Simple Tutorial

for

Circulatory Model Code

Writen by Ata Moradi

26/09/2022

Initializing and startup:

The main project must be run in the Linux operating system, Although you can install the virtual machine in windows and then install the Linux in the virtual machine. One of these virtual machines is VirtualBox Oracle which you can download from the below link:

https://www.virtualbox.org/

Also, you can download the latest version of Ubuntu using this link:

https://ubuntu.com/download/desktop

Then, you need to install openCOR software from this link:

https://opencor.ws/downloads/index.html

And there is a good tutorial PDF that includes many examples, which you can download here:

Download openCOR tutorial

For cloning or pulling the project, the latest version of the code is available on GitHub:

https://github.com/FinbarArgus/circulatory autogen

Note:

If you did not work with git and GitHub, firstly download the git, install it in your windows, and then open the empty folder on your computer. Next, open the terminal and write these commands to clone the project on your pc:

Git init

Git remote add origin https://github.com/FinbarArgus/circulatory_autogen
Git clone https://github.com/FinbarArgus/circulatory_autogen

Directory Definition:

In this tutorial, we use one particular directory for our project, but it can be different on every computer, So the base directory is defined as "MainDir" in all parts. For example, on our computer, this directory is as below:

MainDir: Home/.../Desktop/

The project directory (ProjectDir) is the directory we cloned from the GitHub Circulatory_autogen project to our computer. For example, on our computer:

<u>ProjectDir: Home/.../Desktop/Project/Circulatory_autogen</u>

Also, OpenCOR files directory is needed for opening the project and installing the python and pythonshell, and we show with OpenCOR_dir, which is below on our pc:

OpenCOR Dir: Home/.../Desktop/OpenCOR

Python and libraries installation for this project:

To run openCOR, you need to use the Python version with openCOR. This required python is available at the below address:

Python installation file: OpenCOR_dir/python/bin

So you should install python with this command in the Ubuntu terminal:

Cd [OpenCOR_dir]/python/bin

Sudo apt install python

Then you should add the path:

Cd [OpenCOR_dir]/python/bin

export LD_LIBRARY_PATH=/path/to/opencor/dir/lib

Now, you should install the packages, pandas, and other python libraries which are essential to this project:

-m pip install packagename ./python -m pip install pandas

•••

For parameter identification, you need to use these libraries:

mpi4py, scikit-optimize, emcee, corner, schwimmbad, tqdm

IMPORTANT: installing mpi4py requires mpi to be available. Therefore, the following line may be required to install the mpi software on your computer.

sudo apt install libopenmpi-dev

Circulatory_autogen Project:

The Circulatory_autogen project contains five main folders as presented below:

- generated_models (It includes CellML and other output files, which will be used after running the code.)
- param_id_output (it includes some parameters and codes used for genetic algorithms or other extended parts.)
- resources (it includes resources files which are essential to draw the relation between all parts of our model and determine the boundary conditions between inputs and outputs.),
- src (it includes principal python codes to translate our code to CellML files, and other augmented libraries as well as cellML codes.)
- user_run_files (it includes essential run files and settings which should run to generate CellML files and plot the results.)

Furthermore, there is a README.md file that was written to help users for fast using the project)

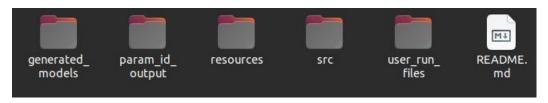


Figure 1

In this section, we want to emphasize how you can generate and simulate your desired model using these projects. We will use several examples to represent the

process of the code and its requirements for running the circulatory_autogen model.

There are several steps to simulate that generate a special circulatory model. These steps are as below:

1) Making at least the **vessel** and **parameters** files in CSV format for the intended model. Those files should be added to the "ProjectDir/resources" directory, and You must pay attention to the file's name.

Proper names of vessel and parameters files are "[model name]_vessel_array.csv" and "[model name]_parameters.csv", respectively. For example, If the model's name is 3compartment, the mentioned files are:

3compartment vessel array.csv

3compartment_parameters.csv

Note: To create a new vessel_array file, follow the next section, "creating a new model."

- **2)** Go to the "ProjectDir/user_run_files" and open the "user_inputs.sh" file to edit. You can use the "nano" command to write the file.
- **3)** you should add the names of the intended vessel and parameters files to the "user_inputs.sh". According to Figure 3, file_prefix is the name of your model. subsequently, input_param_file should be equal to "[model_name]_parameters.csv".
- **4)** At the bottom of the "user_input.sh" file, you should change the "opencor_pythonshell_path" to the directory of pythonshell in the openCOR folder like this: "openCOR/pythonshell".

```
## the below for my local
# opencor_pythonshell_path=/home/ash252/Downloads/OpenCOR-2021-10-05-Linux/pyth
opencor_pythonshell_path=/home/.../Desktop/OpenCOR/pythonshell
## Users should modify opencor_pythonshell_path to the path of their own opencor_
```

Figure 2

Note: Save the file (Ctrl+X and insert Y (yes)) and exit after applying these changes.

```
GNU nano 6.2

# general inputs

# file prefix=3compartment

# file_prefix=acompartment energy

# file_prefix=control_phys

# file_prefix=control_phys

# file_prefix=example2

# file_prefix=example2

# file_prefix=example2

# file_prefix=example2

# input_param_file=3compartment_parameters.csv # this must be stored in resources.

# input_param_file=simple_physiological parameters.csv # this must be stored in resources.

# input_param_file=acompartment_parameters.csv # this must be stored in resources.

# input_param_file=simple_physiological_parameters.csv # this must be stored in resources.

# input_param_file=compartment_energy_parameters.csv # this must be stored in resources.

# input_param_file=simple_physiological_parameters.csv # this must be stored in resources.

# input_param_file=corebral_elic_parameters.csv # this must be stored in resources.

# input_param_file=corebral_elic_parameters.csv # this must be stored in resources.

# input_param_file=example2_parameters.csv # this must be stored in resources.

# input_param_file=example2_parameters.csv # this must be stored in resources.

# input_param_file=example2_parameters.csv # this must be stored in resources.

# input_param_file=example2_parameters.csv # this must be stored in resources.

# input_param_file=example2_parameters.csv # this must be stored in resources.

# input_param_file=example2_parameters.csv # this must be stored in resources.

# input_param_file=example2_parameters.csv # this must be stored in resources.

# input_param_file=example2_parameters.csv # this must be stored in resources.

# input_param_file=ADAVN_parameters.csv # this must be stored in resources.

# input_param_file=ADAVN_parameters.csv # this must be stored in resources.
```

Figure 3

5) You should run the code for generating CellML files and results. At the current directory (ProjectDir/user_run_files), write and insert the "./run_autogeneration.sh" to run the code. As it showed in Figure 4, during running, it creates the CellML files, with all mapping and parameters initialization, and tests the openCOR operation with these generated files. Consequently, If the process goes well, it shows the "Model generation has been successful" message

at the end.

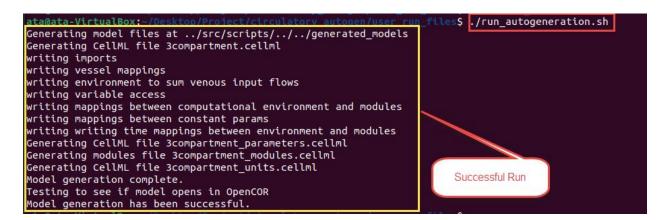


Figure 4

6) Generated CellML files are located in the "ProjectDir/ generated_models" directory. Therefore, You can go to that folder and watch the generated CellML

files. According to Figure 5, There are five different files in this directory after a successful run. In this example, [file_prefix] = 3compartment, so four CellML files, and a CSV file were generated.

```
ata@ata-VirtualBox:~/Desktop/Project/circulatory_autogen/generated_models$ ls

3compartment.cellml 3compartment_parameters.csv

3compartment_modules.cellml 3compartment_units.cellml

3compartment_parameters.cellml
```

Figure 5

CSV file includes parameters essential for running in the openCOR software or augmented codes. Moreover, four CellML files contain the modules, parameters, units and constants, and principle model.

Note: If there are other files before any new run, the new run overrides them, and the last files will be deleted by code. Although, with different [file_prefix], the new files will be generated beside the last files.

7) Now, you can Open the openCOR software and then open the generated CellML files inside the openCOR. As a result, "[file_prefix].cellml" is the main CellML file, and it uses the "[file_prefix]_modules.cellml", "[file_prefix]_parameters.cellml", "[file prefix] units.cellml" files to run correctly (Figure 7).

```
def model Parameters as
   def comp parameters global as
       var rho: Js2_per_m5 {init: 1050, pub: out};
       var T: second {init: 0.8, pub: out};
       var q_ra_0: m3 {init: 4.0e-6, pub: out};
        var q rv 0: m3 {init: 10.0e-6, pub: out};
       var q_la_0: m3 {init: 4.0e-6, pub: out};
       var q_lv_0: m3 {init: 5.0e-6, pub: out};
       var T_ac: second {init: 0.13, pub: out};
       var T_ar: second {init: 0.13, pub: out};
       var t_astart: second {init: 0.64, pub: out};
       var T_vc: second {init: 0.22, pub: out};
       var T_vr: second {init: 0.17, pub: out};
       var t_vstart: second {init: 0.0, pub: out};
       var E_ra_A: J_per_m6 {init: 7.998e+6, pub: out};
       var E ra B: J per m6 {init: 9.331e+6, pub: out};
       var E_rv_A: J_per_m6 {init: 73.315e+6, pub: out};
        var E rv B: J per m6 {init: 6.665e+6, pub: out};
        var E_la_A: J_per_m6 {init: 9.331e+6, pub: out};
        var E la B: J per m6 {init: 11.997e+6, pub: out};
       var E lv A: J per m6 {init: 366.575e+6, pub: out};
       var E_lv_B: J_per_m6 {init: 10.664e+6, pub: out};
       var K_vo_trv: m3_per_Js {init: 0.3, pub: out};
       var K_vo_puv: m3_per_Js {init: 0.2, pub: out};
       var K_vo_miv: m3_per_Js {init: 0.3, pub: out};
        var K_vo_aov: m3_per_Js {init: 0.04, pub: out};
        var K_vc_trv: m3_per_Js {init: 0.4, pub: out};
       var K vc puv: m3 per Js {init: 0.2,
```

Figure 6

Parameters CellML file shown in Figure 7 includes the parameters required in the model, such as resistance, some constants, volume capacity, etc. Furthermore, Units for all variables and constants are written in the "[file_prefix]_units.cellml" (Figure 8).



Figure 7

```
def model Units as
                                               // potential (chemical)
   def unit s2 as
       unit second {expo: 2};
                                              def unit J per mol as
   enddef;
                                                  unit joule;
                                                  unit mole {expo: -1};
   // displacement
   def unit mm as
                                              // potential (voltage)
       unit metre {pref: milli};
   enddef;
                                              def unit J_per_C as
                                                  unit joule;
   // area
                                                  unit coulomb {expo: -1};
                                              enddef;
   def unit m2 as
       unit metre {expo: 2};
                                              def unit J per C s as
   enddef;
                                                  unit joule;
                                                  unit coulomb {expo: -1};
   def unit mm2 as
                                                  unit second {expo: -1};
       unit metre {pref: milli, expo: 2};
                                              enddef;
   enddef;
                                              // potential (force)
   // volume
                                              def unit J per m as
                                                  unit joule;
   def unit m3 as
                                                  unit metre {expo: -1};
       unit metre {expo: 3};
   enddef;
                                              // potential (pressure)
   def unit mm3 as
       unit metre {pref: milli, expo: 3};
                                              def unit J_per_m3 as
                                                  unit joule;
                                                  unit metre {expo: -3};
   enddef;
   // power
                                              def unit m3 per J as
   def unit J per s as
                                                  unit joule {expo: -1};
       unit joule;
                                                  unit metre {expo: 3};
       unit second {expo: -1};
                                              enddef;
                                               def unit J per m3s as
   unit joule;
```

Figure 8

- **8)** When [file_prefix].cellml is opened in the openCOR, click on the simulation bottom on the left side of the code (as shown in Figure 9, with a yellow box). If everything goes well and there is no rational or programming error, openCOR shows you a new page (Figure 9). Several individual parts on this page are:
- Simulation menu
- ODE solver setting
- Parameters part
- Run setting and bottoms

- Graphs and diagrams part
- Results

You should set the simulation's starting, ending, and data output step size. It is essential that this time step is not the ODE solution time step unless the ODE method is chosen as the fix steps method.

ODE solver contains many settings related to the solver, such as maximum step size, iteration method, absolute and relative tolerance, name of solver, etc. It shown with blue box in the below image.

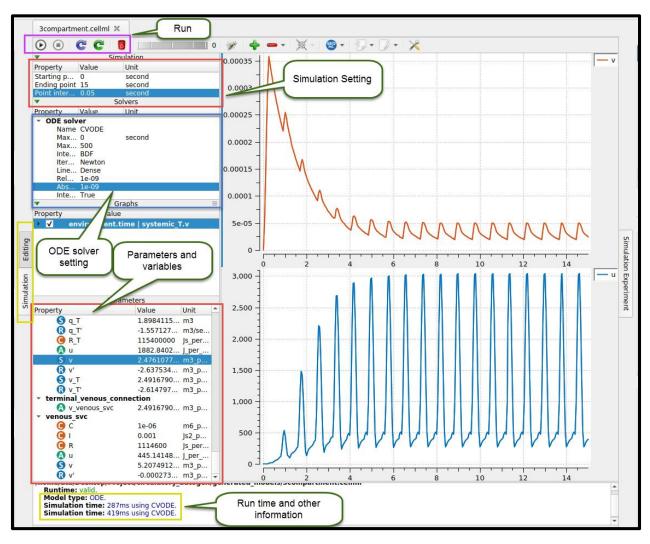


Figure 9

The parameters part represents all constant and variable parameters that are used in the model. Also, all of the environmental parameters can be observed here. You

can plot the intended graphs using this part by right-clicking each parameter you want for the y-axis and then choosing the x-axis variable. For example, time or other variables which you can see after clicking.

The run part is on the top left section, as shown in purple color in Figure 9. The model can be run after accomplishing the required setting. Click on the triangle bottom to run.

The results will be shown after running the model. These results include run-time, settings, and other related parameters, as shown in the yellow box at the bottom (Figure 9).

Simple Example: 3Compartment model

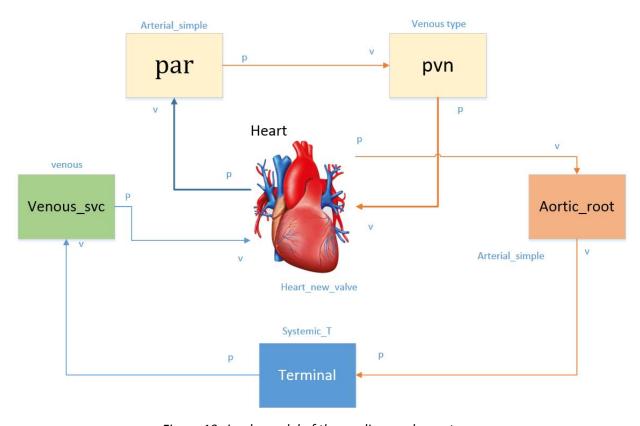


Figure 10 simple model of the cardiovascular system

A schematic view of this model is shown in Figure 10 with details of boundary conditions, parts' names, vein connection, and direction of blood flow through. The heart is modeled as a simple valve module in this example. According to this schematic, the vessel and parameters files are designed as shown in Figure 11.

```
GNU nano 6.2
                                                    3compartment vessel array.csv
name,BC type, vessel type, inp vessels, out vessels
pvn,
                          vp, venous,
                                                                           heart
                                                    par,
                          vp, arterial simple,
                                                    heart,
                                                                           pvn
par,
heart,
                          vp, heart new valve,
                                                    venous svc pvn,
                                                                           aortic root par
aortic root,
                          vv, arterial simple,
                                                    heart,
                                                                           systemic T
systemic T,
                          pp, terminal,
                                                    aortic root,
                                                                           venous svc
venous svc,
                              venous,
                                                    systemic T,
                                                                           heart
```

Figure 11 Example of vessel array file

There are five columns in this vessel_array file: name, BC_type, vessel_type, inp_vessels, and out_vessels. Name is the module's name in each part, for example, heart or aortic_root. BC_type is the boundary condition's type for input and output blood flow. However, those can be used for neural systems or gas exchange modules with other types. BC of pulmonary modules should be one of the vv, vp, pv, and pp types. V and P are the first volume rate and pressure letters, respectively. For example, the pulmonary vein module (pvn) uses vp-type BC. The volume rate of input blood flow and output pressure is the specified boundary conditions for the pulmonary vein module.

The vessel_type must match the equivalent names in the modules_config JSON file, whose directory is:

"ProjectDir/src/generators/resources/module_config.json"

Inp_vessels and out_vessels are the inputs and outputs of each module, respectively. Be careful that some modules might have multiple inputs and outputs, like the heart.

<u>IMPORTANT: The order of input and output vessels is important for the heart module. The order must be</u>

<u>inp vessels: 1:inferior vena cava, 2:superior vena cava, 3:pulmonary vein</u> out vessels: 1:aorta, 2:pulmonary artery.

A simple two-vessel pulmonary system will be used if the pulmonary vessels are not included.

NOTE: Currently, the terminal vessels should only have a BC starting with 'pp'

Results:

Regarding Figure 12, three different variables are plotted versus time in 15 seconds time intervals from the beginning. The step size was adjusted to 0.01 seconds.

These variables are the Aortic_root blood flow rate, pvn flow rate, and the changed volume of the heart, respectively.

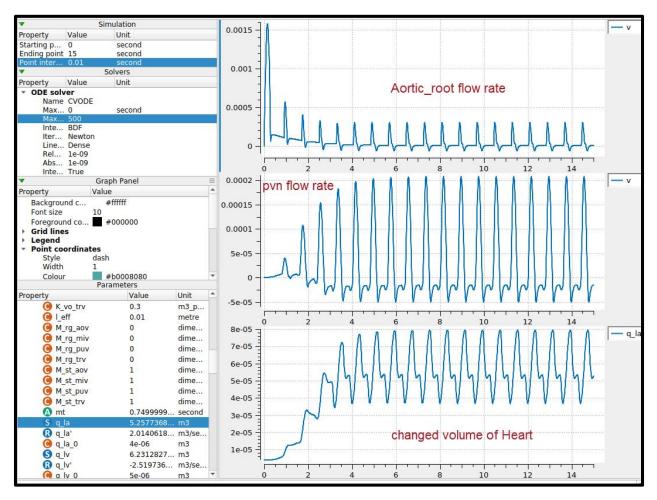


Figure 12 Output results for the 3compartment model

Creating a new model

This part discusses creating the vessel array and parameters files to build a new desired model.

One standard vessel array file contains five important columns elaborated in Table 1. Vessel_name is the name of a common organ or part of the cardiovascular system, BC_type is the type of the boundary condition for the vessel's input and output, and vessel_type can be defined as the desired module which exists in the modules file and JASON file; However, the readily usable vessel_types are possible as below, inp_vessel, and out_vessel, are the input and output of each part, respectively.

Table 1 vessel array file columns and input data types

Column name	Possible inputs	
Vessel_name	It is arbitrary, but it is better to use common names like heart, pvn	
_	par, etc.	
BC_type	'vv', 'vp', 'pv', 'pp', pp_wCont, pp_wLocal, nn	
Vessel_type	'heart', 'arterial', 'arterial_simple', 'venous', 'terminal',	
	'split_junction', 'merge_junction', 2in2out_junction,	
	gas_transport_simple, pulomonary_GE, baroreceptor,	
	chemoreceptor, or other modules in the JSON file.	
Inp_vessels	name of the input vessels, which is one of the vessel_names in	
	other rows	
Out_vessel	name of the output vessels, which is one of the vessel_names in	
_	other rows	

For getting a better view of this vessel file, look into the last example with the name of 3compartment. Furthermore, Figure 11 shows another example of this file type.

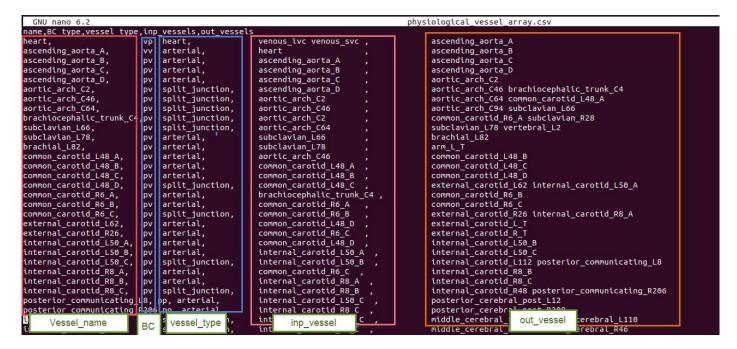


Figure 13 Example of vessel array file

Every row of the vessel array file represents a specific part or module in the defined system. Therefore, each module needs several parameters for modeling and generating a CellML file.

These parameters should be inserted in the parameters file:

"ProjectDir/resources/[file_prefix]_parameters.csv"

This file has the structure as shown in Table 2. Also, An example of the file is shown below.

```
Variable_name,units,value,data_reference
R_pvn,Js_per_m6,1.333e+6,Blanco_2013_Table_8
C_pvn,m6_per_J,0.60015e-8,to_be_identified
I_pvn,Js2_per_m6,1.0e-6,Blanco_2013_Table_8
R_par,Js_per_m6,10.664e+6,Blanco_2013_Table_8
C_par,m6_per_J,0.0309077e-8,to_be_identified
I_pvn,Js2_per_m6,1.0e-6,Blanco_2013_Table_8
C_par,m6_per_J,0.0309077e-8,to_be_identified
I_par,Js2_per_m6,1.0e-6,Blanco_2013_Table_8
rho,Js2_per_m5,1050,known
T,second,0.8,defined_by_user
q_ra_0,m3,4.0e-6,Korakianitis_2006_Table_1
q_rv_0,m3,10.0e-6,Korakianitis_2006_Table_1
q_la_0,m3,4.0e-6,Korakianitis_2006_Table_1
q_la_0,m3,5.0e-6,Korakianitis_2006_Table_1
T_ac,second,0.13,defined_by_user_from_BB128
T_ar,second,0.13,defined_by_user_from_BB128
T_ar,second,0.13,defined_by_user_from_BB128
T_vr,second,0.22,defined_by_user_from_BB128
T_vr,second,0.22,defined_by_user_from_BB128
T_vr,second,0.17,defined_by_user_from_BB128
t_vstart,second,0.0,Liang_2009_Table_2
E_ra_A,J_per_m6,7.998e+6,Liang_2009_Table_2
E_ra_B,J_per_m6,73.315e+6,Liang_2009_Table_2
E_rv_B,J_per_m6,6.665e+6,Liang_2009_Table_2
E_rv_B,J_per_m6,6.665e+6,Liang_2009_Table_2
E_rv_B,J_per_m6,6.665e+6,Liang_2009_Table_2
E_la_B,J_per_m6,11.997e+6,Liang_2009_Table_2
E_la_B,J_per_m6,366.575e+6,Liang_2009_Table_2
E_lu_B,J_per_m6,10.664e+6,Liang_2009_Table_2
E_lu_B,J_per_m6,10.664e+6,Liang_2009_Table_2
E_lv_B,J_per_m6,10.664e+6,Liang_2009_Table_2
E_lv_B,J_per_m6,10.664e+6,Liang_2009_Tabl
```

Table 2 Structure of parameter file

Column Name	Description	
Variable_name	Parameter or	
	constant name	
Units	Unit in the defined	
	units in CellML's unit	
	file	
Value	Value of parameter	
Data_reference	Reference of the	
	parameter value	

Note: If you forget to add or insert any needed parameter in the file when you run the code, It shows you this message at the end:

```
ata@ata-VirtualBox:
                                                                                files$ ./run_autogeneration.sh
Generating model files at ../src/scripts/../../generated_models
Generating CellML file 3compartment.cellml
writing imports
writing vessel mappings
writing environment to sum venous input flows writing variable access
writing mappings between computational environment and modules
writing mappings between constant params
writing writing time mappings between environment and modules
Required parameters are missing.
Creating a file ../src/scripts/../../src/generators/../../resources/3compartment_parameters_unfinished.csv, which has EMPTY_MUST_BE_FILLED tags where parameters need to be included. The user should include these parameters then remove
the "_unfinished" ending of the file name, then rerun the model generation
with the new parameters file as input.
Generating CellML file 3compartment_parameters.cellml
Generating modules file 3compartment_modules.cellml
Generating CellML file 3compartment_units.cellml
                                                                                             Error says that one or several
                                                                                            parameters not inserted correctly
Model generation complete.
Testing to see if model opens in OpenCOR
The OpenCOR model is not yet working because all parameters have not been given values,
Enter the values in ../src/scripts/../../src/generators/../../resources/3compartment_parameters_unfinished.csv
```

At this time, you should go to the below file:

"ProjectDir/resources/[file_prefix]_parameters_unfinished.csv"

Then go to the bottom of the file. You can see the parameters which were not inserted in the file. So, you should add the parameters' value in the file. Subsequently, delete the last part of the file's name ("unfinished") and rerun the code to solve the issue.

Modules and definition of a new module

There are many modules in the below directory, and they can be used in the model. The main directory is:

"ProjectDir/Circulatory autogen/src/generation.resources"

In this directory, there are several CellML files and a unique JSON file, as shown below:

Some of these files are necessary to run our model. They are "units.cellml" includes all defined units, "BG_modules.cellml" consists of many essential modules, such as heart, pvn, par, boundary conditions, sensors, etc, as well as "base script.cellml"

for environment and other aspects of main code. The base_script.cellml file is shown in Figure 14. It uses the "units.cellml" in the main generated code to add all types of units. Also, "module_config.json" is the main file used by python code to call the cellml files and vessel_arrays, and all inputs and outputs for each required module are determined in that file.

```
def model CardiovascularSystem as
        def import using "units.cellml" for
3
           unit m2 using unit m2;
            unit m3 using unit m3;
            unit m3_per_s using unit m3_per_s;
            unit m per s2 using unit m per s2;
            unit m per s using unit m per s;
            unit m6 per J using unit m6 per J;
            unit m6_per_Js using unit m6_per_Js;
10
            unit per_m using unit per_m;
11
            unit per s using unit per s;
            unit J per m3 using unit J per m3;
13
            unit J_per_m3s using unit J_per_m3s;
14
            unit m3_per_J using unit m3_per_J;
15
            unit J2 per m6 using unit J2 per m6;
            unit Js per m6 using unit Js per m6;
16
17
            unit Js2_per_m6 using unit Js2_per_m6;
18
            unit Js2 per m5 using unit Js2 per m5;
19
            unit J_per_s using unit J_per_s;
20
            unit J per m6 using unit J per m6;
21
            unit Js_per_m3 using unit Js_per_m3;
22
            unit UnitValve using unit UnitValve;
            unit J per m9 using unit J per m9;
24
            unit m3 per Js using unit m3 per Js;
25
            unit kg_per_m3 using unit kg_per_m3;
26
            unit m3 per kg using unit m3 per kg;
        enddef;
27
28
29
        def import using "parameters_autogen.cellml" for
30
           comp parameters using comp parameters;
31
            comp parameters global using comp parameters global;
32
        enddef;
33
34
        def comp environment as
35
           var time: second {pub: out};
36
        enddef;
37
        //#STARTGENBELOW
38
39
    enddef:
```

Figure 14 "base_script.cellml"

If you want to create a new module, you must add the related JSON data in the "module_config.json" and write the module whether in the "BG_modules.cellmll" or separated new cellml file.

As shown in Figure 15, there are three different parts for each module. The primary specification includes vessel_type, boundary condition type, and module_file. The ports and their types, and finally, variables and constants.

```
25
          "vessel_type":"arterial_simple",
26
          "BC type": "vp",
27
                                                                           Main
          "module format": "cellml",
28
          "module_file": "BG_modules.cellml",
                                                                       Specification
29
30
          "module type": "vp simple type",
31
          "entrance ports":
32
33
               "port_type":"vessel_port",
34
35
               "variables":["v in","u"]
36
            }
37
38
          "exit_ports":
39
                                                                        ports and types
40
41
               "port type": "vessel port",
               "variables":["v","u out"]
42
43
44
               "port_type": "flow_port",
45
46
               "variables":["v"]
47
            }
48
49
          "variables_and_units":
50
                                                                        Variables and
            ["u", "J_per_m3", "access", "variable"],
51
            ["v", "m3_per_s", "access", "variable"],
52
                                                                             units
            ["q_C", "m3", "access", "variable"],
["R", "Js_per_m6", "access", "constant"],
["C", "m6_per_J", "access", "constant"],
53
54
55
            ["I", "Js2 per m6", "access", "constant"]
56
57
         1
58
       },
59
          "vessel type": "arterial",
60
```

Figure 15 one of the "module config.json" datasets

Furthermore, the modules file's structure must be written in the standard shape. One of the modules is shown in Figure 16. The main body of a specific module contains variables declaration, constitutive parameters, and state variables. Then, you should write the constitutive relations and, eventually, ODE equations.

In the next, we show a simple example to create a new module you can find in the JSON file.

```
// State Variables
def comp vp type as
    var t: second {pub: in};
                                                   var v in: m3 per s {pub: in};
                                                   var u: J per m3 {pub: out};
   // Constitutive parameters
                                                   var u_C: J_per_m3 {pub: out};
                                                   var v: m3_per_s {init: 0.0, pub: out};
   var mu: Js_per_m3 {pub: in};
   var rho: Js2 per m5 {pub: in};
                                                   var u_out: J_per_m3 {pub: in};
                                                   var q C: m3 {init: 0.0, pub: out};
   var g: m_per_s2 {pub: in};
   var beta g: dimensionless {pub: in};
                                                   // Constitutive Relations
   var theta: dimensionless {pub: in};
   var E: J_per_m3 {pub: in};
   var E_m: J_per_m3 {pub: out};
                                                   h = r*(a vessel*exp(b vessel*r)+c vessel*exp(d vessel*)
                                                   I = rho*l/(pi*sqr(r));
    var l: metre {pub: in};
   var length: metre {pub: out};
                                                   //C = 2{dimensionless}*pi*pow(r, 3{dimensionless})*l/(I
   var h: metre {pub: out};
   var thickness: metre {pub: out};
                                                   C = 2{dimensionless}*pi*pow(r, 3{dimensionless})*l/(E*|
   var r: metre {pub: in};
                                                   R = 8{dimensionless}*mu*l/(pi*pow(r, 4{dimensionless})
   var radius: metre {pub: out};
                                                   R_v = 0.01\{second\}/C;
   var I: Js2 per_m6 {pub: out};
                                                   length = 1;
   var C: m6_per_J {pub: out};
   var R: Js per m6 {pub: out};
                                                   E m = E;
                                                   radius = r;
   var R_v: Js_per_m6 {pub: out};
                                                   thickness = h;
   var a_vessel: dimensionless {pub: in};
   var b_vessel: per_m {pub: in};
                                                   // Conservation Laws
   var c_vessel: dimensionless {pub: in};
   var d_vessel: per_m {pub: in};
                                                   ode(v, t) = (u-u_out-R*v-beta_g*rho*g*l*cos(theta*pi/1)
    // State Variables
                                                   // ode(u_C, t) = (v_in-v)/C;
   var v_in: m3_per_s {pub: in};
                                                   ode(q_C, t) = v in-v;
   var u: J_per_m3 {pub: out};
   var u_C: J_per_m3 {pub: out};
                                                   u C = q C/C;
                                                   u = u_C+R_v*(v_in-v);
    var v: m3 per s {init: 0.0, pub: out};
                                               enddef;
    var u_out: J_per_m3 {pub: in};
    var q_C: m3 {init: 0.0, pub: out};
```

Figure 16 one of the modules in the BG modules file

Example:

We want to define a new vessel type with the name of "arterial" with boundary condition type "vp". Additionally, we want to use the "vp_type" module, whose cellml code is shown in Figure 16. Also, the module is located in the "BG_module" file.

Vessel_type, BC_type, module_format, the module_file location, module_type, and other related information are added to this "module_config.json" file, as shown in Figure 17. We can now use this vessel_type in the vessel_array file in the resources directory to add the module with specified inputs, outputs, and parameters. Consider that In the ports, you should add the "vessel_port" type for connecting to the other parts. Additionally, each module can be used in many vessel_types.

```
"vessel_type":"arterial",
 60
 61
                     "BC type": "vp",
                     "module_format":"cellml",
 62
                      "module_file":"BG_modules.cellml",
 63
                                                                                                                              Arterial vessel type
 64
                      "module_type":"vp_type",
                                                                                                                                     specification
 65
                     "entrance ports":
 66
 67
 68
                              "port_type":"vessel_port",
 69
                              "variables":["v in", "u"]
 70
 71
                    ],
 72
                     "exit_ports":
 73
                    [
 74
 75
                              "port type": "vessel port",
                                                                                                                                    Vessel ports and
                              "variables":["v","u_out"]
 76
                                                                                                                                     flow port added
 77
 78
                         {
                              "port_type":"flow_port",
 79
 80
                              "variables":["v"]
 81
 82
                       variables and units":
 83
                       ["u", "J_per_m3", "access", "variable"],
["v", "m3_per_s", "access", "variable"],
["E", "J_per_m3", "access", "constant"],
["l", "metre", "no_access", "constant"],
["theta", "dimensionless", "no_access", "constant"],
["beta_g", "dimensionless", "no_access", "global_constant"],
["rho", "Js2_per_m5", "no_access", "global_constant"],
["mu", "Js_per_m3", "no_access", "global_constant"],
["g", "m_per_s2", "no_access", "global_constant"],
["g, "m_per_s2", "no_access", "global_constant"],
["b_vessel", "dimensionless", "no_access", "global_constant"],
["c_vessel", "dimensionless", "no_access", "global_constant"],
["d_vessel", "dimensionless", "no_access", "global_constant"],
["d_vessel", "per_m", "no_access", "global_constant"],
 84
 85
 86
 87
 88
 89
 90
 91
 92
 93
 94
 95
 96
 97
 98
 99
100
```

Figure 17 Example of adding a new vessel_type to JSON file

Appendix A: Cardiovascular system and CN model

The article below is a good source for getting more information about the human cardiopulmonary system and the CN model. You can download the article from the link.

Albanese, A., Cheng, L., Ursino, M., & Chbat, N. W. (2016). An integrated mathematical model of the human cardiopulmonary system: model development. American Journal of Physiology-Heart and Circulatory Physiology, 310(7), H899-H921.

https://journals.physiology.org/doi/epdf/10.1152/ajpheart.00230.2014

Moreover, some schematic pictures of the heart, pulmonary system, and neural networks can be observed in

Figure 18 to Figure 21. These images can help you better understand the cardiovascular system and every part's connection.

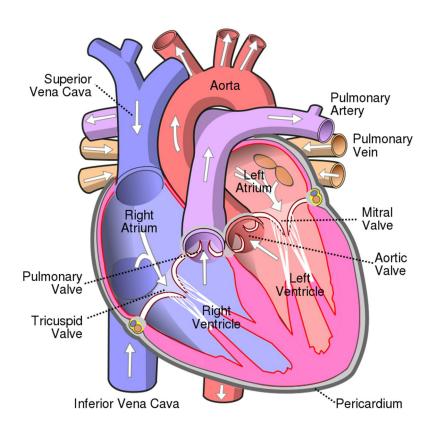


Figure 18 Heart Mechanism

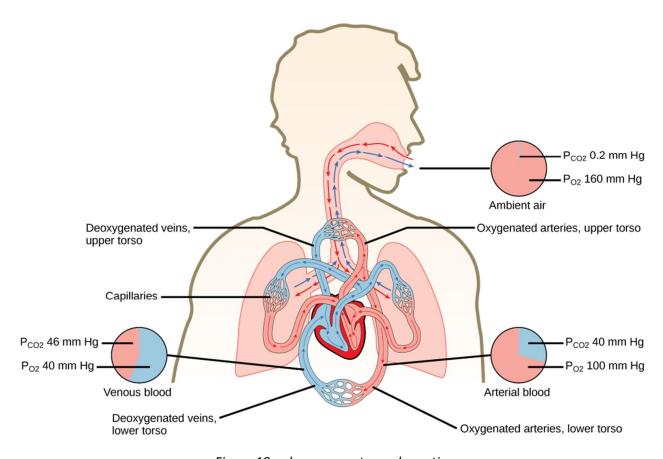


Figure 19 pulmonary system schematics

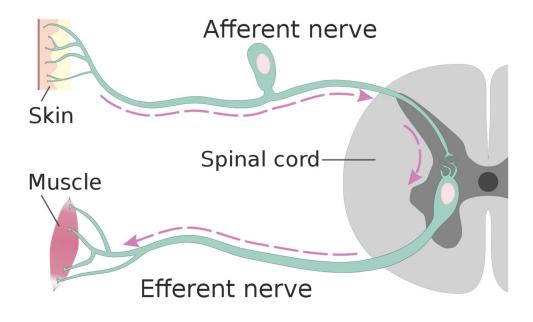


Figure 20 Afferent and Efferent neural network

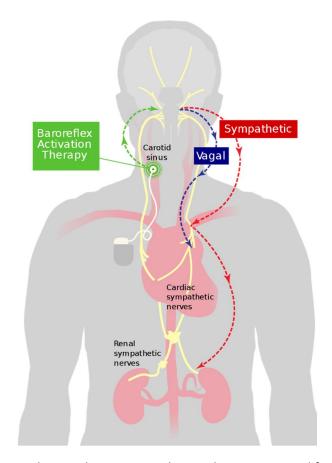


Figure 21 Cardiovascular system with neural connection and feedback

Furthermore, many abbreviation names are used in the articles and source code. Some of them are mentioned in the below table.

Cardiovascular abbreviation Table

Abbreviation Name	Main Name	
pvn	Pulmonary vein	
par	Pulmonary arteries	
MV	Mitral valve	
TV	Tricuspid valve	
AV	Aortic valve	
PV	Pulmonary valve	
la	Left atrium	
lv	Left ventricle	
ra	right atrium	
rv	right ventricle	
ер	Extrasplanchnic peripheral	

ev	Extraplanchnic veins	
mv	Skeletal Muscle peripheral	
bp	Brain peripheral compartment	
bv	Brain veins	
hp	Coronary peripheral	
hv	Coronary veins	
tv	Thoracic veins	
рр	Pulmonary peripheral	
pv	Pulmonary veins	
rvo	Right ventricle output	
lvo	Left ventricle output	
CNS	Central neural system	
aov	Aortic valve	
vub	Venous upper body	
SVC	Superior vena cava	
vlb	Venous lower body	
ivc	Inferior vena cava	
alv	alveolar	
cw Chest wall		
ABP	Arterial blood pressure	
СР	Cardiopulmonary	

Appendix B: Other Notes

There are many modules in the BG_module.cellml file. Here we mention several of these modules' names.

	1	
Pv_0D_1D_coupler_type	Pv_simple_type	
Imposter_1D	Pp_simple_type	
Heart_simple_wcon	Vv_simple_type	
Heart_simple	Vp_simple_type	
Heart_new_valve	Pp_T_type	
Heart_simple_Lvprop	Pp_T_wcont_type	
Constant_flow_BC_type	Pv_split_type	
Constant_flow_2_BC_type	Vv_2in2out_type	
Constant_pressure_BC_type	vv_merge_type	
P_observer_type	Vp_merge_type	
F_observer_type	Zero_flow	
Controller_type	Flow_sum_2_type	
Controller2_type	Baroreceptor_type	
Pv_type	Chemoreceptor_type	
Vp_type		
Pp_type		
Vv_type		

Boundary conditions type:

BC Type		
PV	Pressure	Flow rate
PP	Pressure	Pressure
VV	Flow rate	Flow rate
VP	Flow rate	pressure

Some of the equivalent circuits for boundary conditions in vessels are shown in the below image.

You can find the good notes and documents in the attached files about the bond graph, the openCOR tutorial, related articles, and my notes.

