BPL_CHO_Perfusion_cspr_openloop script with PyFMI

The key library PyFMI is installed.

After the installation a small application BPL_CHO_Pefusion_cspr_openloop is loaded and run. You can continue with this example if you like.

In [1]:
```
!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
```

In [2]:
```
%env PYTHONPATH=
```

```
env: PYTHONPATH=
```

In [3]:
```
!python --version
```

```
Python 3.11.11
```

In [4]:
```
!wget https://repo.anaconda.com/miniconda/Miniconda3-py311_24.11.1-0-Linux-x86_64.s
!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/')
```

```
--2025-03-26 15:47:30--  https://repo.anaconda.com/miniconda/Miniconda3-py311_24.11.
1-0-Linux-x86_64.sh
Resolving repo.anaconda.com (repo.anaconda.com)... 104.16.32.241, 104.16.191.158, 26
06:4700::6810:bf9e, ...
Connecting to repo.anaconda.com (repo.anaconda.com)|104.16.32.241|: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  77.7MB/s    in 1.8s

2025-03-26 15:47:32 (77.7 MB/s) - 'Miniconda3-py311_24.11.1-0-Linux-x86_64.sh' saved
[145900576/145900576]

PREFIX=/usr/local
Unpacking payload ...

Installing base environment...

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

In [5]:
```
!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-2025.2.25  |      h06a4308_0         129 KB
    certifi-2025.1.31          |  py311h06a4308_0         163 KB
    openssl-3.0.16             |      h5eee18b_0         5.2 MB
    ------------------------------------------------------------
                                           Total:         5.5 MB

The following packages will be UPDATED:

  ca-certificates                    2024.11.26-h06a4308_0 --> 2025.2.25-h06a4308_0
  certifi                      2024.8.30-py311h06a4308_0 --> 2025.1.31-py311h06a4
308_0
  openssl                            3.0.15-h5eee18b_0 --> 3.0.16-h5eee18b_0



Downloading and Extracting Packages:
openssl-3.0.16       | 5.2 MB    | :   0% 0/1 [00:00<?, ?it/s]
certifi-2025.1.31    | 163 KB    | :   0% 0/1 [00:00<?, ?it/s]

ca-certificates-2025 | 129 KB    | :   0% 0/1 [00:00<?, ?it/s]

ca-certificates-2025 | 129 KB    | :  50% 0.49527293063186295/1 [00:00<00:00,  4.71i
t/s]
openssl-3.0.16       | 5.2 MB    | :   2% 0.0178955563700972384/1 [00:00<00:05,  6.08
s/it]

ca-certificates-2025 | 129 KB    | : 100% 1.0/1 [00:00<00:00,  4.71it/s]
certifi-2025.1.31    | 163 KB    | : 100% 1.0/1 [00:00<00:00,  5.51it/s]

ca-certificates-2025 | 129 KB    | : 100% 1.0/1 [00:00<00:00,  4.71it/s]



Preparing transaction: - ▒▒done
Verifying transaction: | ▒▒/ ▒▒- ▒▒done
Executing transaction: | ▒▒done
```

```
In [6]: !conda --version
        !python --version

        conda 24.11.1
        Python 3.11.11

In [7]: !conda config --set channel_priority strict

In [8]: !conda install -c conda-forge pyfmi --yes # Install the key package
```

```
Channels:
 - conda-forge
 - defaults
Platform: linux-64
Collecting package metadata (repodata.json): - ██\ ██| ██/ ██- ██\ ██| ██/ ██- ██\
██| ██/ ██- ██\ ██| ██/ ██- ██\ ██| ██/ ██- ██\ ██| ██/ ██- ██\ ██| ██/ ██- ██\ ██|
██/ ██- ██\ ██| ██/ ██- ██\ ██done
Solving environment: / ██- ██\ ██| ██done

## Package Plan ##

  environment location: /usr/local

  added / updated specs:
    - pyfmi


The following packages will be downloaded:

    package                    |            build
    ---------------------------|-----------------
    _x86_64-microarch-level-3  |      2_broadwell          8 KB   conda-forge
    assimulo-3.6.0             |    py311h083bc19_0        1.1 MB   conda-forge
    certifi-2025.1.31          |      pyhd8ed1ab_0         159 KB   conda-forge
    conda-25.1.1               |    py311h38be061_1        1.1 MB   conda-forge
    fmilib-2.4.1               |        hac33072_1         383 KB   conda-forge
    gmp-6.3.0                  |        hac33072_2         449 KB   conda-forge
    libamd-3.3.3               | haaf9dc3_7100102           49 KB   conda-forge
    libblas-3.9.0              |31_h59b9bed_openblas         16 KB   conda-forge
    libbtf-2.3.2               | h32481e8_7100102           27 KB   conda-forge
    libcamd-3.3.3              | h32481e8_7100102           46 KB   conda-forge
    libcblas-3.9.0             |31_he106b2a_openblas         16 KB   conda-forge
    libccolamd-3.3.4           | h32481e8_7100102           42 KB   conda-forge
    libcholmod-5.3.1           | h59ddab4_7100102          1.1 MB   conda-forge
    libcolamd-3.3.4            | h32481e8_7100102           33 KB   conda-forge
    libcxsparse-4.4.1          | h32481e8_7100102          118 KB   conda-forge
    libgcc-14.2.0              |        h767d61c_2         828 KB   conda-forge
    libgcc-ng-14.2.0           |        h69a702a_2          52 KB   conda-forge
    libgfortran-14.2.0         |        h69a702a_2          52 KB   conda-forge
    libgfortran-ng-14.2.0      |        h69a702a_2          53 KB   conda-forge
    libgfortran5-14.2.0        |        hf1ad2bd_2         1.4 MB   conda-forge
    libgomp-14.2.0             |        h767d61c_2         449 KB   conda-forge
    libklu-2.3.5               | hf24d653_7100102          142 KB   conda-forge
    liblapack-3.9.0            |31_h7ac8fdf_openblas         16 KB   conda-forge
    libldl-3.3.2               | h32481e8_7100102           24 KB   conda-forge
    libopenblas-0.3.29         |pthreads_h94d23a6_0        5.6 MB   conda-forge
    libparu-1.0.0              | h17147ab_7100102           91 KB   conda-forge
    librbio-4.3.4              | h32481e8_7100102           47 KB   conda-forge
    libspex-3.2.3              | had10066_7100102           79 KB   conda-forge
    libspqr-4.3.4              | h852d39f_7100102          213 KB   conda-forge
    libstdcxx-14.2.0           |        h8f9b012_2         3.7 MB   conda-forge
    libstdcxx-ng-14.2.0        |        h4852527_2          53 KB   conda-forge
    libsuitesparseconfig-7.10.1| h92d6892_7100102           42 KB   conda-forge
    libumfpack-6.3.5           | heb53515_7100102          424 KB   conda-forge
    metis-5.1.0                |      hd0bcaf9_1007        3.7 MB   conda-forge
    mpfr-4.2.1                 |        h90cbb55_3         620 KB   conda-forge
```

```
        numpy-2.2.4                |    py311h5d046bc_0          8.6 MB  conda-forge
        openssl-3.4.1              |         h7b32b05_0          2.8 MB  conda-forge
        pyfmi-2.16.3               |    py311h9f3472d_0          5.2 MB  conda-forge
        python_abi-3.11            |            2_cp311             5 KB  conda-forge
        scipy-1.15.2               |    py311h8f841c2_0         16.4 MB  conda-forge
        suitesparse-7.10.1         |  ha0f6916_7100102            12 KB  conda-forge
        sundials-7.1.1             |         ha52427a_0          907 KB  conda-forge
        ------------------------------------------------------------
                                           Total:          56.1 MB

The following NEW packages will be INSTALLED:

  _x86_64-microarch~  conda-forge/noarch::_x86_64-microarch-level-3-2_broadwell
  assimulo            conda-forge/linux-64::assimulo-3.6.0-py311h083bc19_0
  fmilib              conda-forge/linux-64::fmilib-2.4.1-hac33072_1
  gmp                 conda-forge/linux-64::gmp-6.3.0-hac33072_2
  libamd              conda-forge/linux-64::libamd-3.3.3-haaf9dc3_7100102
  libblas             conda-forge/linux-64::libblas-3.9.0-31_h59b9bed_openblas
  libbtf              conda-forge/linux-64::libbtf-2.3.2-h32481e8_7100102
  libcamd             conda-forge/linux-64::libcamd-3.3.3-h32481e8_7100102
  libcblas            conda-forge/linux-64::libcblas-3.9.0-31_he106b2a_openblas
  libccolamd          conda-forge/linux-64::libccolamd-3.3.4-h32481e8_7100102
  libcholmod          conda-forge/linux-64::libcholmod-5.3.1-h59ddab4_7100102
  libcolamd           conda-forge/linux-64::libcolamd-3.3.4-h32481e8_7100102
  libcxsparse         conda-forge/linux-64::libcxsparse-4.4.1-h32481e8_7100102
  libgcc              conda-forge/linux-64::libgcc-14.2.0-h767d61c_2
  libgfortran         conda-forge/linux-64::libgfortran-14.2.0-h69a702a_2
  libgfortran-ng      conda-forge/linux-64::libgfortran-ng-14.2.0-h69a702a_2
  libgfortran5        conda-forge/linux-64::libgfortran5-14.2.0-hf1ad2bd_2
  libklu              conda-forge/linux-64::libklu-2.3.5-hf24d653_7100102
  liblapack           conda-forge/linux-64::liblapack-3.9.0-31_h7ac8fdf_openblas
  libldl              conda-forge/linux-64::libldl-3.3.2-h32481e8_7100102
  libopenblas         conda-forge/linux-64::libopenblas-0.3.29-pthreads_h94d23a6_0
  libparu             conda-forge/linux-64::libparu-1.0.0-h17147ab_7100102
  librbio             conda-forge/linux-64::librbio-4.3.4-h32481e8_7100102
  libspex             conda-forge/linux-64::libspex-3.2.3-had10066_7100102
  libspqr             conda-forge/linux-64::libspqr-4.3.4-h852d39f_7100102
  libstdcxx           conda-forge/linux-64::libstdcxx-14.2.0-h8f9b012_2
  libsuitesparsecon~  conda-forge/linux-64::libsuitesparseconfig-7.10.1-h92d6892_7100
102
  libumfpack          conda-forge/linux-64::libumfpack-6.3.5-heb53515_7100102
  metis               conda-forge/linux-64::metis-5.1.0-hd0bcaf9_1007
  mpfr                conda-forge/linux-64::mpfr-4.2.1-h90cbb55_3
  numpy               conda-forge/linux-64::numpy-2.2.4-py311h5d046bc_0
  pyfmi               conda-forge/linux-64::pyfmi-2.16.3-py311h9f3472d_0
  python_abi          conda-forge/linux-64::python_abi-3.11-2_cp311
  scipy               conda-forge/linux-64::scipy-1.15.2-py311h8f841c2_0
  suitesparse         conda-forge/linux-64::suitesparse-7.10.1-ha0f6916_7100102
  sundials            conda-forge/linux-64::sundials-7.1.1-ha52427a_0

The following packages will be UPDATED:

  conda               pkgs/main::conda-24.11.1-py311h06a430~ --> conda-forge::conda-2
5.1.1-py311h38be061_1
  libgcc-ng           pkgs/main::libgcc-ng-11.2.0-h1234567_1 --> conda-forge::libgcc-
ng-14.2.0-h69a702a_2
```

```
  libgomp              pkgs/main::libgomp-11.2.0-h1234567_1 --> conda-forge::libgomp
-14.2.0-h767d61c_2
  libstdcxx-ng         pkgs/main::libstdcxx-ng-11.2.0-h12345~ --> conda-forge::libstdc
xx-ng-14.2.0-h4852527_2
  openssl              pkgs/main::openssl-3.0.16-h5eee18b_0 --> conda-forge::openssl
-3.4.1-h7b32b05_0

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

  certifi              pkgs/main/linux-64::certifi-2025.1.31~ --> conda-forge/noarch::
certifi-2025.1.31-pyhd8ed1ab_0


Downloading and Extracting Packages:
scipy-1.15.2          | 16.4 MB   | :    0% 0/1 [00:00<?, ?it/s]
numpy-2.2.4           | 8.6 MB    | :    0% 0/1 [00:00<?, ?it/s]

libopenblas-0.3.29    | 5.6 MB    | :    0% 0/1 [00:00<?, ?it/s]


pyfmi-2.16.3          | 5.2 MB    | :    0% 0/1 [00:00<?, ?it/s]


metis-5.1.0           | 3.7 MB    | :    0% 0/1 [00:00<?, ?it/s]



libstdcxx-14.2.0      | 3.7 MB    | :    0% 0/1 [00:00<?, ?it/s]



openssl-3.4.1         | 2.8 MB    | :    0% 0/1 [00:00<?, ?it/s]



libgfortran5-14.2.0   | 1.4 MB    | :    0% 0/1 [00:00<?, ?it/s]




conda-25.1.1          | 1.1 MB    | :    0% 0/1 [00:00<?, ?it/s]
```

```
assimulo-3.6.0          | 1.1 MB    | :   0% 0/1 [00:00<?, ?it/s]

libcholmod-5.3.1        | 1.1 MB    | :   0% 0/1 [00:00<?, ?it/s]

sundials-7.1.1          | 907 KB    | :   0% 0/1 [00:00<?, ?it/s]

libgcc-14.2.0           | 828 KB    | :   0% 0/1 [00:00<?, ?it/s]

mpfr-4.2.1              | 620 KB    | :   0% 0/1 [00:00<?, ?it/s]
```

```
gmp-6.3.0                  | 449 KB    | :    0% 0/1 [00:00<?, ?it/s]

libgomp-14.2.0             | 449 KB    | :    0% 0/1 [00:00<?, ?it/s]

libumfpack-6.3.5           | 424 KB    | :    0% 0/1 [00:00<?, ?it/s]
```

```
fmilib-2.4.1          | 383 KB    | :   0% 0/1 [00:00<?, ?it/s]




libspqr-4.3.4         | 213 KB    | :   0% 0/1 [00:00<?, ?it/s]




scipy-1.15.2          | 16.4 MB   | :   0% 0.0019058779654147827/1 [00:00<00:56, 57.0
5s/it]
numpy-2.2.4           | 8.6 MB    | :   0% 0.0018194029373407579/1 [00:00<01:05, 65.5
7s/it]




metis-5.1.0           | 3.7 MB    | :   0% 0.004175799528999174/1 [00:00<00:26, 26.70
s/it]


pyfmi-2.16.3          | 5.2 MB    | :   0% 0.002983953056648666/1 [00:00<00:38, 39.10
s/it]

scipy-1.15.2          | 16.4 MB   | :  16% 0.1629525660429639/1 [00:00<00:00,  1.09s/
it]
numpy-2.2.4           | 8.6 MB    | :  24% 0.2419805906663208/1 [00:00<00:00,  1.32i
t/s]
```

```
metis-5.1.0         | 3.7 MB   | :  59% 0.5929635331178827/1 [00:00<00:00,  3.31i
t/s]


pyfmi-2.16.3        | 5.2 MB   | :  44% 0.4386410993273539/1 [00:00<00:00,  2.41i
t/s]

libopenblas-0.3.29  | 5.6 MB   | :  43% 0.4345603728015937/1 [00:00<00:00,  2.24i
t/s]



scipy-1.15.2        | 16.4 MB  | :  33% 0.3306698269994648/1 [00:00<00:00,  1.25i
t/s]
numpy-2.2.4         | 8.6 MB   | :  58% 0.5767507311370202/1 [00:00<00:00,  2.19i
t/s]




libstdcxx-14.2.0    | 3.7 MB   | :   0% 0.0042177278432850495/1 [00:00<01:24, 85.2
0s/it]


pyfmi-2.16.3        | 5.2 MB   | : 100% 1.0/1 [00:00<00:00,  2.97it/s]


scipy-1.15.2        | 16.4 MB  | :  53% 0.5326928913334318/1 [00:00<00:00,  1.55i
t/s]
numpy-2.2.4         | 8.6 MB   | :  95% 0.9479089303545348/1 [00:00<00:00,  2.77i
t/s]




openssl-3.4.1       | 2.8 MB   | :   1% 0.00557410490775713766/1 [00:00<01:17, 77.9
8s/it]




libstdcxx-14.2.0    | 3.7 MB   | :  75% 0.7507555561047389/1 [00:00<00:00,  2.13i
t/s]


libopenblas-0.3.29  | 5.6 MB   | : 100% 1.0/1 [00:00<00:00,  2.21it/s]

scipy-1.15.2        | 16.4 MB  | :  70% 0.6994572133072252/1 [00:00<00:00,  1.52i
t/s]
```

```
openssl-3.4.1         | 2.8 MB     | :   97% 0.9698942539497418/1 [00:00<00:00,  2.39i
t/s]



libgfortran5-14.2.0   | 1.4 MB     | :    1% 0.011206734985068174/1 [00:00<00:47, 48.20
s/it]



scipy-1.15.2          | 16.4 MB    | :   88% 0.8776568030735074/1 [00:00<00:00,  1.60i
t/s]



openssl-3.4.1         | 2.8 MB     | : 100% 1.0/1 [00:00<00:00,  2.39it/s]



libgfortran5-14.2.0   | 1.4 MB     | : 100% 1.0/1 [00:00<00:00, 48.20s/it]



conda-25.1.1          | 1.1 MB     | :    1% 0.013622478419712683/1 [00:00<00:46, 46.85
s/it]
numpy-2.2.4           | 8.6 MB     | : 100% 1.0/1 [00:00<00:00,  2.77it/s]



libcholmod-5.3.1      | 1.1 MB     | :    1% 0.014870549794649543/1 [00:00<00:45, 45.97
s/it]
```

```
assimulo-3.6.0      | 1.1 MB    | :    1% 0.014703493605362324/1 [00:00<00:46, 47.11
s/it]


conda-25.1.1        | 1.1 MB    | : 100% 1.0/1 [00:00<00:00, 46.85s/it]


sundials-7.1.1      | 907 KB    | :    2% 0.017633738300085844/1 [00:00<00:40, 41.06
s/it]


metis-5.1.0         | 3.7 MB    | : 100% 1.0/1 [00:00<00:00,  1.23it/s]


metis-5.1.0         | 3.7 MB    | : 100% 1.0/1 [00:00<00:00,  1.23it/s]


libcholmod-5.3.1    | 1.1 MB    | : 100% 1.0/1 [00:00<00:00, 45.97s/it]


sundials-7.1.1      | 907 KB    | : 100% 1.0/1 [00:00<00:00, 41.06s/it]
```

```
libgcc-14.2.0        | 828 KB    | :   2% 0.019323375221875561/1 [00:00<00:39, 40.36
s/it]

assimulo-3.6.0       | 1.1 MB    | : 100% 1.0/1 [00:00<00:00,  1.70it/s]

assimulo-3.6.0       | 1.1 MB    | : 100% 1.0/1 [00:00<00:00,  1.70it/s]

libgcc-14.2.0        | 828 KB    | : 100% 1.0/1 [00:00<00:00, 40.36s/it]

mpfr-4.2.1           | 620 KB    | :   3% 0.025811696239942908/1 [00:00<00:30, 31.72
s/it]
```

```
gmp-6.3.0                | 449 KB   | :   4% 0.03561313321233331/1 [00:00<00:22, 23.12
s/it]
```

```
gmp-6.3.0                | 449 KB   | : 100% 1.0/1 [00:00<00:00, 23.12s/it]
```

```
libgomp-14.2.0           | 449 KB   | :   4% 0.03562807972826631/1 [00:00<00:22, 23.64
s/it]
```

```
libumfpack-6.3.5      | 424 KB     | :    4% 0.037731330084655984/1 [00:00<00:22, 23.00
s/it]
```

```
libgomp-14.2.0        | 449 KB     | : 100% 1.0/1 [00:00<00:00, 23.64s/it]
```

```
mpfr-4.2.1            | 620 KB     | : 100% 1.0/1 [00:00<00:00, 31.72s/it]
```

```
libumfpack-6.3.5      | 424 KB     | : 100% 1.0/1 [00:00<00:00, 23.00s/it]
```

```
fmilib-2.4.1          | 383 KB    | :    4% 0.04180391656566945/1 [00:00<00:20, 21.51
s/it]


pyfmi-2.16.3          | 5.2 MB    | : 100% 1.0/1 [00:00<00:00,  2.97it/s]
```

```
fmilib-2.4.1          | 383 KB    | : 100% 1.0/1 [00:00<00:00, 21.51s/it]
```

```
libspqr-4.3.4         | 213 KB    | :    8% 0.07503068271326775/1 [00:00<00:11, 12.36
s/it]
```

```
        ... (more hidden) ...




        ... (more hidden) ...









scipy-1.15.2           | 16.4 MB   | : 100% 1.0/1 [00:01<00:00,  1.60it/s]




libstdcxx-14.2.0       | 3.7 MB    | : 100% 1.0/1 [00:01<00:00,  2.13it/s]

libopenblas-0.3.29     | 5.6 MB    | : 100% 1.0/1 [00:01<00:00,  2.21it/s]
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libgfortran5-14.2.0  | 1.4 MB     | : 100% 1.0/1 [00:01<00:00,  1.30s/it]

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openssl-3.4.1        | 2.8 MB     | : 100% 1.0/1 [00:01<00:00,  2.39it/s]

conda-25.1.1         | 1.1 MB     | : 100% 1.0/1 [00:01<00:00,  1.72s/it]

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assimulo-3.6.0        | 1.1 MB    | : 100% 1.0/1 [00:02<00:00,  1.70it/s]


libgcc-14.2.0         | 828 KB    | : 100% 1.0/1 [00:02<00:00,  2.16s/it]


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libgomp-14.2.0        | 449 KB    | : 100% 1.0/1 [00:02<00:00,  2.37s/it]




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libumfpack-6.3.5      | 424 KB    | : 100% 1.0/1 [00:02<00:00,  2.41s/it]
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fmilib-2.4.1          | 383 KB    | : 100% 1.0/1 [00:02<00:00,  2.48s/it]




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libspqr-4.3.4        | 213 KB    | : 100% 1.0/1 [00:02<00:00,  2.55s/it]




libspqr-4.3.4        | 213 KB    | : 100% 1.0/1 [00:02<00:00,  2.55s/it]
scipy-1.15.2         | 16.4 MB   | : 100% 1.0/1 [00:04<00:00,  1.60it/s]
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Verifying transaction: / ░░- ░░\ ░░| ░░/ ░░done
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```

BPL_CHO_Perfusion_cspr_openloop setup

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

- FMU - BPL_CHO_Perfusion_cspr_openloop_linux_om_me.fmu
- Setup-file - BPL_CHO_Perfusion_cspr_openloop_explore

In [9]:
```python
# Filter out DepracationWarnings for 'np.float as alias' is needed - wish I could m
import warnings
warnings.filterwarnings("ignore")
```

In [10]:
```bash
%%bash
git clone https://github.com/janpeter19/BPL_CHO_Perfusion_cspr
```

```
Cloning into 'BPL_CHO_Perfusion_cspr'...
```

```
In [11]:  %cd BPL_CHO_Perfusion_cspr
```

/content/BPL_CHO_Perfusion_cspr

BPL CHO Perfusion cspr openloop - demo

Author: Jan Peter Axelsson

This notebook is about CHO perfusion cultivation and focus on the concept of Cell Specific Perfusion Rate (CSPR). Recombinant protein production is included in the model but not shown in the diagrams here.

The model used here was orignally developed and validated for fed-batch cultivation of CHO cultures [1], but also got some influence from perfusion cultivation [2]. The model emphasize the bottlenecks of metabolism and growth and inspired from similar models of microbial cultures. One interesting aspect is that the model brings a theoretical base for the usefulness of the CSPR concept often used experimentally [4] and [5]. The results of simulation shown here are in accordance with experiments in a qualititative way, howerver not tested more quantitatively, to the authors knowledge.

The main result is that when the perfusion rate should be increased from one set-point to another, it should be changed slowly. An abrupt step-wise increase should be avoided. A slow increase in the pefusion rate minimize the risk of unnecessary by-product formation of lactate and amonia and make the culture increase in cell concentration quicker to a new steady-state compared to a step-wise perfusion rate change. The rate of change of perfusion rate should not exceed the maximal culture growth rate.

The strategy to limit rate of change of perfusion rate is much more important for mammalian cultures than for microbial cultures. The reason is that mammalian cell cutures increase in cell density after an inrease in perfusion rate, while mibrobial cultures remains constant in cell density. This difference is most likely due to the fact that maintenance metabolism is a larger part in mammalian cultures and at higher growth rates the percentage of maintenance becomes smaller and the overall yield increase, while microbial cultures has a much more contsant yield over a broad range of growth rates. These ideas are discussed in section 2.2 in [3], together with other insights into perfusion cultivation obtained from simulation studies of the current model.

Once again, it would be good to compare simulations with relevant experimental data from perfusion cultivation. Hopefully, the material presented here can stimulate work in this direction.

Setup of the simulation model

```
In [12]:  run -i BPL_CHO_perfusion_cspr_openloop_explore.py
```

```
Linux - run FMU pre-compiled OpenModelica

Model for the process 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 [13]:
```python
%matplotlib inline
plt.rcParams['figure.figsize'] = [25/2.54, 20/2.54]
```

About the process model

Here a process diagram is shown of the process. Further information about the culutre
stored in the model code is extracted.

In [14]:
```python
process_diagram()
```

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

In [15]: ```
describe('culture'); print(); #describe('liquidphase')
```

Reactor culture CHO-MAb - cell line HB-58 American Culture Collection ATCC

## Simulaton study

The simulations are run with default parameters from [1]. The parameters for the change of perfusion rate is done here. The parameter mu_ref gives the rate of increase in [1/h]. With the value mu_ref=1 you get an abrupt step directly to the set-point. The parameters F1 and F2 give the flow rate [L/h] before and after the change. The corresponding time parameters t1 and t2 are given by default.

In [16]: ```
newplot('Perfusion cultivation', plotType='Extended')

par(samplePeriod=1); par(F1=0.0020, F2=0.030)    # General parameters
par(mu_ref=0.04); simu()                         # First simulation (solid)
par(mu_ref=1); simu()                            # Second simulation (dashed)
```

Perfusion cultivation
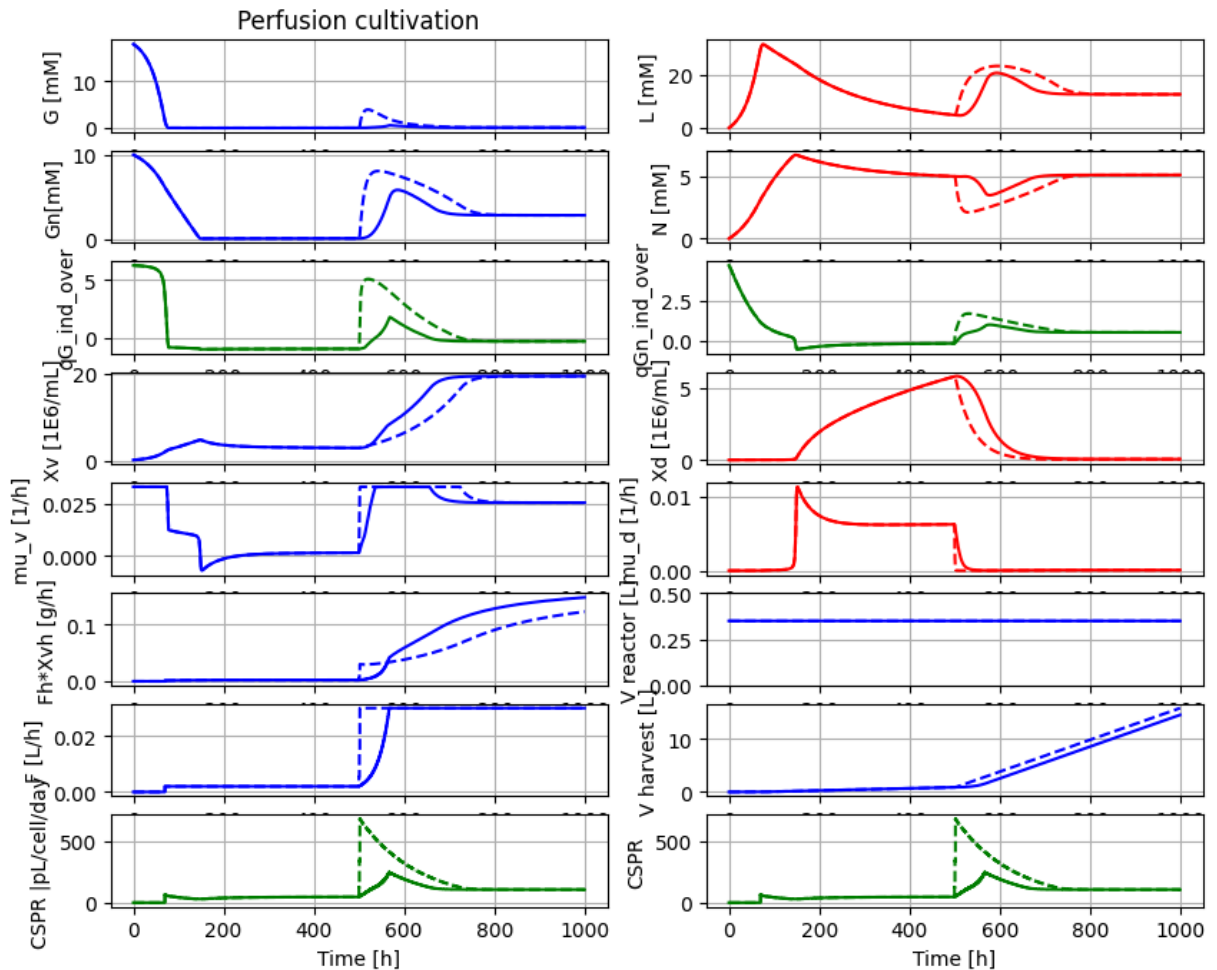
We see here the shorter settling time for cell conc Xv when the slower exponential increase of perfusion rate is used, compared to an abrupt change.

The different sets of parameters that can be changed are shown below

In [17]: `disp(mode='long')`

```
bioreactor.V_start : V_start : 0.35
bioreactor.m_start[1] : VXv_start : 0.07
bioreactor.m_start[2] : VXd_start : 0.0
bioreactor.m_start[3] : VXl_start : 0.0
bioreactor.m_start[4] : VG_start : 6.3
bioreactor.m_start[5] : VGn_start : 3.5
bioreactor.m_start[6] : VL_start : 0.0
bioreactor.m_start[7] : VN_start : 0.0
bioreactor.culture.qG_max1 : qG_max1 : 0.297
bioreactor.culture.qG_max2 : qG_max2 : 0.038
bioreactor.culture.qGn_max1 : qGn_max1 : 0.124
bioreactor.culture.qGn_max2 : qGn_max2 : 0.022
bioreactor.culture.mu_d_max : mu_d_max : 0.13
bioreactor.culture.k_toxic : k_toxic : 0.0
bioreactor.culture.alpha : alpha : 0.0
bioreactor.culture.beta : beta : 0.417
bioreactor.broth_decay.k_lysis_v : k_lysis_v : 0.0
bioreactor.broth_decay.k_lysis_d : k_lysis_d : 0.0
filter.eps : eps : 0.1
filter.alpha[1] : alpha_Xv : 0.03
filter.alpha[2] : alpha_Xd : 0.03
filter.alpha[3] : alpha_Xl : 0.1
filter.alpha[4] : alpha_G : 0.1
filter.alpha[5] : alpha_Gn : 0.1
filter.alpha[6] : alpha_L : 0.1
filter.alpha[7] : alpha_N : 0.1
filter.alpha[8] : alpha_Pr : 0.1
feedtank.c_in[4] : G_in : 15.0
feedtank.c_in[5] : Gn_in : 11.0
cspr_openloop.samplePeriod : samplePeriod : 1.0
cspr_openloop.mu_ref : mu_ref : 1.0
cspr_openloop.t1 : t1 : 70.0
cspr_openloop.F1 : F1 : 0.002
cspr_openloop.t2 : t2 : 500.0
cspr_openloop.F2 : F2 : 0.03
```
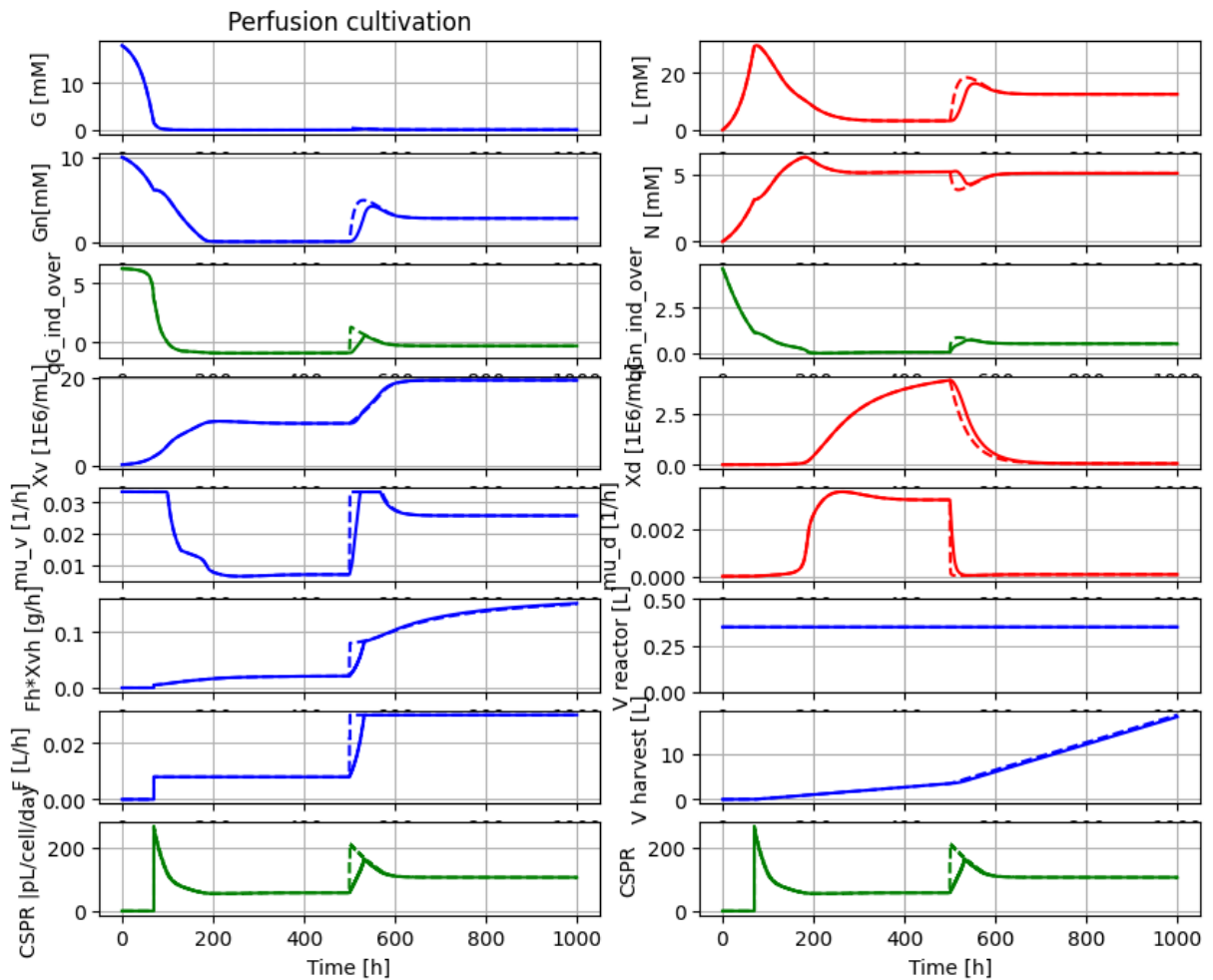
Some other important parameters for information, but cannot be changed.

In [18]: `describe('bioreactor.broth_decay.k_decay')`

```
Rate of decay of viable cells : 0.0 [ 1E9 cells/(L*h) ]
```

In [19]: `describe('k_lysis_d')`

```
Specific rate of lysis of dead cells : 0.0 [ 1/h ]
```

Now a new simulation where the flow rate F1 is higher before change to the new set-point F2.

In [20]:
```
newplot('Perfusion cultivation', plotType='Extended')

par(samplePeriod=1); par(F1=0.0080, F2=0.03)     # General parameters
par(mu_ref=0.04); simu()                          # First simulation (solid)
par(mu_ref=1); simu()                             # Second simulation (dashed)
```

Perfusion cultivation

We see that a somewhat smaller change in perfusion rate make the differnce in settling time of Xv for the two strategies to almost disappear.

Summary

The simulation study shows that a slow increase in the perfusion rate that match the maximal culture growth rate gives a quicker increase in cell density than an abrupt step-wise change of perfusion rate.

The effect is more pronounced for a larger change of perfusion rate than for a smaller.

Here the change of perfusion rate was done usering a pre-calculated exponential scheme, i.e. open-loop control. A more robust method would be to measure the cell concentration on-line and adjust the perfusion rate change to more exactly maintan constant CSPR.

It is of interest to confirm the results with experimental data.

References

[1] Amribt, Z., Niu, H. and Bogaerts P.: "Macroscopic modelling of overflow metabolism and model based optimization of hybridoma cell fed-batch cultures.", Biochem. Eng. Journal, 2013.

[2] Niu,H., Amribt, Z., Fickers, P., Tan, W. and Bogaerts P.: "Metabolic pathway analysis and reduction for mammalian cell cultures - towards macroscopic modelling", Chem. Eng. Science, 2013.

[3] Axelsson, J. P.: "Simplified model of CHO-cultivation in Bioproces Library for Modelica - some experience", conference paper 22nd NPCW Lyngby, Denmark, August 22-23, 2019.

[4] Hu, W-S: "Cell culture bioprocess engineering", 2nd edition, CRC Press, 2020.

[5] Konstantinov, K. et al: "The push-to-low" approach for optimization of high density perfusion cultures of animal cells", Adv Biochem Engin/Biotechnol, 2006.

Appendix

In [21]:
```
describe('parts')
```

```
['bioreactor', 'bioreactor.broth_decay', 'bioreactor.culture', 'CSPR', 'cspr_openloop', 'D', 'feedtank', 'filter', 'harvesttank']
```

In [22]:
```
describe('MSL')
```

```
MSL: 3.2.3 - used components: RealInput, RealOutput
```

In [23]:
```
system_info()
```

```
System information
 -OS: Linux
 -Python: 3.11.11
 -Scipy: not installed in the notebook
 -PyFMI: 2.16.3
 -FMU by: OpenModelica Compiler OpenModelica 1.25.0~dev-422-ge7d6d52
 -FMI: 2.0
 -Type: FMUModelME2
 -Name: BPL_CHO.Perfusion_cspr_openloop
 -Generated: 2025-03-03T07:33:31Z
 -MSL: 3.2.3
 -Description: Bioprocess Library version 2.3.0
 -Interaction: FMU-explore version 1.0.0
```