

BPL_TEST2_Perfusion - demo

This notebook explore perfusion cultivation in comparison with ordinary continuous cultivation (chemostat) and use comparable settings to earlier notebook. Further you see here examples of interaction with the simplified commands `par()`, `init()`, `simu()` etc as well as direct interaction with the FMU which is called "model" here. The last simulation is always available in the workspace and called "sim_res". Note that `describe()` brings mainly up from descriptive information from the Modelica code from the FMU but is complemented by some information given in the Python setup file.

```
In [1]: run -i BPL_TEST2_Perfusion_fmpy_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 and the command `process_diagram()` brings up the main configuration

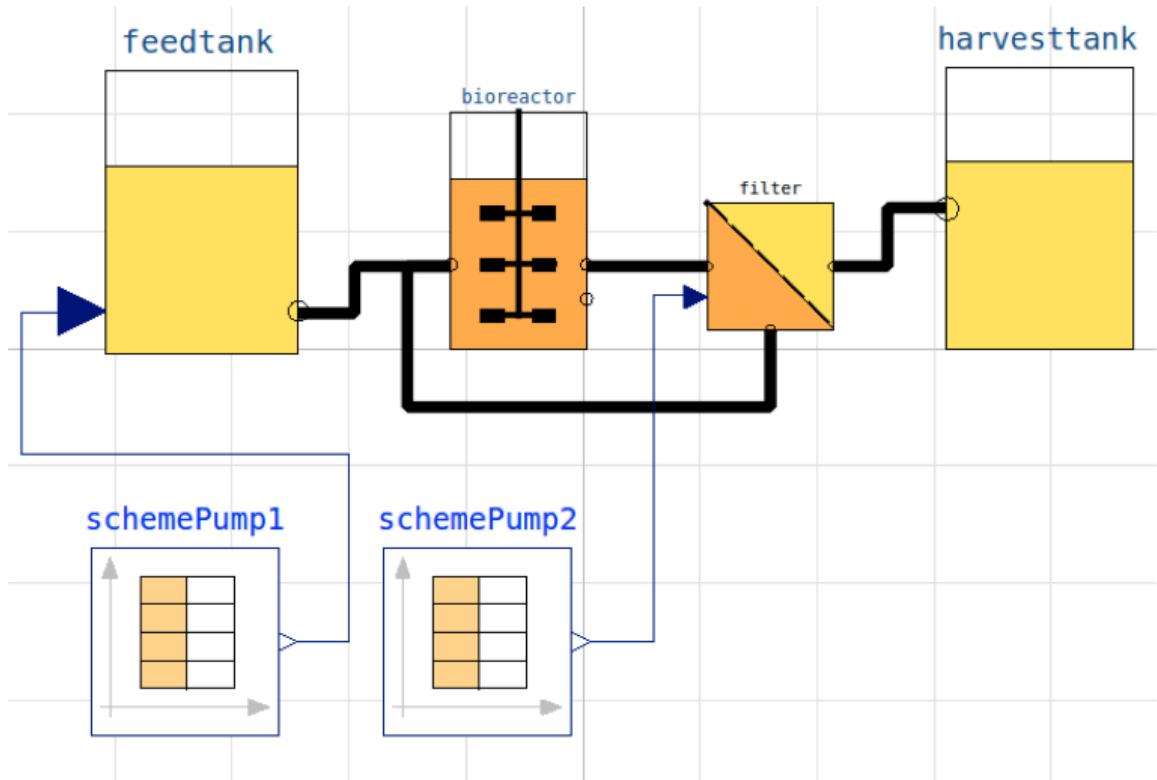
Brief information about a command by `help()`, eg `help(simu)`

Key system information is listed with the command `system_info()`

```
In [2]: %matplotlib inline
plt.rcParams['figure.figsize'] = [25/2.54, 20/2.54]
```

```
In [3]: process_diagram()
```

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



```
In [4]: # Process parameters used throughout
par(Y=0.5, qSmax=0.75, Ks=0.1) # Culture
par(filter_eps=0.10, filter_alpha_X=0.02, filter_alpha_S=0.10) # Filter
par(S_in=30.0) # Inlet subs
init(V_start=1.0, VX_start=1.0) # Process in
eps = parDict['filter_eps'] # Pump sched
```

```
In [5]: # Simulation of process with flow rate clot to wash-out for chemostat

init(VS_start=20) # Process initial
par(pump1_t1=10, pump2_t1=10) # Pump schedule - recyc
par(pump1_F1=2.5*0.155, pump2_F1=2.5*0.155/eps)
par(pump1_t2=940, pump2_t2=940, pump1_t3=950, pump2_t3=950, pump1_t4=960, pump2_

newplot(title='Perfusion cultivation - flow rate corresponding to maximal rate f
simu(5)
```

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  File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\sundials\__init__.py", line 134, in f
    self.set_time(t)
  File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\fmi2.py", line 497, in setTime
    return self.fmi2SetTime(self.component, time)
  File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\fmi2.py", line 215, in w
    raise FMICallException(function=fname, status=res)
fmpy.fmi1.FMICallException: fmi2SetTime failed with status 3 (error).
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```



```

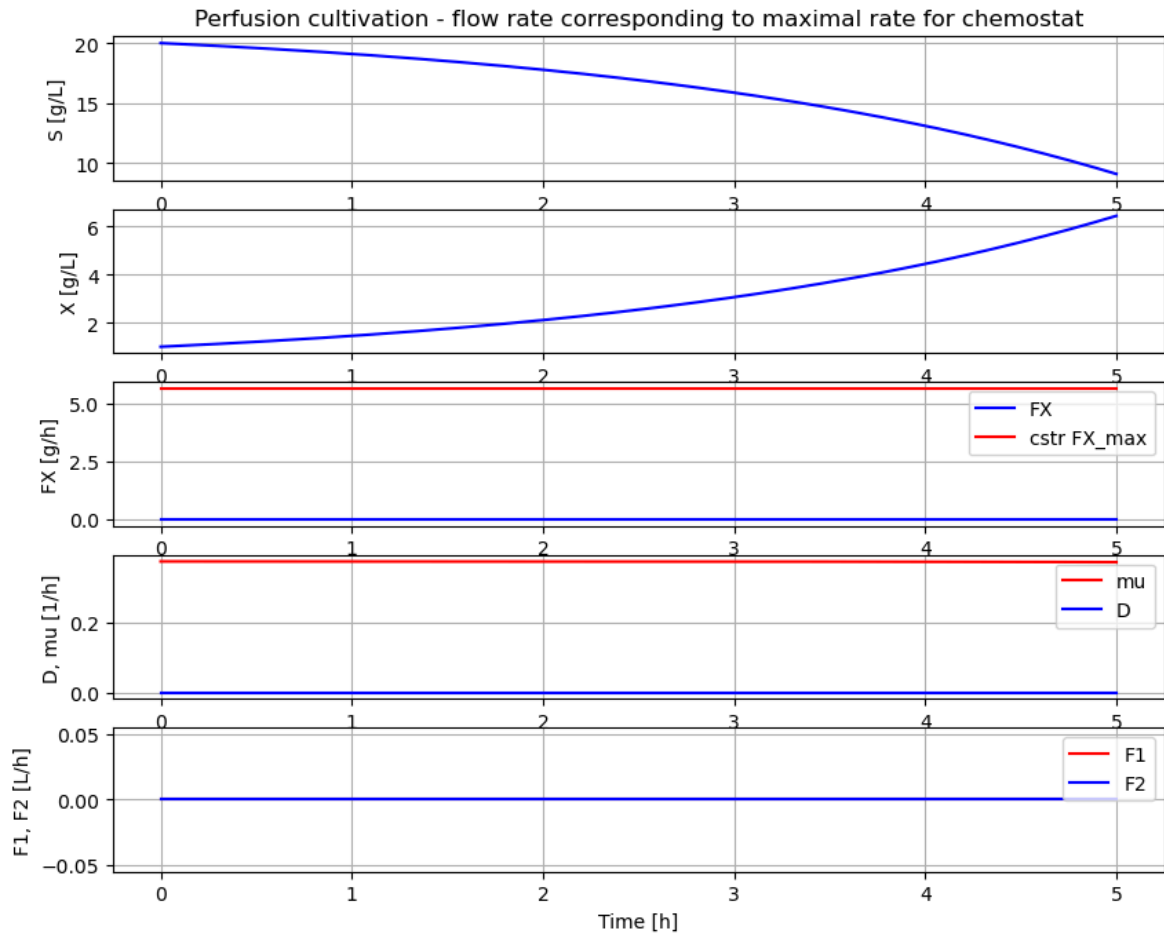
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215, in w
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Exception ignored on calling ctypes callback function: <bound method CCodeSolver.
f of <fmpy.sundials.CCodeSolver object at 0x0000021F785A7E50>>
Traceback (most recent call last):
  File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\sundials\__ini

```

```

t__.py", line 134, in f
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215, in w
    raise FMICallException(function=fname, status=res)
fmpy.fmi1.FMICallException: fmi2SetTime failed with status 3 (error).

```



```
In [6]: # Concentration factor of the filter
c=model_get('filter.retentate.c[1]')/model_get('filter.inlet.c[1]')
print('Conc factor of perfusion filter =', np.round(c,3))
```

Conc factor of perfusion filter = 1.186

```
In [7]: c_data=sim_res['filter.retentate.c[1]']/sim_res['filter.inlet.c[1]']
print('Conc factor variation', np.round(min(c_data[151:]), 3),'to', np.round(max
```

Conc factor variation 1.186 to 1.186

```
In [8]: # Simulation of process with step-wise increase of perfusion rate until wash-out.
# This means that re-circulation rate change at the same time as the perfusion rate

init(VS_start=150) # Process initial variables

par(pump1_t1=12, pump2_t1=12) # Pump schedule - recirculation
par(pump1_F1=2.5*0.155, pump2_F1=2.5*0.155/eps)
par(pump1_t2=22, pump2_t2=22)
par(pump1_F2=2.5*0.35, pump2_F2=2.5*0.35/eps)
par(pump1_t3=32, pump2_t3=32)
par(pump1_F3=2.5*0.63, pump2_F3=2.5*0.63/eps)
par(pump1_t4=42, pump2_t4=42)
par(pump1_F4=2.5*0.83, pump2_F4=2.5*0.83/eps)

newplot(title='Perfusion cultivation - step wise increase of perfusion rate and
simu(60)
```

```

Exception ignored on calling ctypes callback function: <bound method CCodeSolver.
f of <fmpy.sundials.CCodeSolver object at 0x0000021F78A32320>>
Traceback (most recent call last):
  File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\sundials\__ini
t__.py", line 141, in f
    self.get_dx(NV_DATA_S(ydot), self.nx)
  File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\fmi2.py", line
505, in getDerivatives
    return self.fmi2GetDerivatives(self.component, dx, nx)
  File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\fmi2.py", line
215, in w
    raise FMICallException(function=fname, status=res)
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  File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\fmi2.py", line
505, in getDerivatives

```



```
File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\sundials\__init__.py", line 153, in g
    self.get_z(gout, self.nz)
File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\fmi2.py", line 508, in getEventIndicators
    return self.fmi2GetEventIndicators(self.component, z, nz)
File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\fmi2.py", line 215, in w
    raise FMICallException(function=fname, status=res)
fmpy.fmi1.FMICallException: fmi2GetEventIndicators failed with status 3 (error).
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  File "C:\Users\janpa\miniconda3\envs\fmpy\lib\site-packages\fmpy\fmi2.py", line 215, in w
    raise FMICallException(function=fname, status=res)
fmpy.fmi1.FMICallException: fmi2GetEventIndicators failed with status 3 (error).
```

```

-----
FMIException                                         Traceback (most recent call last)
Cell In[8], line 16
    13 par(pump1_F4=2.5*0.83, pump2_F4=2.5*0.83/eps)
    15 newplot(title='Perfusion cultivation - step wise increase of perfusion ra
te and max productivity 4x chemostat')
--> 16 simu(60)

File \\VBoxSvr\Modelica\GitHub\Colab\BPL_TEST2_Perfusion\BPL_TEST2_Perfusion_fmpy
_explore.py:568, in simu(simulationTime, mode, options, diagrams)
    565 start_values = {parLocation[k]:parDict[k] for k in parDict.keys()}
    567 # Simulate
--> 568 sim_res = simulate_fmu(
    569     filename = fmu_model,
    570     validate = False,
    571     start_time = 0,
    572     stop_time = simulationTime,
    573     output_interval = simulationTime/options['ncp'],
    574     record_events = True,
    575     start_values = start_values,
    576     fmi_call_logger = None,
    577     output = list(set(extract_variables(diagrams) + list(stateDict.keys
(()) + key_variables))
    578 )
    580 simulationDone = True
    582 elif mode in ['Continued', 'continued', 'cont']:

File ~\miniconda3\envs\fmpy\lib\site-packages\fmpy\simulation.py:759, in simulate
_fmu(filename, validate, start_time, stop_time, solver, step_size, relative_toler
ance, output_interval, record_events, fmi_type, start_values, apply_default_start
_values, input, output, timeout, debug_logging, visible, logger, fmi_call_logger,
step_finished, model_description, fmu_instance, set_input_derivatives, remote_pla
tform, early_return_allowed, use_event_mode, initialize, terminate, fmu_state, se
t_stop_time)
    757 # simulate_fmu the FMU
    758 if fmi_type == 'ModelExchange':
--> 759     result = simulateME(model_description, fmu, start_time, stop_time, so
lver, step_size, relative_tolerance, start_values, apply_default_start_values, in
put, output, output_interval, record_events, timeout, step_finished, validate, se
t_stop_time)
    760 elif fmi_type == 'CoSimulation':
    761     result = simulateCS(model_description, fmu, start_time, stop_time, re
lative_tolerance, start_values, apply_default_start_values, input, output, output
_interval, timeout, step_finished, set_input_derivatives, use_event_mode, early_r
eturn_allowed, validate, initialize, terminate, set_stop_time)

File ~\miniconda3\envs\fmpy\lib\site-packages\fmpy\simulation.py:1159, in simulat
eME(model_description, fmu, start_time, stop_time, solver_name, step_size, relati
ve_tolerance, start_values, apply_default_start_values, input_signals, output, ou
tput_interval, record_events, timeout, step_finished, validate, set_stop_time)
   1155 recorder.sample(time, force=True)
   1157 if abs(time - round(time / output_interval) * output_interval) < eps and
time > recorder.lastSampleTime + eps:
   1158     # record values for this step
-> 1159     recorder.sample(time, force=True)
   1161 if step_finished is not None and not step_finished(time, recorder):
   1162     break

File ~\miniconda3\envs\fmpy\lib\site-packages\fmpy\simulation.py:165, in Recorde
r.sample(self, time, force)

```



```

163 names, vrs, shapes, nValues, getter = self.info[t]
164 if self.modelDescription.fmiVersion in ['1.0', '2.0']:
--> 165     values = getter(vr=vrs)
166 else:
167     values = getter(vr=vrs, nValues=nValues)

```

File ~\miniconda3\envs\fmipy\lib\site-packages\fmipy\fmipy2.py:293, in _FMU2.getReal(self, vr)

```

291 vr = (fmi2ValueReference * len(vr))(*vr)
292 value = (fmi2Real * len(vr))()
--> 293 self.fmi2GetReal(self.component, vr, len(vr), value)
294 return list(value)

```

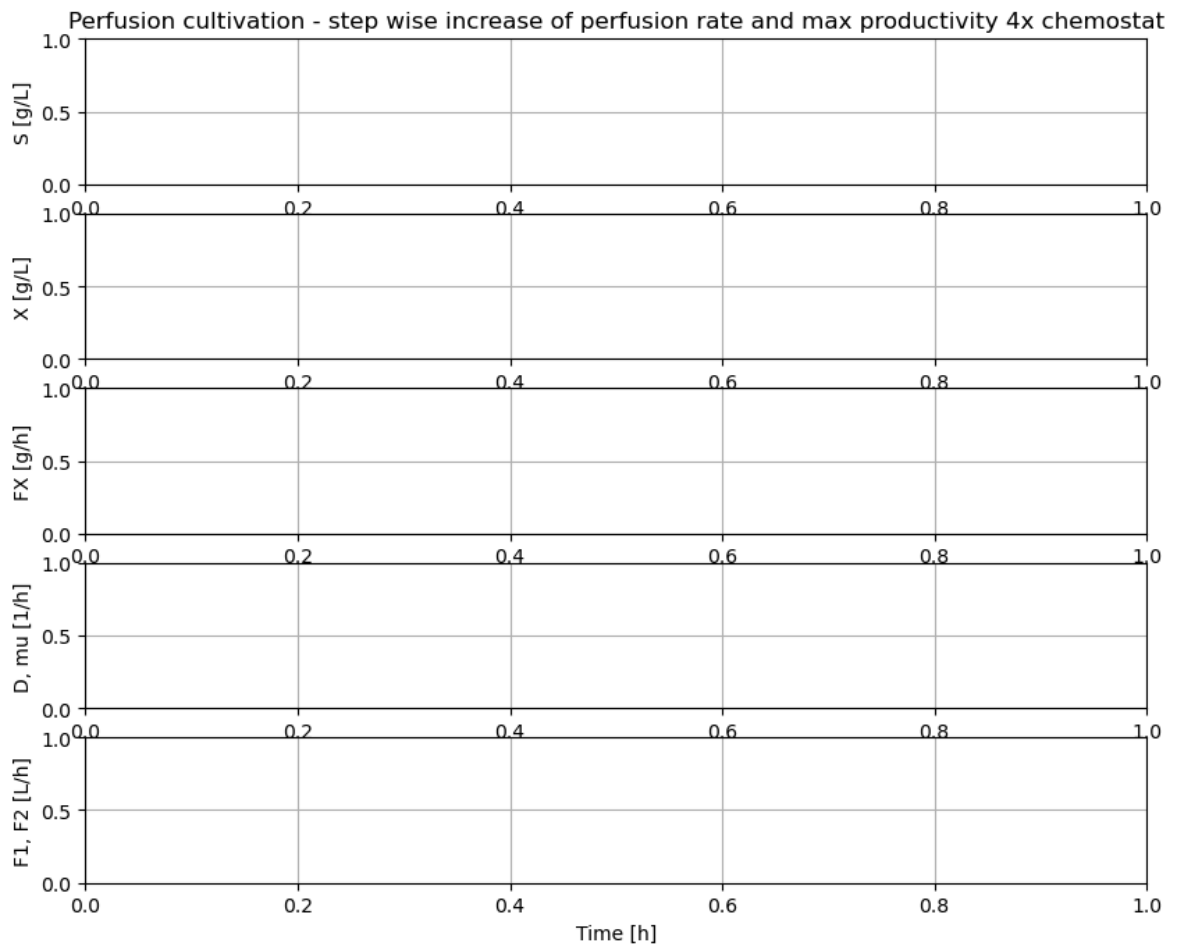
File ~\miniconda3\envs\fmipy\lib\site-packages\fmipy\fmipy2.py:215, in _FMU2._fmi2Function.<locals>.w(*args)

```

212 if restype == fmi2Status: # status code
213     # check the status code
214     if res > fmi2Warning:
--> 215         raise FMICallException(function=fname, status=res)
217 return res

```

FMICallException: fmi2GetReal failed with status 3 (error).



```

In [ ]: # Simulation without a plot and just to check typical values at high production
simu(40)
c_data=sim_res['filter.retentate.c[1]'][304:]/sim_res['filter.inlet.c[1]'][304:]
print('Conc factor variation', np.round(min(c_data[304:]), 3), 'to', np.round(max(c_data[304:]), 3))

```

```

In [ ]: #describe('cstrProdMax')

```

```
In [ ]: # The maximal biomass productivity before washout is obtained around 40 hours
np.round(model_get('harvesttank.inlet.F')*model_get('harvesttank.inlet.c[1]'),1)

In [ ]: # Thus perfusion (with this filter) brings a productivity improvement of about
np.round(23.5/5.6,1)

In [ ]: # Finally we check the filter flow rates at time 40 hour - note the negative sig
model_get('filter.inlet.F')

In [ ]: model_get('filter.filtrate.F')

In [ ]: model_get('filter.retentate.F')
```

Summary

- The perfusion filter had a concentration factor of cells around 1.08 and re-cycling flow was set to a factor 10 higher than the perfusion rate and changed when perfusion rate was change to keep the ratio factor 10.
- The first simulation showed that by cell retention using perfusion filter the process could be run at a perfusion flow rate at the maximal flow rate possible for corresponding chemostat culture and cell concentration increased steadily.
- The second simulation showed that with a proper startup cell concentration, the cell concentration remained constant when perfusion rate increased in a similar way as what we see in a chemostat.
- The second simulation also showed that biomass productivity in this case was increased by a factor 4.2 compared to chemostat.
- If the perfusion rate increased to higher levels washout started but the decrease of cell concentration was slow.

Some of you who read this may have your perfusion experience with CHO-cultures. For such cultures the cell concentration do increase with increase of perfusion rate and there are understood reasons for that. But for this simplified process as well as microbial processes they typically keep cell concentration constant when flow rate is chaged, and that under quite wide conditions. I will try come back to this phenomena in a later notebook.

Appendix

```
In [ ]: disp('culture')

In [ ]: describe('mu')

In [ ]: # List of components in the process setup and also a couple of other things like
describe('parts')

In [ ]: describe('MSL')

In [9]: system_info()
```

System information

- OS: Windows
- Python: 3.10.13
- Scipy: not installed in the notebook
- FMPy: 0.3.19
- FMU by: JModelica.org
- FMI: 2.0
- Type: ME
- Name: BPL_TEST2.Perfusion
- Generated: 2024-03-11T09:55:45
- MSL: 3.2.2 build 3
- Description: Bioprocess Library version 2.1.2 prel
- Interaction: FMU-explore for FMPy version 0.9.9

In []: