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
```

```
  lzma                pkgs/main/noarch::lzma-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
```

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

```
Collecting package metadata (current_repodata.json): done
Solving environment: done

## Package Plan ##

  environment location: /usr/local

  added / updated specs:
    - conda


The following packages will be downloaded:

    package                    |            build
    ---------------------------|-----------------
    _openmp_mutex-5.1          |            1_gnu          21 KB
    ca-certificates-2022.07.19 |       h06a4308_0         124 KB
    certifi-2022.6.15          |   py37h06a4308_0         153 KB
    cffi-1.15.1                |   py37h74dc2b5_0         227 KB
    conda-4.14.0               |   py37h06a4308_0         909 KB
    cryptography-37.0.1        |   py37h9ce1e76_0         1.3 MB
    cytoolz-0.11.0             |   py37h7b6447c_0         328 KB
    ld_impl_linux-64-2.38      |       h1181459_1         654 KB
    libgcc-ng-11.2.0           |       h1234567_1         5.3 MB
    libgomp-11.2.0             |       h1234567_1         474 KB
```

```
  libstdcxx-ng-11.2.0         |       h1234567_1         4.7 MB
  ncurses-6.3                 |       h5eee18b_3         781 KB
  openssl-1.1.1q              |       h7f8727e_0         2.5 MB
  pip-22.1.2                  |   py37h06a4308_0         2.4 MB
  requests-2.28.1             |   py37h06a4308_0          92 KB
  setuptools-63.4.1           |   py37h06a4308_0         1.1 MB
  sqlite-3.39.2               |       h5082296_0         1.1 MB
  tk-8.6.12                   |       h1ccaba5_0         3.0 MB
  toolz-0.11.2                |     pyhd3eb1b0_0          49 KB
  tqdm-4.64.0                 |   py37h06a4308_0         126 KB
  urllib3-1.26.11             |   py37h06a4308_0         181 KB
  xz-5.2.5                    |       h7f8727e_1         339 KB
  zlib-1.2.12                 |       h7f8727e_2         106 KB
  ------------------------------------------------------------
                                        Total:        25.9 MB

The following NEW packages will be INSTALLED:

  cytoolz            pkgs/main/linux-64::cytoolz-0.11.0-py37h7b6447c_0
  toolz              pkgs/main/noarch::toolz-0.11.2-pyhd3eb1b0_0

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 --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
```

```
  libgfortran-ng      conda-forge/linux-64::libgfortran-ng-12.1.0-h69a702a_16
  libgfortran5        conda-forge/linux-64::libgfortran5-12.1.0-hdcd56e2_16
  libiconv            conda-forge/linux-64::libiconv-1.16-h516909a_0
  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 SUPERSEDED by a higher-priority channel:
```

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

    ca-certificates    pkgs/main::ca-certificates-2022.07.19~ --> conda-forge::c
    certifi            pkgs/main::certifi-2022.6.15-py37h06a~ --> 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
  assimulo-3.2.9       | 2.6 MB    | : 100% 1.0/1 [00:00<00:00,  1.26it/s]
  pyfmi-2.7.4          | 12.4 MB   | : 100% 1.0/1 [00:02<00:00,  2.80s/it]
  python_abi-3.7       | 4 KB      | : 100% 1.0/1 [00:00<00:00, 15.04it/s]
  icu-68.2             | 13.1 MB   | : 100% 1.0/1 [00:03<00:00,  3.21s/it]
  libxml2-2.9.12       | 772 KB    | : 100% 1.0/1 [00:00<00:00,  2.90it/s]
  fmilib-2.2.3         | 532 KB    | : 100% 1.0/1 [00:00<00:00,  3.99it/s]
  libiconv-1.16        | 1.4 MB    | : 100% 1.0/1 [00:00<00:00,  3.40it/s]
  libxslt-1.1.33       | 522 KB    | : 100% 1.0/1 [00:00<00:00,  4.04it/s]
  conda-4.14.0         | 1010 KB   | : 100% 1.0/1 [00:00<00:00,  2.62it/s]
  sundials-5.8.0       | 1.0 MB    | : 100% 1.0/1 [00:00<00:00,  1.70it/s]
  numpy-1.21.6         | 6.1 MB    | : 100% 1.0/1 [00:02<00:00,  2.01s/it]
  libopenblas-0.3.20   | 10.1 MB   | : 100% 1.0/1 [00:03<00:00,  3.06s/it]
  libblas-3.9.0        | 12 KB     | : 100% 1.0/1 [00:00<00:00, 12.56it/s]
  metis-5.1.0          | 4.1 MB    | : 100% 1.0/1 [00:01<00:00,  1.10s/it]
  liblapack-3.9.0      | 12 KB     | : 100% 1.0/1 [00:00<00:00, 20.75it/s]
  libcblas-3.9.0       | 12 KB     | : 100% 1.0/1 [00:00<00:00, 18.69it/s]
  gmp-6.2.1            | 806 KB    | : 100% 1.0/1 [00:00<00:00,  4.18it/s]
  openssl-1.1.1o       | 2.1 MB    | : 100% 1.0/1 [00:00<00:00,  1.83it/s]
  ca-certificates-2022 | 149 KB    | : 100% 1.0/1 [00:00<00:00, 13.57it/s]
  mpfr-4.1.0           | 2.6 MB    | : 100% 1.0/1 [00:00<00:00,  1.46it/s]
  certifi-2022.6.15    | 155 KB    | : 100% 1.0/1 [00:00<00:00,  9.59it/s]
  libgfortran-ng-12.1. | 23 KB     | : 100% 1.0/1 [00:00<00:00, 17.35it/s]
  libgfortran5-12.1.0  | 1.8 MB    | : 100% 1.0/1 [00:00<00:00,  1.68it/s]
  scipy-1.7.3          | 21.8 MB   | : 100% 1.0/1 [00:06<00:00,  6.28s/it]
  tbb-2021.5.0         | 1.9 MB    | : 100% 1.0/1 [00:00<00:00,  2.05it/s]
  suitesparse-5.10.1   | 2.4 MB    | : 100% 1.0/1 [00:00<00:00,  1.17it/s]
  lxml-4.8.0           | 1.4 MB    | : 100% 1.0/1 [00:00<00:00,  1.90it/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::certifi-2022.6.15-py37h8~ --> pkgs/main::cer
  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,  5.57it/s]
numpy-base-1.19.1     | 4.1 MB    | : 100% 1.0/1 [00:00<00:00,  1.21it/s]
blas-1.0              | 46 KB     | : 100% 1.0/1 [00:00<00:00, 10.91it/s]
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
```

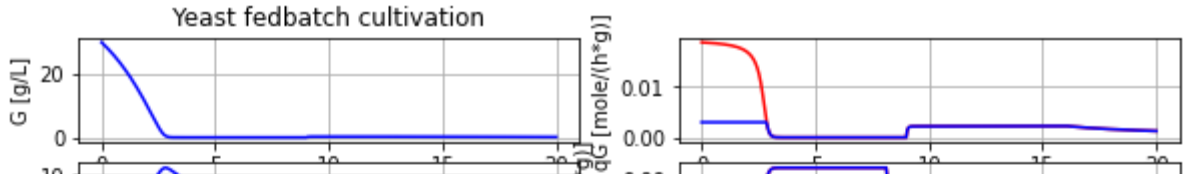
```
run -i BPL_YEAST_AIR_Fedbatch_DOcontrol_explore.py
```

```
    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'] = [25/2.54, 20/2.54]
```

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

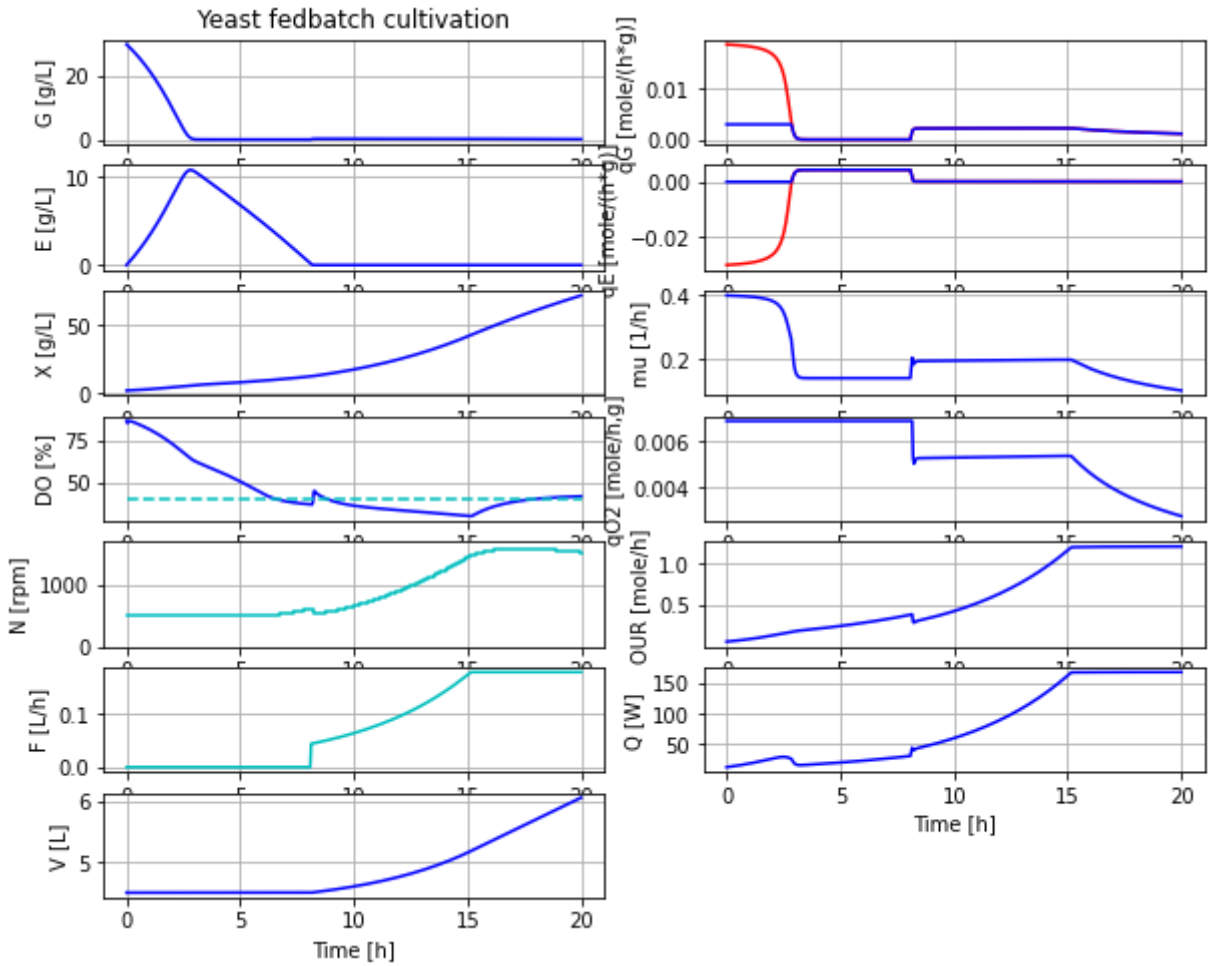
```
    Saccharomyces cerevisae - default parameters for strain H1022

    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

# 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)
```




```
disp('culture', decimals=4)
```

```
qGmax : 0.02
Ks : 0.01
qO2lim : 0.0069
```

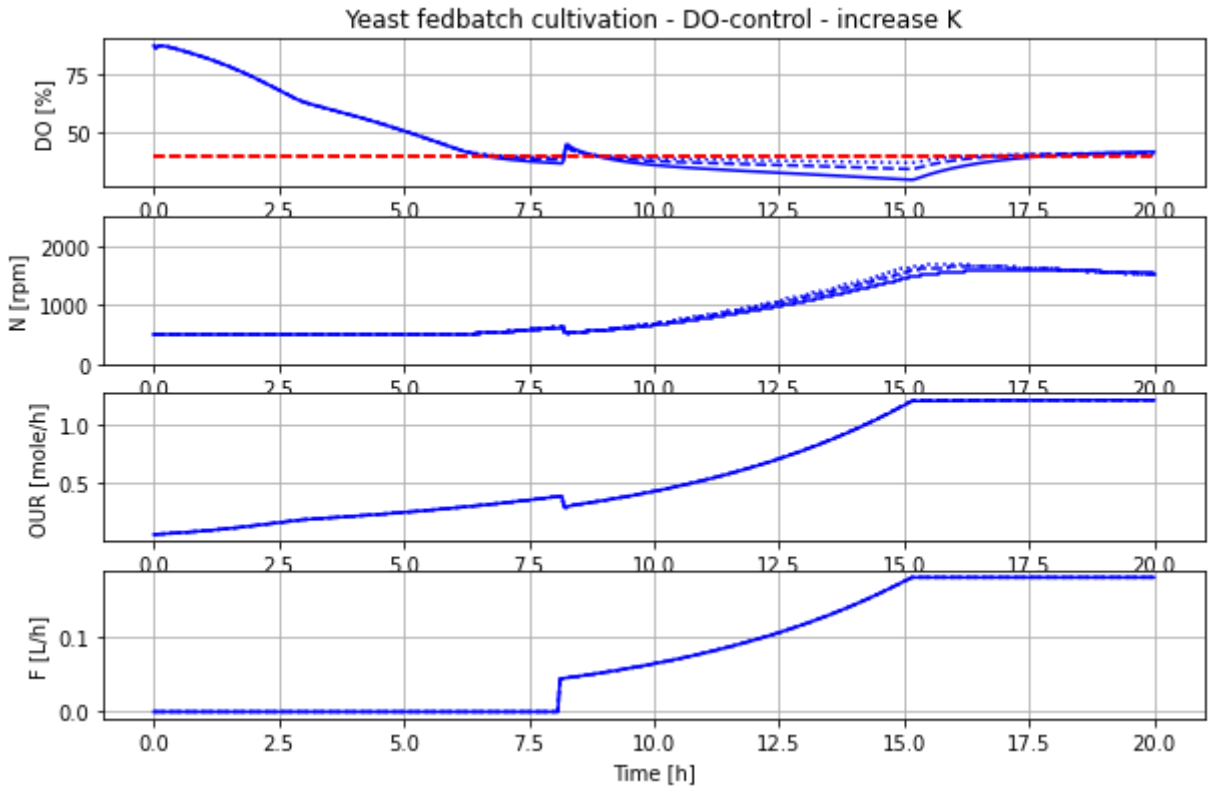
```
# Let us start the feeding just after the batch phase has ended and keep other para
par(t_start=8.1)

# 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.

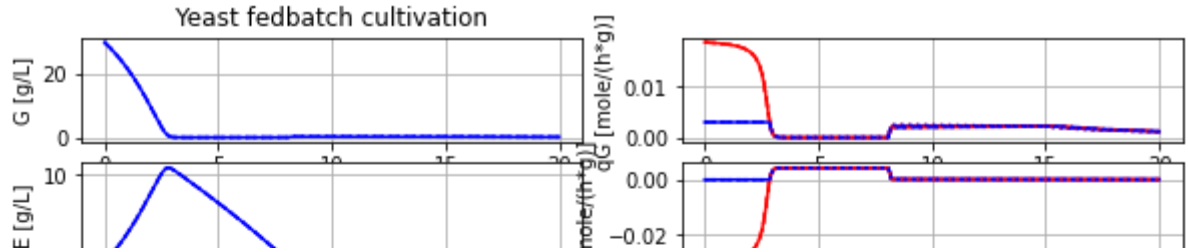
```
# Let us take a closer look at the DO-control system and try to make control error
newplot(title='Yeast fedbatch cultivation - DO-control - increase K', plotType='Foc
for value in [10, 20, 40]: par(K=value); simu(20)
```

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



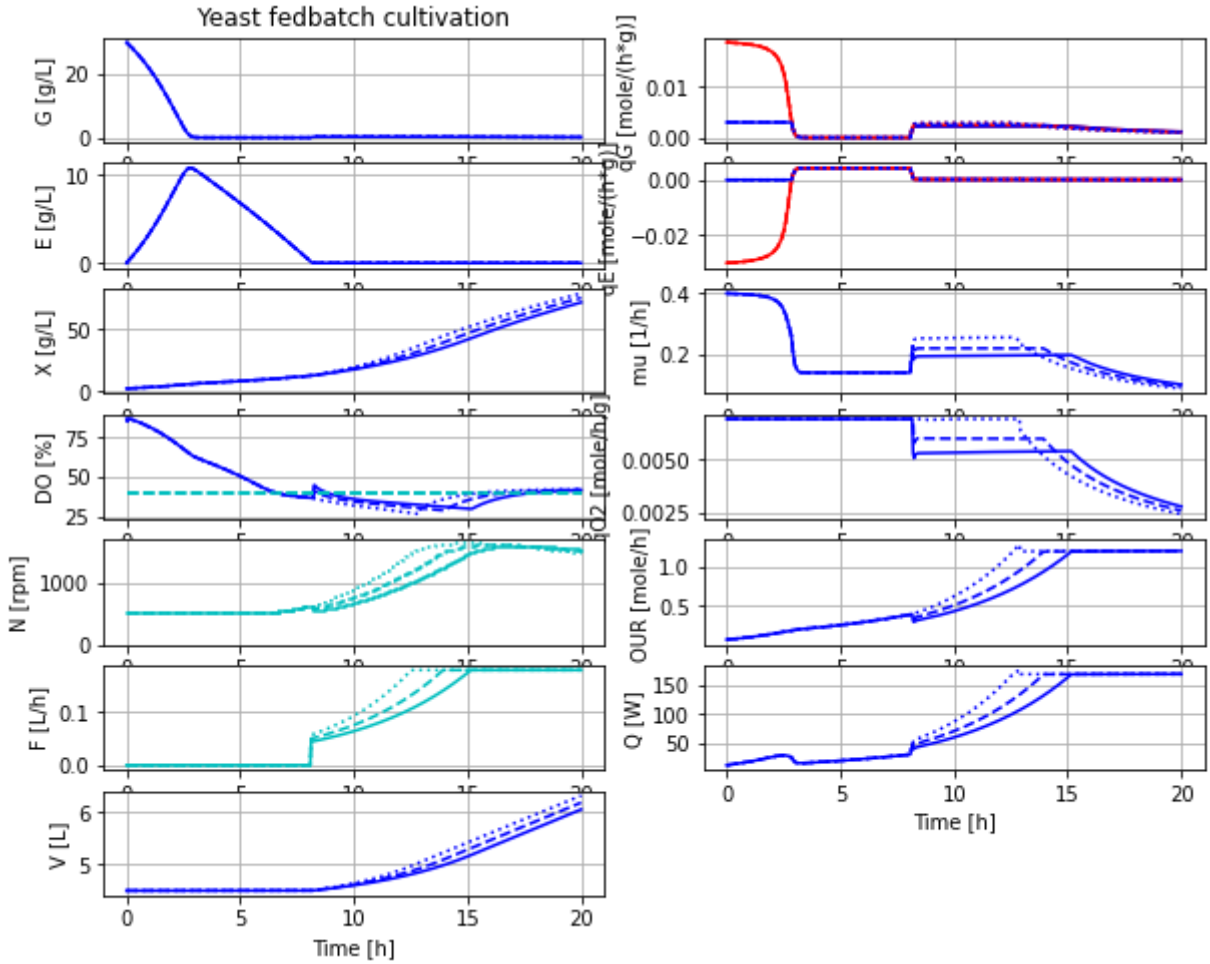
We see that by a higher control gain K the DO-control error get smaller and the stability of the control system is maintained.

```
# 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)
```

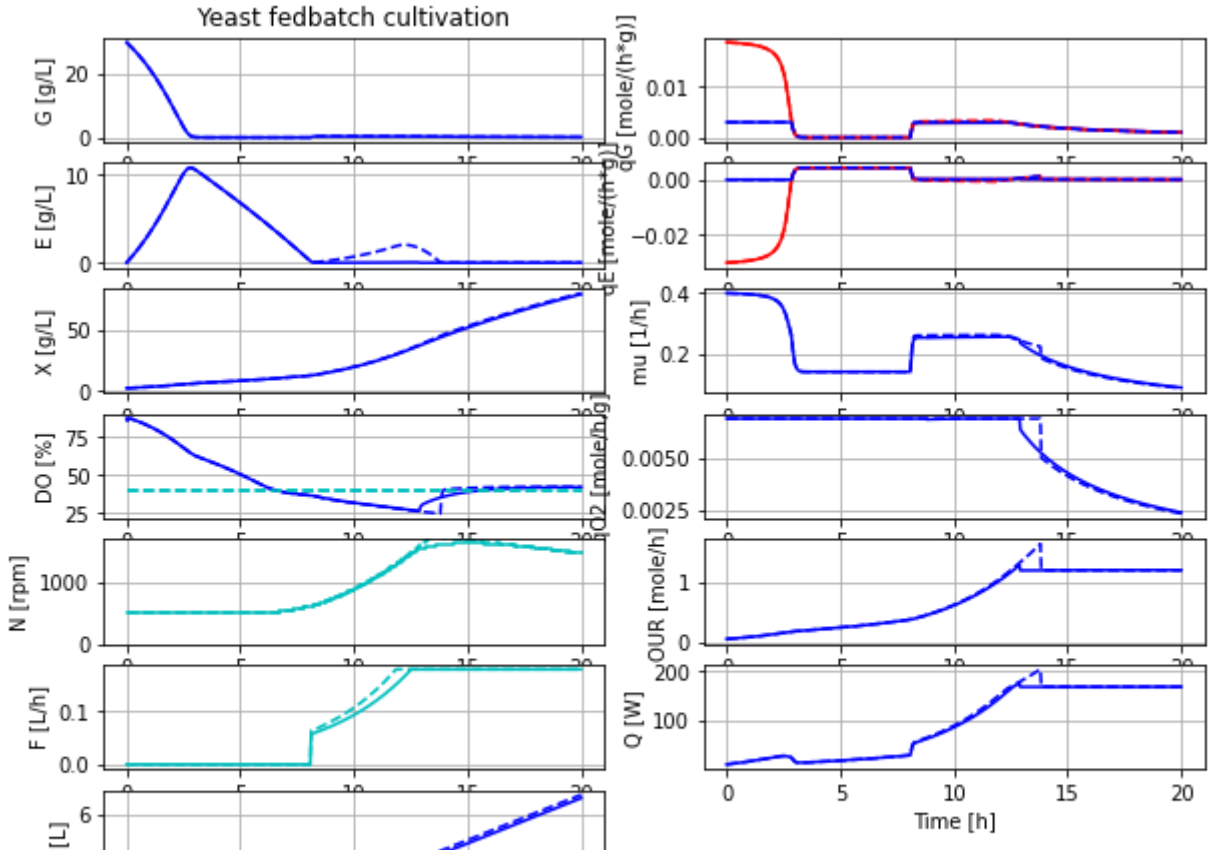


The variation in F_start has an impact and we see that the actual growth rate during fedbatch phase do converge to the set growth rate of the feed, but i takes more than 5 hours.

```
# 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)
```

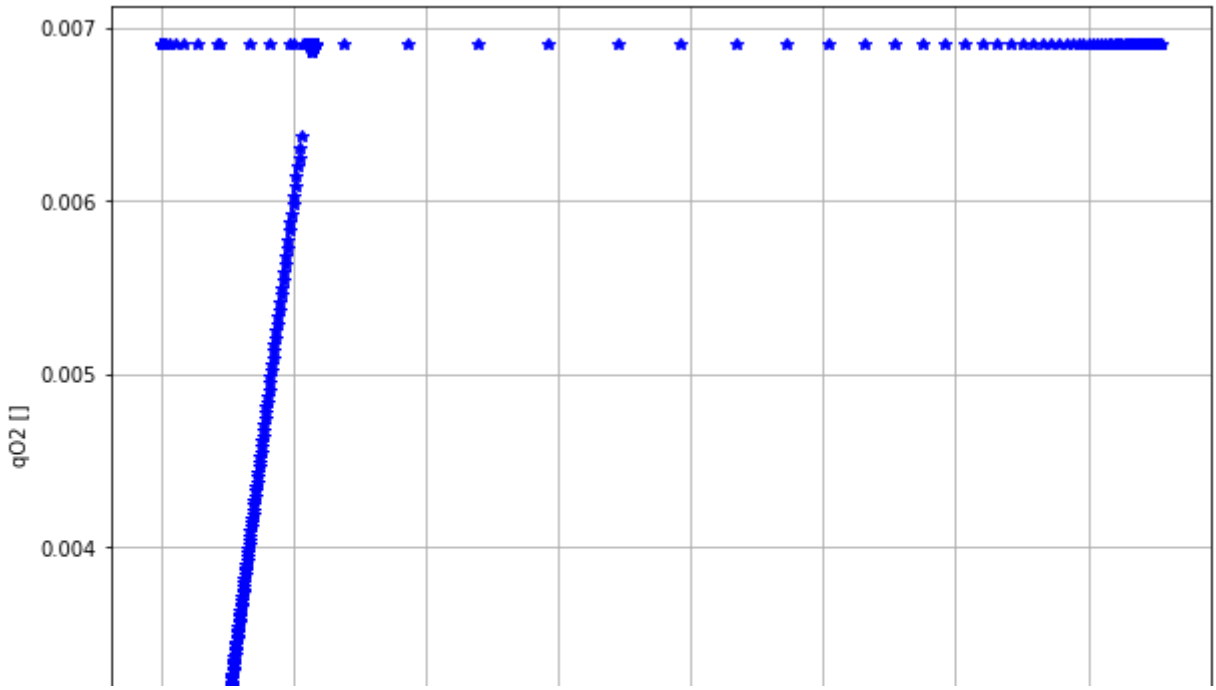



```
# And let us see what happens if the feedprofile exceed the culture capacity
newplot(title='Yeast fedbatch cultivation', plotType='Overview')
par(F_start=0.057, mu_feed=0.26); simu(20)
par(F_start=0.063, mu_feed=0.28); simu(20)
par(F_start=0.044, mu_feed=0.20)
```



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.

```
# Improvise and make your own diagram - 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)
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 wanted to confirm our understanding of the relation between qO2 and qG and could easily make an improvised diagram to show this using data from the standard simulation.

```
# 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
```