BPL_IEC_operation script with PyFMI

The key library PyFMI is installed.

After the installation a small application BPL_IEC_operation 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 20.04.5 LTS
Release:        20.04
Codename:       focal
```

```
%env PYTHONPATH=
```

```
env: PYTHONPATH=
```

```
!wget https://repo.anaconda.com/miniconda/Miniconda3-py39_23.1.0-1-Linux-x86_64.sh
!chmod +x Miniconda3-py39_23.1.0-1-Linux-x86_64.sh
!bash ./Miniconda3-py39_23.1.0-1-Linux-x86_64.sh -b -f -p /usr/local
import sys
sys.path.append('/usr/local/lib/python3.9/site-packages/')
```

```
--2023-04-24 18:25:10--  https://repo.anaconda.com/miniconda/Miniconda3-py39_23.1.0-1-Linux-x86_64.sh
Resolving repo.anaconda.com (repo.anaconda.com)... 104.16.131.3, 104.16.130.3, 2606:4700::6810:8203, ...
Connecting to repo.anaconda.com (repo.anaconda.com)|104.16.131.3|:443... connected.
HTTP request sent, awaiting response... 200 OK
Length: 69888122 (67M) [application/x-sh]
Saving to: ‘Miniconda3-py39_23.1.0-1-Linux-x86_64.sh’

Miniconda3-py39_23. 100%[===================>]  66.65M   204MB/s    in 0.3s

2023-04-24 18:25:10 (204 MB/s) - ‘Miniconda3-py39_23.1.0-1-Linux-x86_64.sh’ saved [69888122/69888122]

PREFIX=/usr/local
Unpacking payload ...

Installing base environment...


Downloading and Extracting Packages


Downloading and Extracting Packages

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

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

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

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

```
     conda 23.3.1
     Python 3.9.16
```

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

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

Notes of BPL_IEC_operation

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

- FMU - BPL_IEC_operation_linux_jm_cs.fmu
- Setup-file - BPL_IEC_operation_explore

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

```
Cloning into 'BPL_IEC_operation'...
```

```
%cd BPL_IEC_operation
```

```
/content/BPL_IEC_operation
```

BPL_IEC_operation

Authors: Karl Johan Brink and Jan Peter Axelsson

In this notebook we show operation of a typical ion-exchange chromatography step. The impact of pH is also illustrated.

The model is based on the simplified model [1].

```
run -i BPL_IEC_explore.py
```

```
Linux - run FMU pre-comiled 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

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]
```

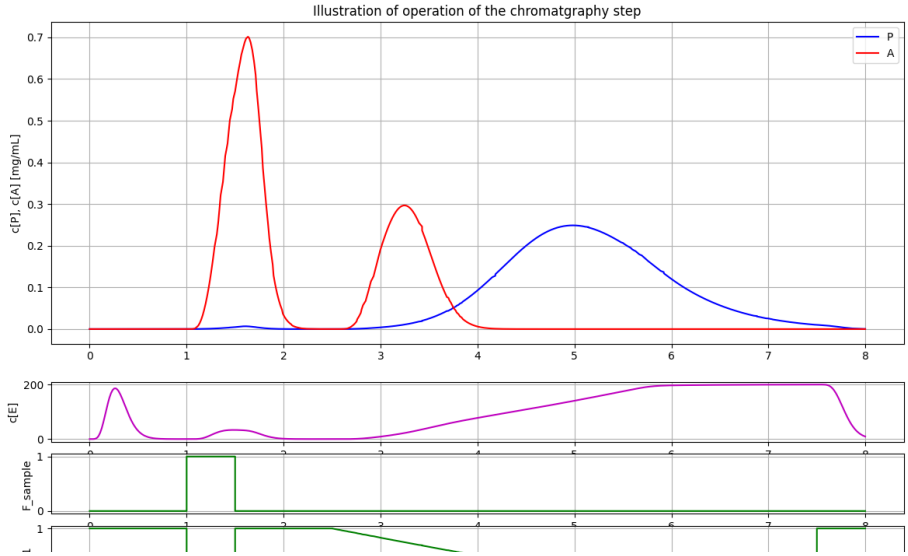
Typical parameters for a pilot scale ion exchange chromatography column process setup

```
# From  given colunn height (h) diameter (d) and linear flow rate (lfr)
# actual column volume (V) and volume flow rate (VFR) are calculated below.
```

```
from numpy import pi
h = 20.0
d = 1.261
a = pi*(d/2)**2
V = h*a
print('V =', np.round(V,1), '[mL]')

lfr = 48
VFR = a*lfr/60
print('VFR =', np.round(VFR,1), '[mL/min]')                                    # Pump schedule parameter
```

```
V = 25.0 [mL]
VFR = 1.0 [mL/min]
```

```
# Sample concentration product P_in and antagonist A_in
par(P_in = 1.0)
par(A_in = 1.0)

# Column properties are described by the size and binding capacity of the resin Q_av
par(height = h)
par(diameter = d)
par(Q_av = 6.0)

# Remaining salt koncentration in the column from prvious batch and eliminated during the initial equilibration peri
init(E_0 = 50)

# Salt koncentration of the desorption buffer
par(E_in_desorption_buffer = 8.0)

# Flow rate rate through the
par(LFR=lfr)

# Switching points during operation are conveniently described in terms of multiples of the column volume V
CV_ekv = 1.0
CV_ads = 0.5
CV_wash = 1.0
CV_desorb = 3.0
CV_start_pool = 1.2
CV_stop_pool = 4.5
CV_wash2 = 2.5
par(scale_volume=True, start_adsorption=CV_ekv*V, stop_adsorption=(CV_ekv+CV_ads)*V)
par(start_desorption=(CV_ekv+CV_ads+CV_wash)*V, stationary_desorption=(CV_ekv+CV_ads+CV_wash+CV_desorb)*V)
par(stop_desorption=7.5*V)
par(start_pooling=(CV_ekv+CV_ads+CV_wash+CV_start_pool)*V, stop_pooling=(CV_ekv+CV_ads+CV_wash+CV_stop_pool)*V)

# Simulation and plot of results
newplot(title='Illustration of operation of the chromatgraphy step', plotType='Elution-conductivity-vs-CV-combined-a
simu((CV_ekv+CV_ads+CV_wash+CV_desorb+CV_wash2)*V/VFR)
```



Comments of steps of operations:

1) Time: 0-1 hours - equilibration. Just to illustrate the equilibration process the first part of the column is given an initial value of salt concentration.

2) Time: 1-1.5 hours - sample is loaded on the column. The product P is adsorbed to the columne and just a small amount passes through and goes to the waste. The antagonist A is much less adsrobed.

3) Time: 1.5-2.5 hours - washing 1. The column comes to equilibrium and both antagonist and product comes down to low levels.

4) Time: 2.5-5.5 hours - desorption. A linear gradient of increaseing salt concentration is applied. First the antagonist and later the product comes out.

5) Time: 5.5-7.5 hours - washing 2 The The column has constant salt concentration and stationary desorption.

6) Time: 3.7-7.0 hours - pooling of product. The start- and stop of pooling are chosen with trade-off between maximizing the product pooled and minimize the amount of antagonist in the pooling.

7) Time: 7.5-8.0 hours - desorption stopped and salt is washed out and preparation of the next batch to come.

Note that step 4 and 5 is parallel to step 6.

```
# Check mass-balance of P and A
P_mass = model.get('tank_harvest.m[1]') + model.get('tank_waste.m[1]')
A_mass = model.get('tank_harvest.m[2]') + model.get('tank_waste.m[2]')
print('P_mass [mg] =', P_mass)
print('A_mass [mg] =', A_mass)
```

```
P_mass [mg] = [12.42212162]
A_mass [mg] = [12.48878113]
```

These values should be compared with the expected value 12.5 mg, i.e. half a column volume with sample concentration 1 mg/L. The difference is due to numerical errors during simulation.

Impact of change of binding strength due to pH

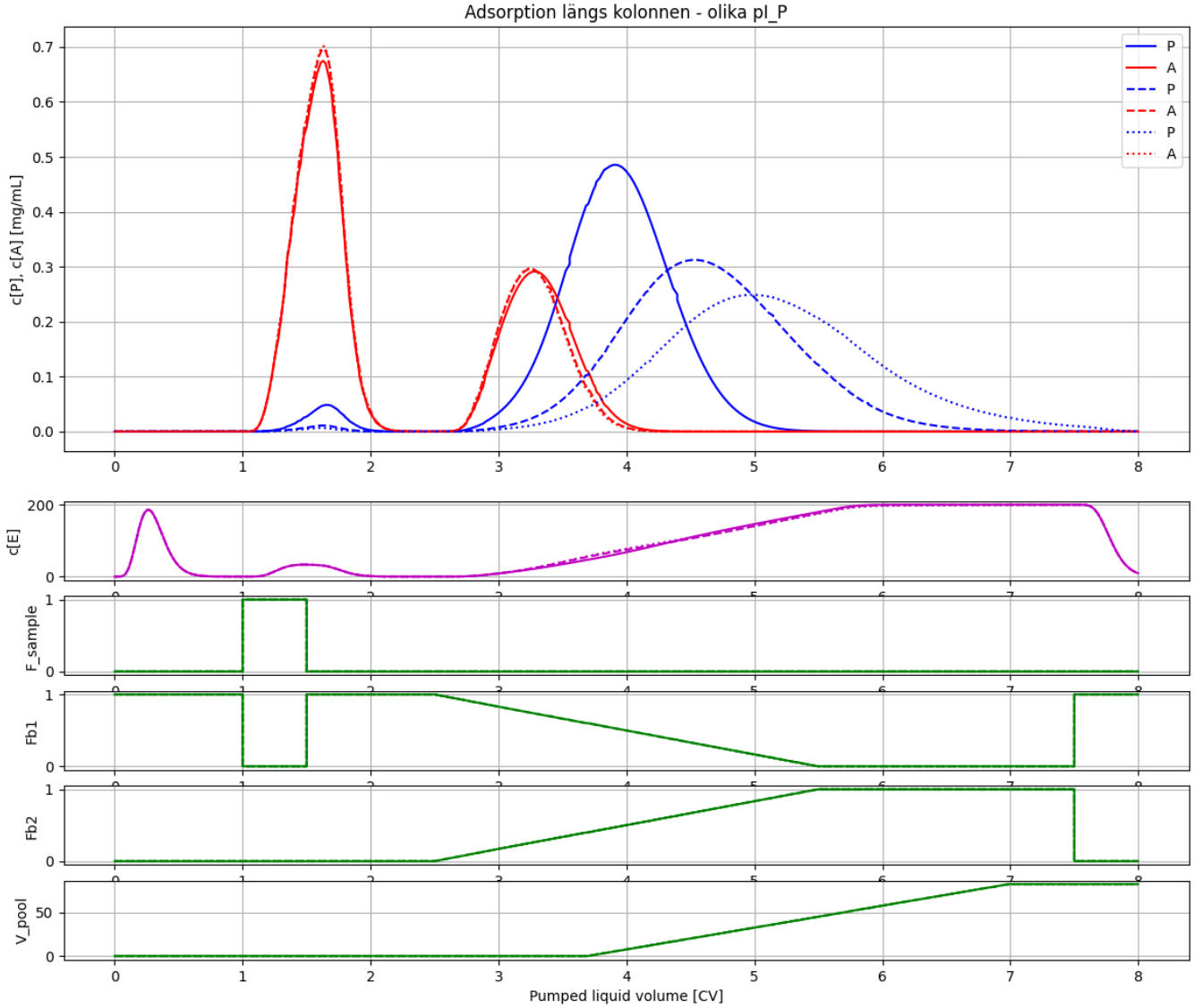
There are many factors that contribute to the binding strength. A most important factor is the pH-value of the resin and the characteristic iso-electric point of the protein. The binding strenght can be seen as proportional to the difference.

The binding strength of the resin is described by the quotient KP=k1/k2 for the protein P and similarly KA=k3/k4 for the protein A, see [1].

```
# Define function that describe the proportionality of binding strength ot
# the pH difference of the iso-electric point and the resin

def KP_pH_sensitivity(pI_P=8.0, pH_resin=7.0):
    K_P_nom = 0.0
    coeff_pH = 6.0
    return K_P_nom + coeff_pH*(pI_P-pH_resin)

def KA_pH_sensitivity(pI_A=7.1667, pH_resin=7.0):
```

```
    K_A_nom = 0.0
    coeff_pH = 1.0
    return K_A_nom + coeff_pH*(pI_A-pH_resin)


# Let us investigate the impact of change of the iso-electric pH for protein P

# Default value of TP
TP=3.33

# Simulate and plot the results
newplot(title='Adsorption längs kolonnen - olika pI_P', plotType='Elution-conductivity-vs-CV-combined-all')

for value in [7.2, 7.6, 8.0]:
    par(k2 = 1/(TP*KP_pH_sensitivity(pI_P=value, pH_resin=7.0)));
    simu((CV_ekv+CV_ads+CV_wash+CV_desorb+CV_wash2)*V/VFR)
    print(sim_res['tank_harvest.m[1]'][-1], 'mg')

# Restore default values
par(k2 = 1/(TP*KP_pH_sensitivity(pI_P=8.0)))
```

```
8.734961016147334 mg
11.650336552488831 mg
11.769880473010728 mg
```



Summary

The simplified simulation model was found useful to describe operational aspects of ion exchange cromtography. The model describe qualitatively well the impact of typical operational changes in flow rate.

Acknowledgement

The author thank Karl Johan Brink for sharing his know-how of chromatography operation. He has especially given input of how to parametrize the model in terms often used in the industry and provided typical values used here.

References

1) Månsson, Jonas, "Control of chromatography comlumn in production scale", Master thesis TFRT-5599, Department of Automatic Control, LTH, Lund Sweden, 1998. 2) Pharmacia LKB Biotechnology. "Ion Exchange chromatography. Principles and Mathods.", 3rd edition, 1991.

Appendix

```
system_info()
```

```
System information
 -OS: Linux
 -Python: 3.9.16
 -Scipy: not installed in the notebook
 -PyFMI: 2.10.3
 -FMU by: OpenModelica Compiler OpenModelica 1.21.0
 -FMI: 2.0
 -Type: FMUModelME2
 -Name: BPL_IEC.Column_system
 -Generated: 2023-04-21T10:58:26Z
 -MSL: 3.2.3
 -Description: Bioprocess Library version 2.1.1
 -Interaction: FMU-explore version 0.9.7
```


✓ 0s completed at 20:26