

✓ BPL_YEAST_AIR_Fedbatch script with PyFMI

The key library PyFMI is installed.

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 22.04.4 LTS
   Release:        22.04
   Codename:       jammy
```

```
%env PYTHONPATH=
```

```
⇒ env: PYTHONPATH=
```

```
!python --version
```

```
⇒ Python 3.11.11
```

```
!wget https://repo.anaconda.com/miniconda/Miniconda3-py311_24.11.1-0-Linux-x86_64
!chmod +x Miniconda3-py311_24.11.1-0-Linux-x86_64.sh
!bash ./Miniconda3-py311_24.11.1-0-Linux-x86_64.sh -b -f -p /usr/local
import sys
sys.path.append('/usr/local/lib/python3.11/site-packages/')
```

```
⇒ --2025-02-18 12:54:39-- https://repo.anaconda.com/miniconda/Miniconda3-py311\_24.11.1-0-Linux-x86\_64.sh
Resolving repo.anaconda.com (repo.anaconda.com)... 104.16.191.158, 104.16.32.1
Connecting to repo.anaconda.com (repo.anaconda.com)|104.16.191.158|:443... connected
HTTP request sent, awaiting response... 200 OK
Length: 145900576 (139M) [application/octet-stream]
Saving to: 'Miniconda3-py311_24.11.1-0-Linux-x86_64.sh'
```

```
Miniconda3-py311_24 100%[=====>] 139.14M  90.9MB/s    in 1.5s
```

```
2025-02-18 12:54:40 (90.9 MB/s) - 'Miniconda3-py311_24.11.1-0-Linux-x86_64.sh'
```

```
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	
ca-certificates-2024.12.31	h06a4308_0	128 KB
certifi-2025.1.31	py311h06a4308_0	163 KB
Total:		291 KB

The following packages will be UPDATED:

```

ca-certificates          2024.11.26-h06a4308_0 --> 2024.12.31-h06a4308_0
certifi                  2024.8.30-py311h06a4308_0 --> 2025.1.31-py311h06a4308_0

```

Downloading and Extracting Packages:

```

certifi-2025.1.31      | 163 KB | : 0% 0/1 [00:00<?, ?it/s]
certifi-2025.1.31      | 163 KB | : 100% 1.0/1 [00:00<00:00, 19.52it/s]
ca-certificates-2024   | 128 KB | : 100% 1.0/1 [00:00<00:00, 18.30it/s]

```

```

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

```

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

```

➡ conda 24.11.1
   Python 3.11.11

```

```
!conda config --set channel_priority strict
```

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



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

✓ Notes of BPL_YEAST_AIR_Fedbatch

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

```
%%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

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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 cells respiratory capacity [1] as well as oxygen limitation in the reactor. The model is exapanded to describe also the gas phase as well as the culture heat production [2]. The model was derived mainly from continuous culture data but proved to capture dynamic aspects well of ethanol production and consumption [3]. Several cultivations where donw with ethnol control that facilitated high cell density cultivations [4].

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-compiled OpenModelica

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

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.

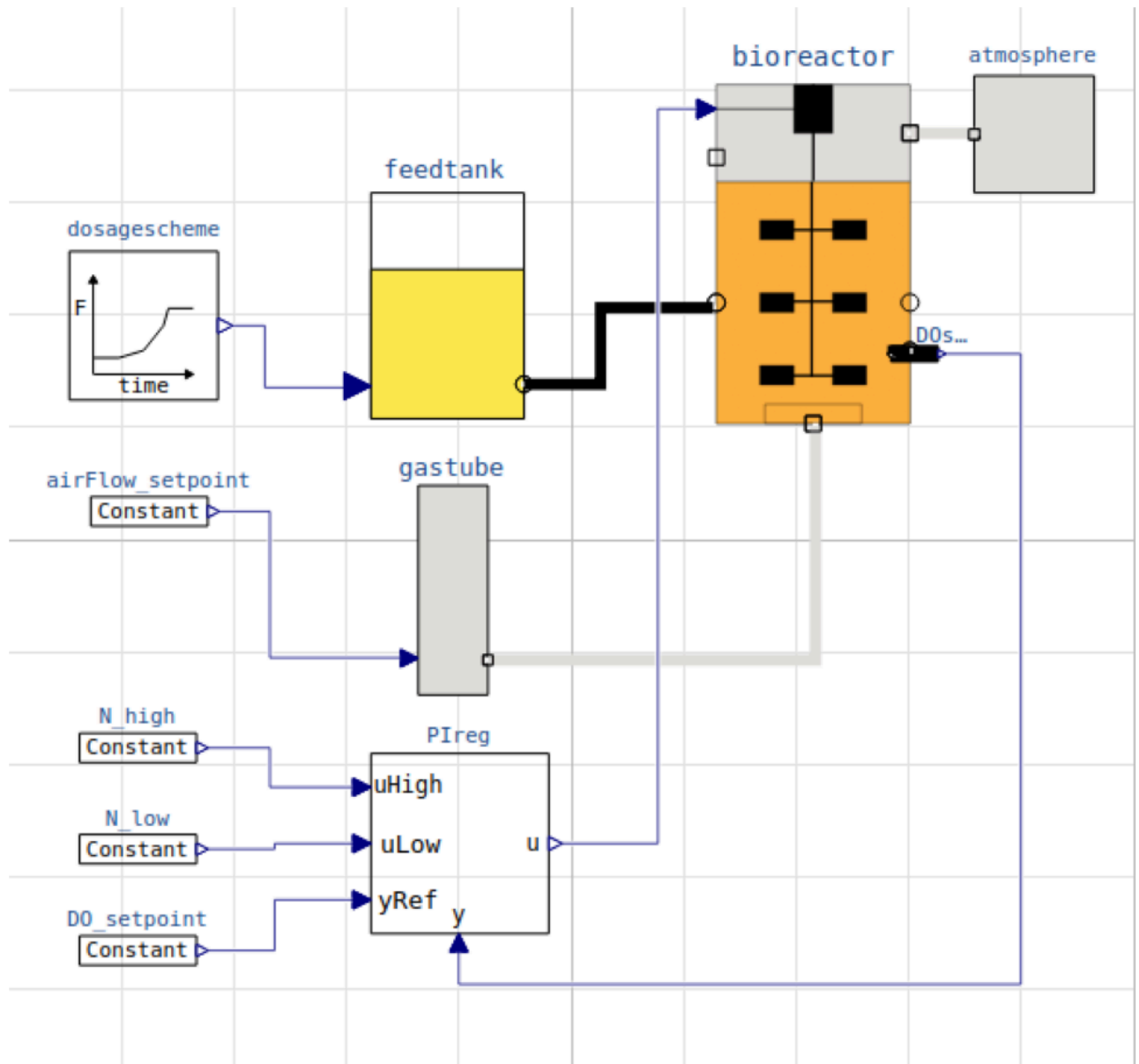
However, you should use describe() after a simulation to get the values used during the simulation.

```
describe('culture'); print(); #describe('liquidphase'); print(); describe('gaspha
```

Saccharomyces cerevisiae – default parameters for strain H1022

```
process_diagram()
```

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



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(q02lim=0.0069)

# Process initial conditions
init(V_start=4.5, VG_start=4.5*30, VX_start=4.5*2, VE_start=4.5*0)

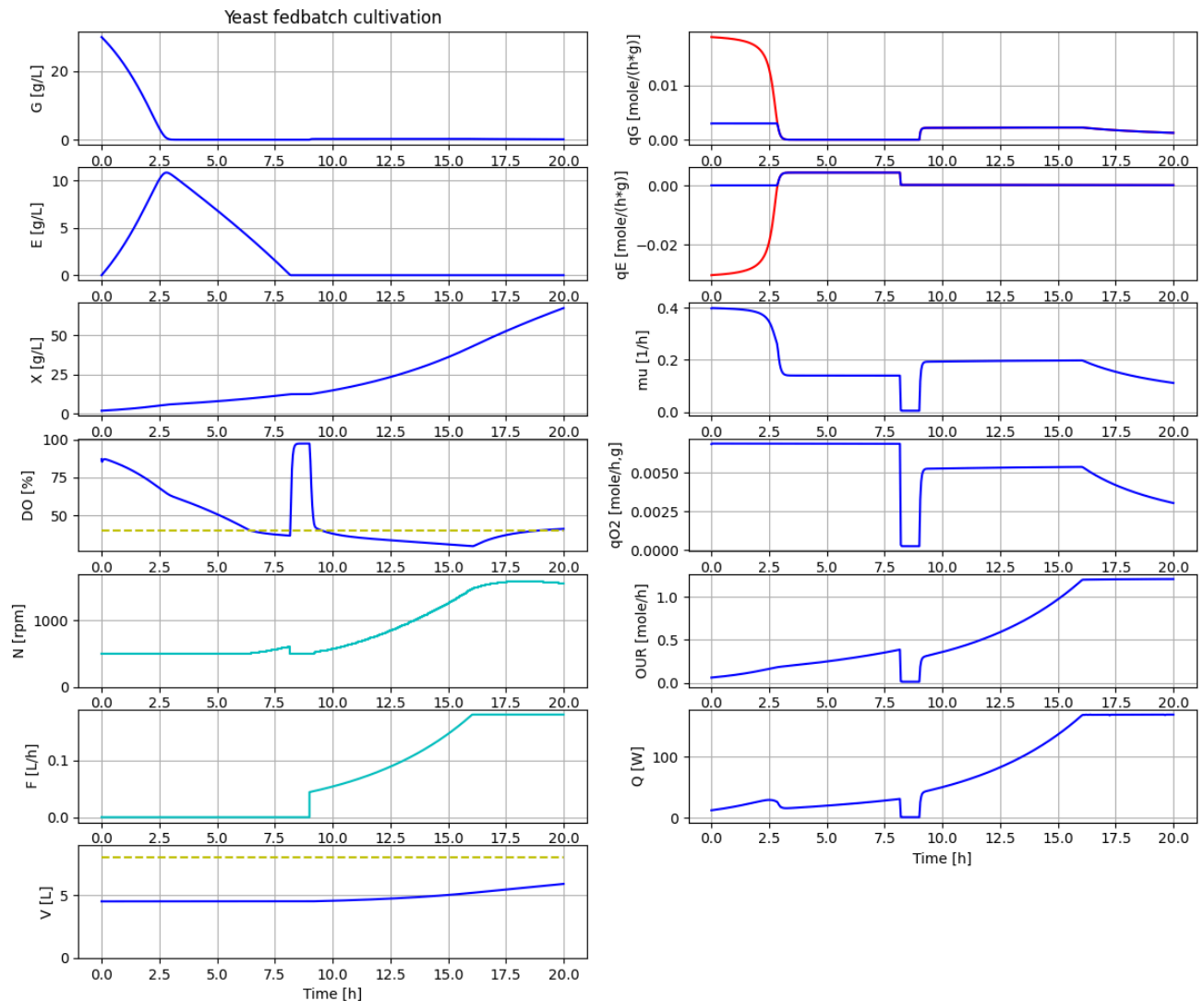
# Feed profile
par(t_startExp=9, F_startExp=0.044, mu_feed=0.20, F_max=0.18)

# DO-control parameters
par(K=10, Ti=0.5)

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



Error: q02lim – seems not an accessible parameter – check the spelling
 Could not find cannot import name 'dopri5' from 'assimulo.lib' (/usr/local/lib,
 Could not find cannot import name 'rodas' from 'assimulo.lib' (/usr/local/lib,
 Could not find cannot import name 'odassl' from 'assimulo.lib' (/usr/local/lib,
 Could not find ODEPACK functions.
 Could not find RADAR5
 Could not find GLIMDA.



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')
```

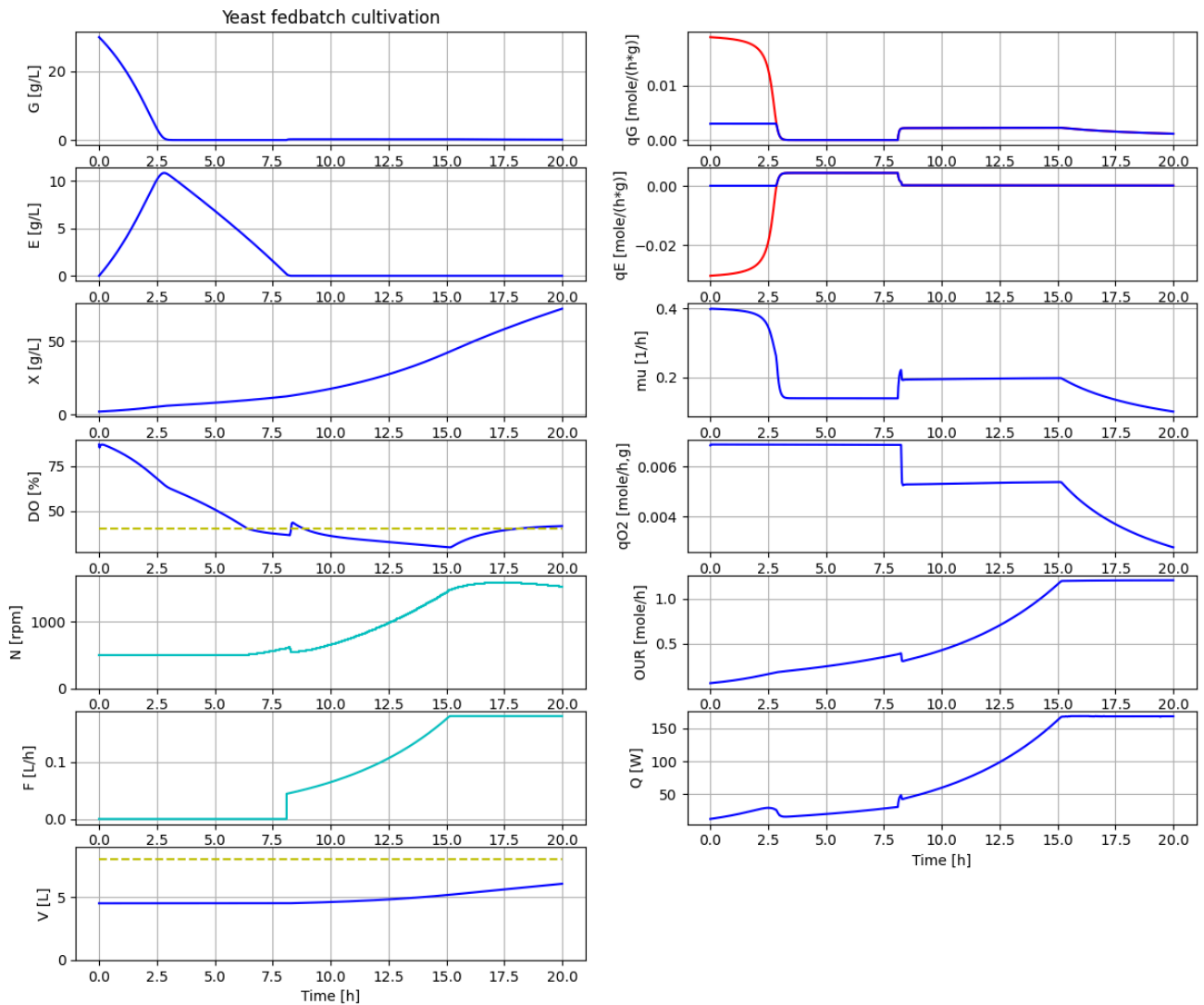
```
⇒ Volume of the gas phase : 2.108 [ L ]
```

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

```
⇒ F_start : 0.0  
   mu_feed : 0.2  
   t_startExp : 9.0  
   F_startExp : 0.044  
   F_max : 0.18
```

```
# Let us start the feeding just after the batch phase has ended and keep other pa  
par(t_startExp=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.

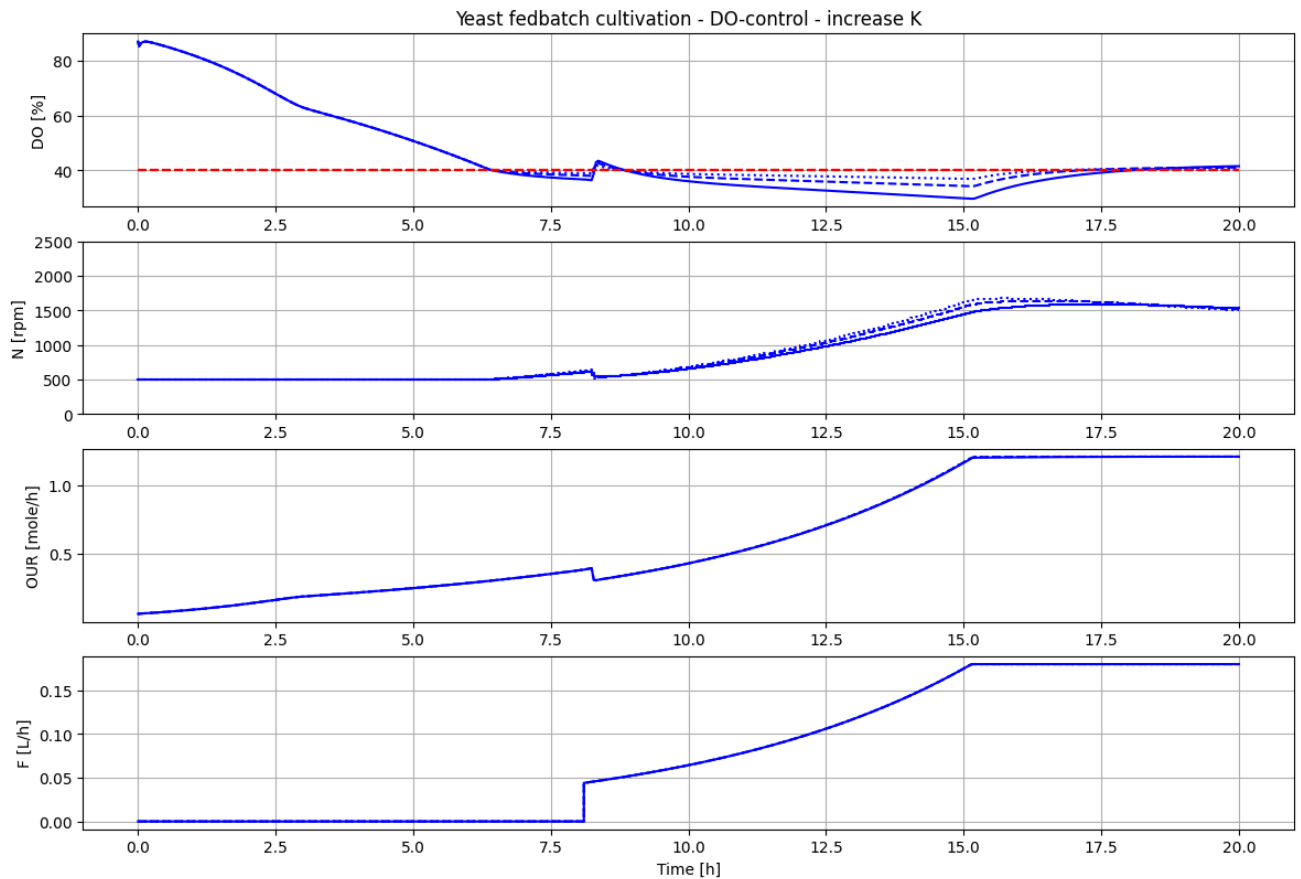
✓ DO-control - tuning of PI-regulator parameters

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 loosing

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='F
for value in [10, 20, 40]: par(K=value); simu(20)
```

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



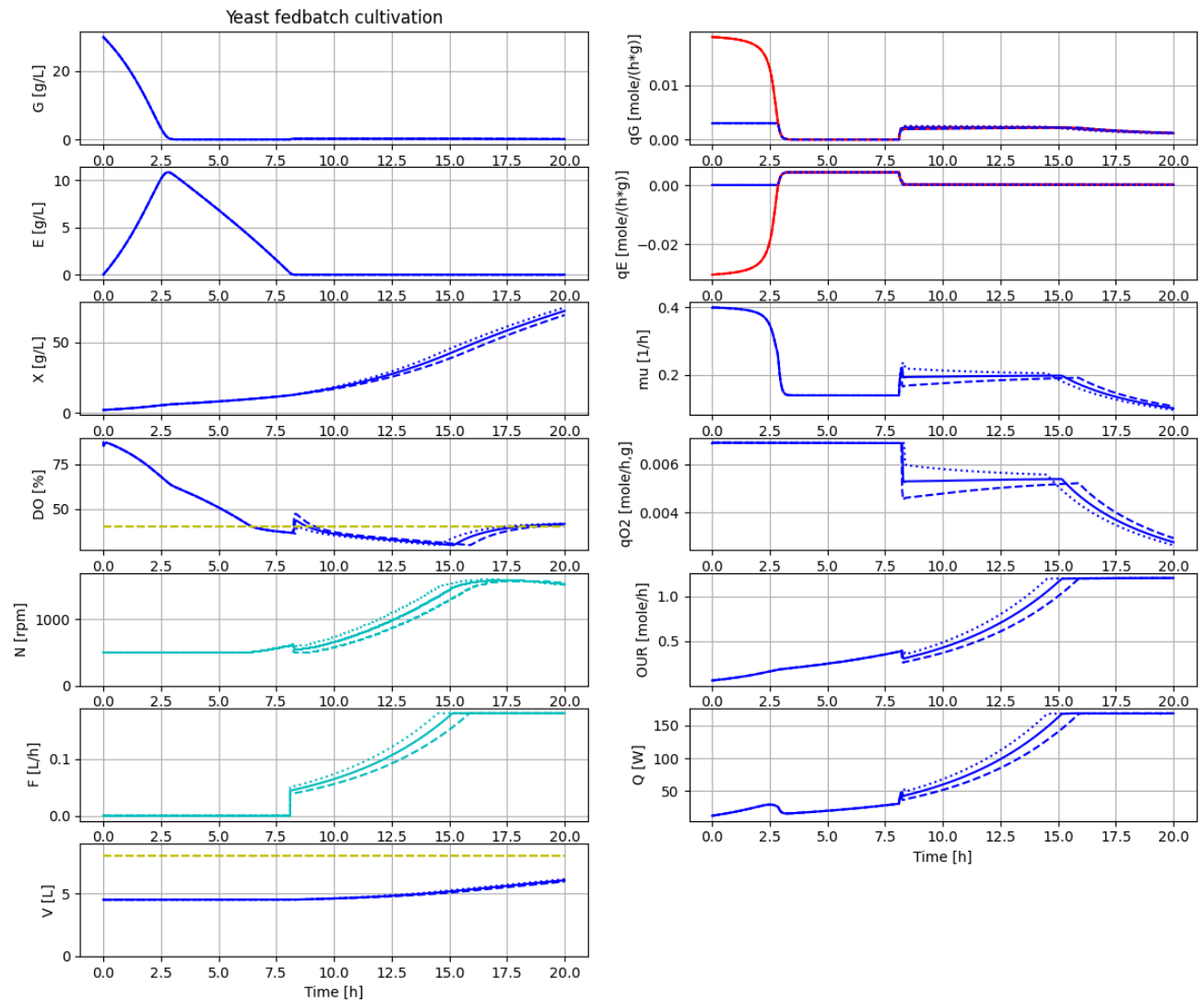
We see that by a higher control gain K the DO-control error get smaller and the stability of the control system is maintained.

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

✓ Sensitivity to changes in feed-profile

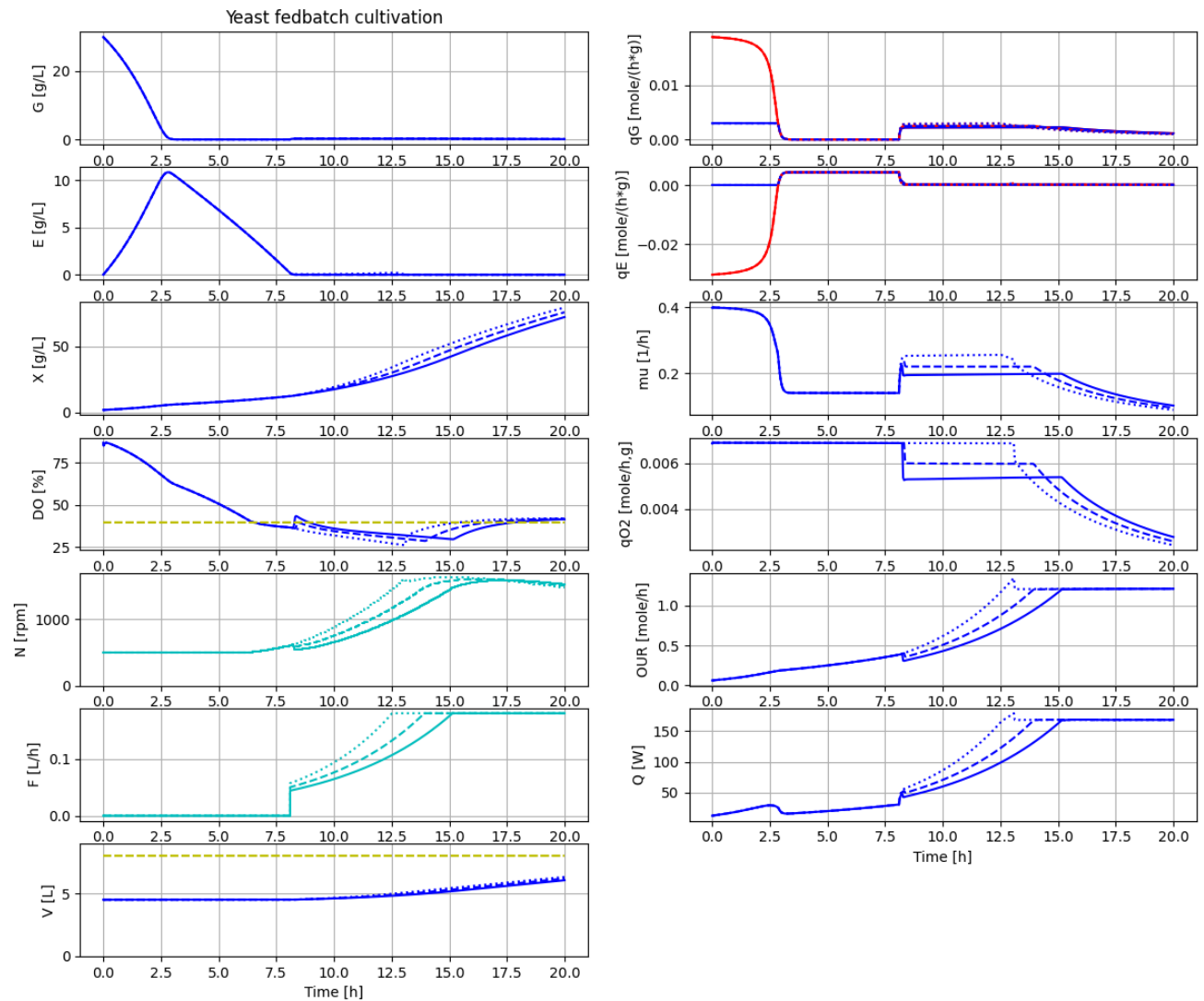
Now, let us focus on investigating impact of changes in the feed-profile. The goal is to increase the produced cell mass without accumulation of by-product ethanol. Simulation can bring some insight into how behaviour of the different variables change when by-product is formed. This insight can help 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_startExp=value); simu(20)
```

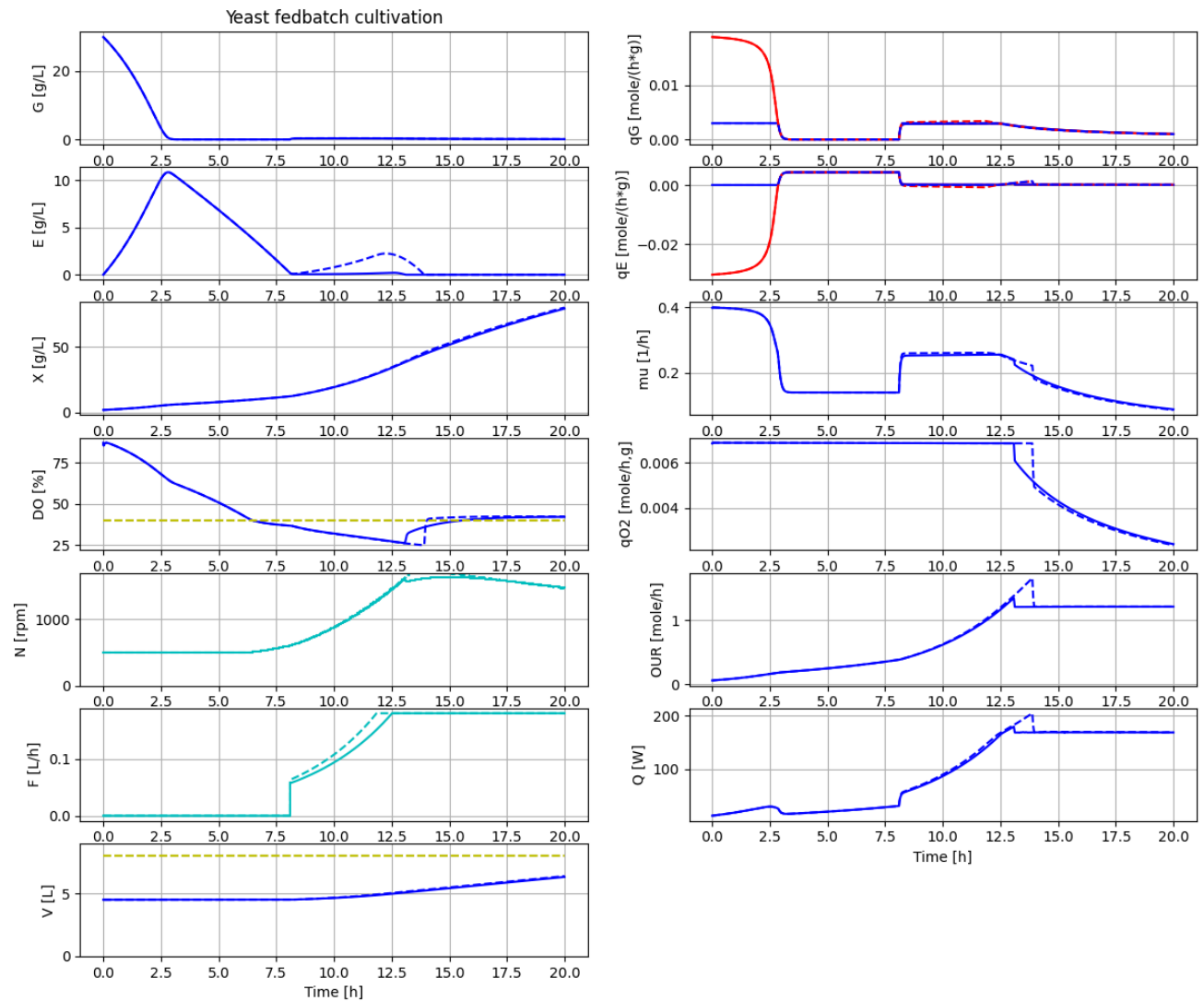


The variation in F_{start} has an impact and we see that the actual growth rate during fedbatch phase do converge to the set growth rate of the feed, but it takes more than 5 hours.

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



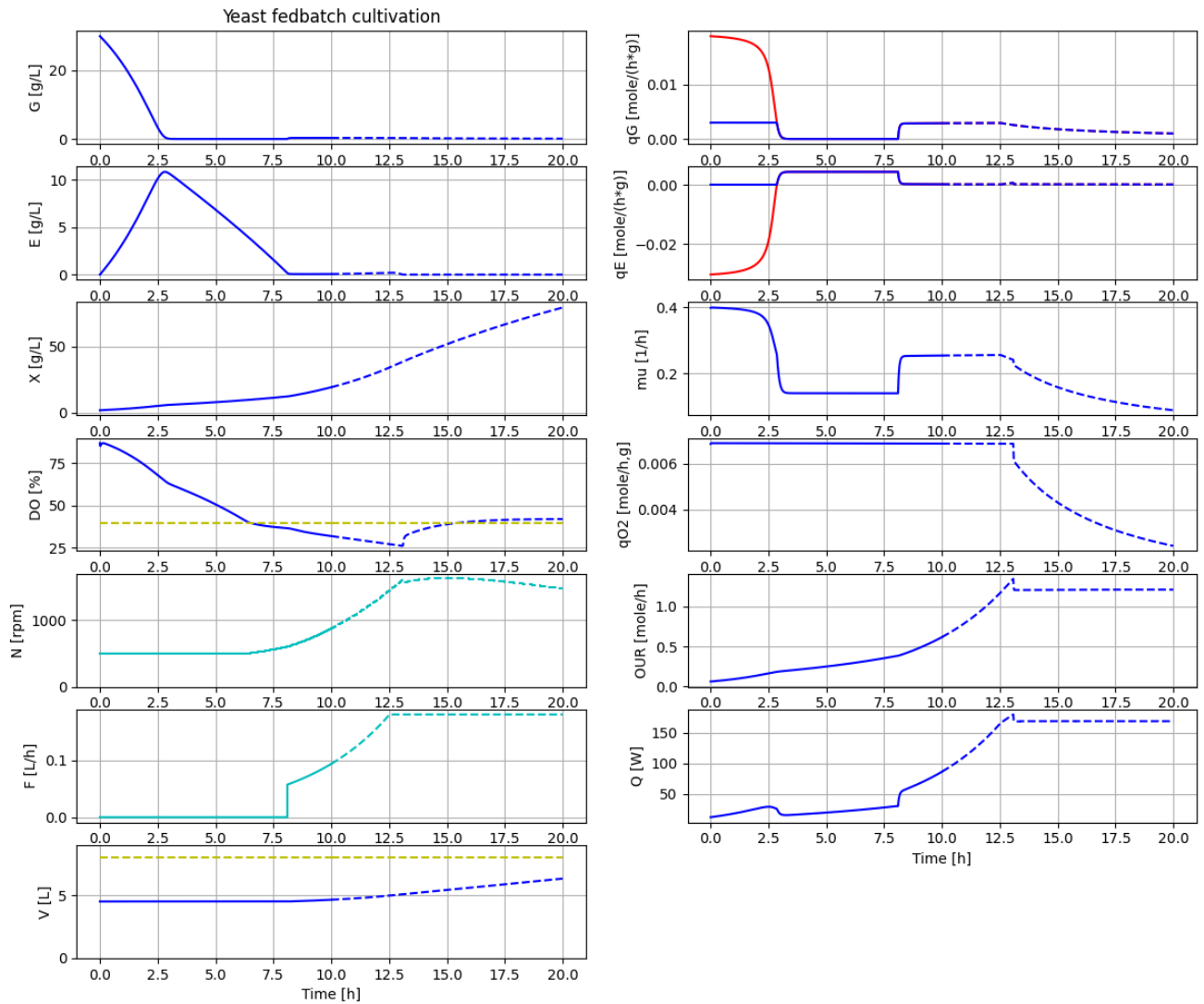
```
# And let us see what happens if the feedprofile exceed the culture capacity
newplot(title='Yeast fedbatch cultivation', plotType='Overview')
par(F_startExp=0.057, mu_feed=0.26); simu(20)
par(F_startExp=0.063, mu_feed=0.28); simu(20)
par(F_startExp=0.044, mu_feed=0.20)
```



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 investigate the impact of changing the maximal feedrate F_{\max} . Make sure that the DO level do not get too low.

```
# Check of simu('cont')
newplot(title='Yeast fedbatch cultivation', plotType='Overview')
par(F_startExp=0.057, mu_feed=0.26); simu(10)
simu(10,'cont')
```



✓ Sensitivity to low dissolved oxygen levels

The detailed understanding of process dynamics at very low dissolved oxygen levels is not that well studied, to the authors knowledge. Here is a section on "Growth under oxygen limiation" in the original paper [1]. This model we use here. The idea is that the oxygen uptake is essentially described with a Monod-function with a parameter here denoted K_{sO2} . At higher dissolved oxygen levels the uptake is saturated by the respiratory capacity and in our model denoted q_{O2max} . Thus, at lower dissolved oxygen levels the respiration capacity is lowered and denoted here q_{O2lim} and at sufficiently high dissolved oxygen levels the q_{O2lim} corresponds to q_{O2max} . The value of q_{O2lim} controls metabolism and growth.

$$q_{O2lim} = q_{O2max} \frac{c[O2]}{K_{sO2} + c[O2]}$$

The process dyanmics for variation of glucose feed rate around the respiratory capacity under well-aerated condnions are well described in [3]. It would be interesting to make similar studies at low dissolved oxygens levels. Also interesting to describe the impact of variation in the aeration during condition of a constant glucose supply to see the impact of ethanol production and consumption this way.

During the time 1980-90 there was an interest to study the impact variation in dissolved oxygen in two-reactor setups [5]. In the smaller reactor dissolved oxygen level was low while higher in the larger reactor and the culture was circulated in the system at a rate related to typical mixing times in a large reactor. This experimental setup has been simulated with Bioprocess Library

```
# Let us instead see what happens when the aeration reach a limit in terms of sti
newplot(title='Yeast fedbatch cultivation', plotType='Overview'); ax22.set_ylim([
par(F_startExp=0.057, mu_feed=0.26); simu(20)
par(F_startExp=0.057, mu_feed=0.26, N_high=900); simu(20)
par(F_startExp=0.044, mu_feed=0.20, N_high=2000)
```

