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 a simplified model [1].

In [1]:
```
run -i BPL_IEC_explore.py
```

```
Windows - run FMU pre-compiled JModelica 2.14

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()
```

In [2]:
```
plt.rcParams['figure.figsize'] = [30/2.54, 24/2.54]
```

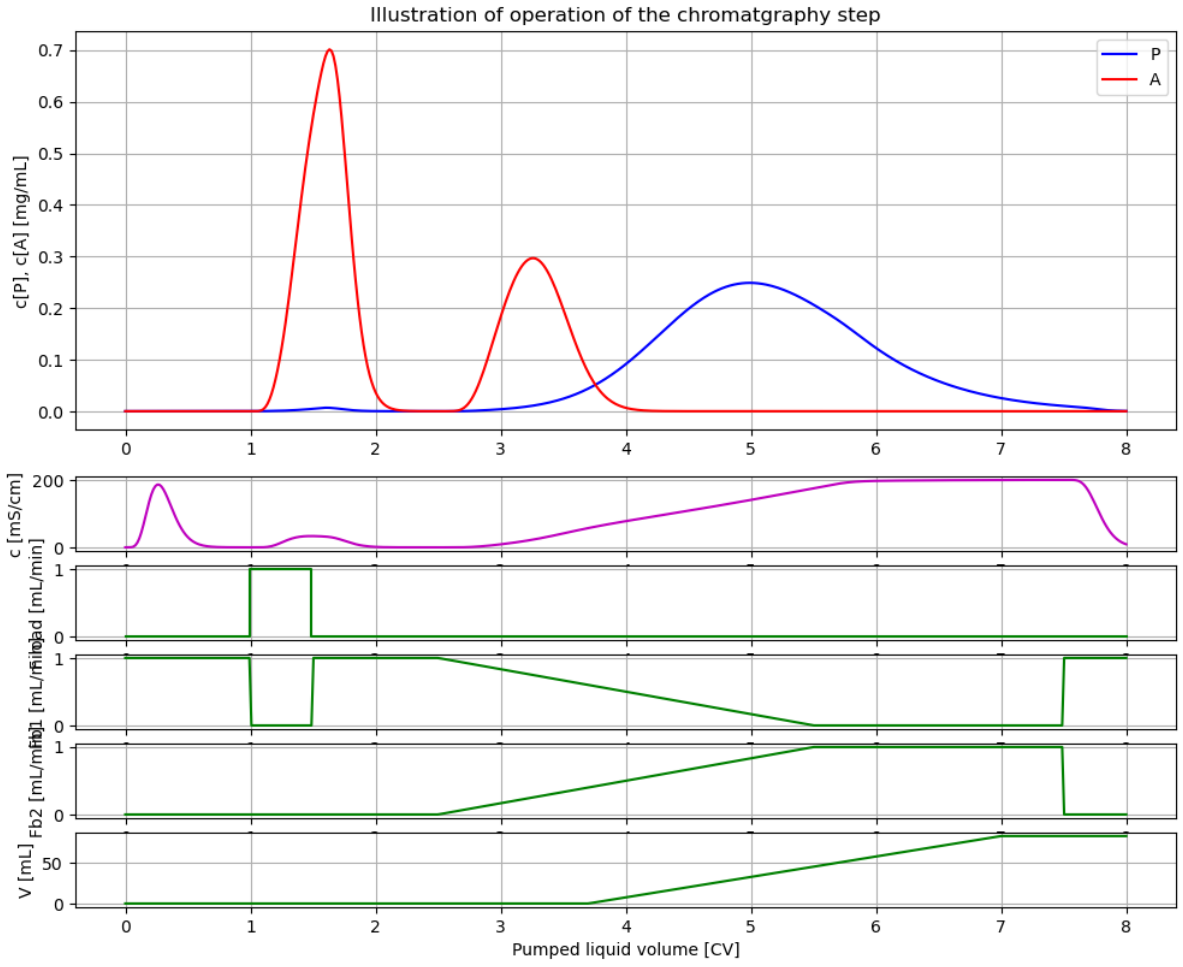
Typical parameters for a pilot scale ion exchange chromatography column proces setup

In [3]:
```
# 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]')
```

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

In [4]:
```
# 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_c
par(height = h)
```

```
par(diameter = d)
par(Q_av = 6.0)

# Remaining salt koncentration in the column from prvious batch and eliminated duri
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 multiple
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_ad
par(stop_desorption=7.5*V)
par(start_pooling=(CV_ekv+CV_ads+CV_wash+CV_start_pool)*V, stop_pooling=(CV_ekv+CV_

# Simulation and plot of results
newplot(title='Illustration of operation of the chromatgraphy step', plotType='Elut
simu((CV_ekv+CV_ads+CV_wash+CV_desorb+CV_wash2)*V/VFR)
```



Comments of steps of operations:

1. Time: 0-1 hours - equilibration.
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.

In [5]:
```
# Check mass-balance of P
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] = [12.42212131]
A_mass [mg] = [12.48878113]
```

Impact of change of binding strength due to pH

In [6]:
```
# Exempel på koppling mellan k1 och olka pI - skrivna så att vi får samma k-värden
pI_P = 8.0
pI_resin = 7.0
pI_A = 8.0

k1_value = 0.3*(pI_P-pI_resin)
k3_value = 0.3*(pI_A-pI_resin)
```

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

In [7]:
```
system_info()
```

```
System information
 -OS: Windows
 -Python: 3.10.6
 -Scipy: not installed in the notebook
 -PyFMI: 2.10.0
 -FMU by: JModelica.org
 -FMI: 2.0
 -Type: FMUModelCS2
 -Name: BPL_IEC.Column_system
 -Generated: 2023-04-21T12:28:38
 -MSL: 3.2.2 build 3
 -Description: Bioprocess Library version 2.1.1
 -Interaction: FMU-explore version 0.9.7
```