
```



During the cultivation we have a number of data points for qG and qO2 at the same time, during different conditions. What we see in the diagram is that qO2 increase with qG until qG reach a level of just above 0.0025 and then qO2 saturats for highter qG. This what expect to see.

We also see that for lower qG we have also qO2 values at saturation level. This points correspond to a situation where ethanol is consumed with the remaining respiratory capacity. Glucose is consumed by priority.

Summary

- We have first seen an overview diagram of a typical yeast fedbatch cultivation where the feed started about an hour after the batch phase was finished. A new simulation was made where the feed started directly after detection of lack of substrate.
- We also took a look at the DO-control system and saw that we could decrease the control error by increasing the PI-controller gain. Stability of the control system remained.
- Then we tested variations in the feed dosage scheme and investigated the possibilities to increae the production.
- We also saw what happens if the feed dosage exceed the culture respiratory capacity and what to look for during the experimental work.
- Finally we saw some examples of how to improvise new diagrams.

References

[1] Sonnleitner, B and O. Käppeli "Growth of *Sacharomyces cerevisiae* is controlled by its limited respiratory capacity: formulationa and verification of a hypothesis", Biotech. Bioeng., 1986.

Appendix

```
# List of components in the process setup and also a couple of other things like li
describe('parts')
```

```
['airFlow_setpoint', 'airtube', 'atmosphere', 'bioreactor', 'bioreactor.cultur
```

```
system_info()
```

```
System information
 -OS: Linux
 -Python: 3.7.13
 -PyFMI: 2.7.4
 -FMU by: JModelica.org
 -FMI: 2.0
 -Type: FMUModelCS2
 -Name: BPL_YEAST_AIR.Fedbatch_DOcontrol
 -Generated: 2022-08-26T11:07:26
 -MSL: 3.2.2 build 3
 -Description: Bioprocess Library version 2.1.0 beta
 -Interaction: FMU-explore ver 0.9.2
```