Heart Assist Lab (BME Cornell)

CVS Simulator Manual (Version 3)

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This is the 3rd version of the cardiovascular (CVS) simulator, developed by the Heart Assist Lab at Cornell University. It is aimed to simulate the hemodynamics of human cardiovascular and provide a non-invasive way to investigate the intervention of heart disease, as well as the intervention of rotary ventricular assist device for the patients with end-stage heart failure. This model includes bi-ventricles, systemic circulation, pulmonary circulation, the regulation of normal baro-reflex[1], biventricular interaction[2-4] and model of rotary left ventricular assist device (VAD)[5]. It enables the user to simulate different scenarios of heart diseases and VAD therapy by changing the set up in each tab (Please see instruction 1-4). We also provide five examples to facilitate your beginning trial of this CVS simulator (Please see the Instructions at the end).

When you finish installation, you'll find a short-cut of the software on your desktop. (Note: make sure you put the installation folder under the C:\ path, since the program links an excel file in the folder and set the path as "C:\CVS Installer\data.xls").

Double click the short-cut; the program begins to run, when you click on the up-left corner of the interface. You could click the symbol on the up-left corner or on the interface to end the simulation. For all the control panels and waveform display, you could adjust the scale of the axis by clicking the maximum or minimum values to input other digits.

This has the following features:

- There are 3 tabs for easy access of the controls and the indicators: User Guide, Controls & Monitor, Dilated HF and Septum Monitor. All the controls are colored yellow, and all the indicators are in pink.
- A data file with for easier understanding.

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User Guide (Figure 1): Brief instructions to get you started right away. This tab will help you navigate through the software and provide important guidelines to avoid errors.

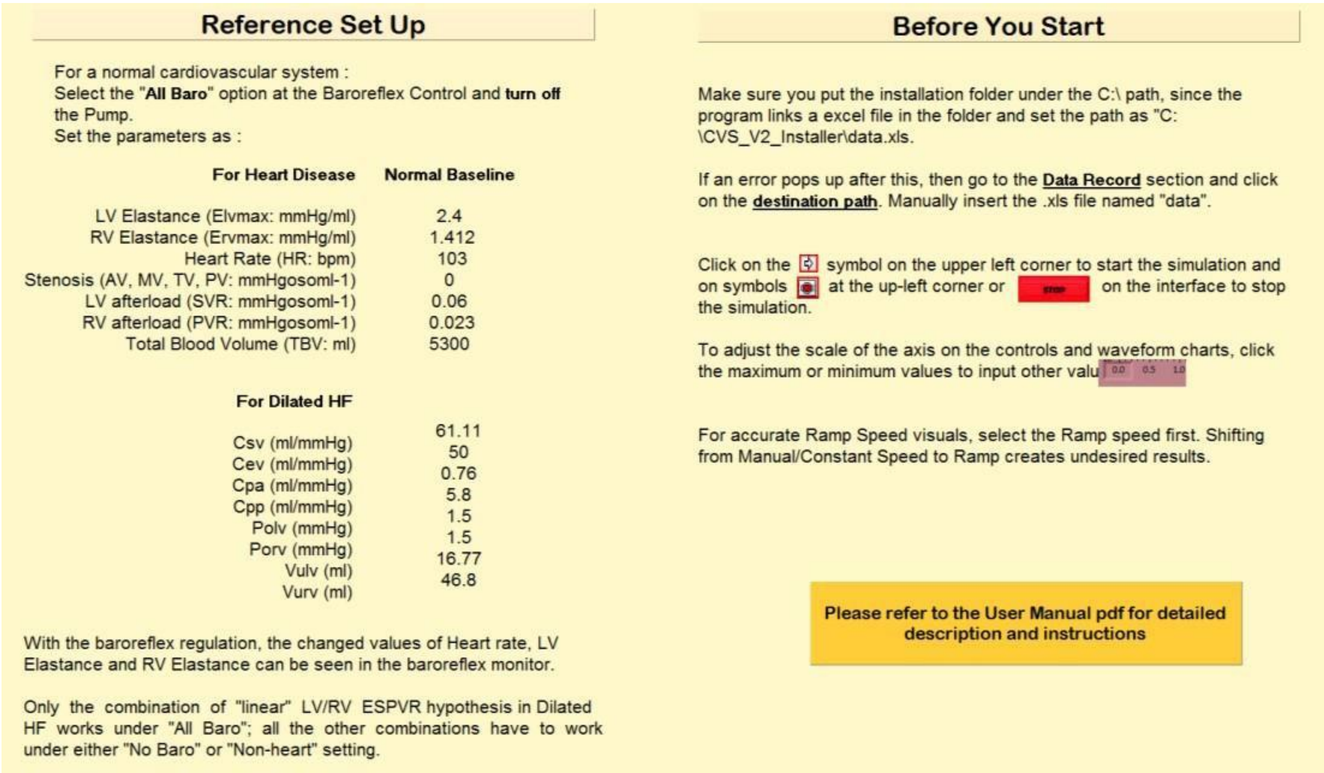


Figure 1: User Guide Tab

Controls and Monitors 1 (Figure 2): Settings for general Heart Disease, LVAD controls, Baroreflex Control and Cardiac Monitor.

1. **Heart Diseases:** This can be created by manipulating the following-
    - Left Ventricle (LV)/ Right Ventricle (RV) contractility based on the hypothesis of the linear end-systolic pressure and volume relationship (ESPVR) (mmHg/mL)
      Note: "Dilated HF" default settings for LV/RV ESPVR Hypothesis are linear.
    - LV/RV afterload (e.g. systemic/pulmonary hypertension) (mmHg*s*mL ^{1})
    - Stenosis of Aortic Valve (AV), Mitral Valve (MV), Tricuspid Valve (TV) & Pulmonary Valve (PV) (mmHg*s*mL^{-1})
    - Regurgitation of Aortic Valve and Mitral Valve
    - Heart rate (HR) (bpm)
    - The total blood volume (hypervolemia/hypovolemia) (mL)

2. **LVAD (Rotary VAD) Controls:** You could turn on the LVAD in heart failure condition to see its intervention on cardiovascular hemodynamics. There are three options for the speed setup:
    - Ramp Speed: It begins at 2k and goes up to 16k. You could get the instantaneous Rotary VAD speed from the meter of "***Pump Speed***".
    - Manual Speed: you can set up the speed from dragging the slider from 2k to 12k.
    - Pulsatile Speed: The rotating speed of the VAD uses the sine function to create pulses. **Switch on the Pulsatile Speed button after switching to constant/manual speed.** This feature does not work with Ramp Speed

All these controls are grouped under the name of Rotary VAD.

3. **Data Record:** This session provides you an option to record the data. To create an excel file on your computer click the symbol  and select the directory named "data" to save the recorded data. If you do not select the directory correctly, when you stop the program, there will be an error showing up.
4. **Baroreflex Control:** There are three control options to maintain 7 parameters of the model to maintain arterial pressure. The barometer monitor shows the instantaneous values of the 7 parameters running in the program.
    - "No Baro": no baro-reflex regulation – "baro-reflex" control is off.
    - "All Baro": regulates Heart Rate, Contractility of LV, RV free wall, Peripheral Systemic Resistance, including both splanchnic R_{sp} and extra-splanchnic vessels *Rep*) and Systemic Venous Unstressed Volume, including both splanchnic V_{usv} and extra-splanchnic vessels $\mathrm{V_{uev}}$. (Note: only the combination of "linear" LV/RV ESPVR hypothesis works under "All Baro"; all the other combinations must work under either "No Baro" or "Non-heart" setting)
    - "Non-heart": regulates R_{sp}, R_{ep}, V_{usv} *and* V_{uev} (default settings)

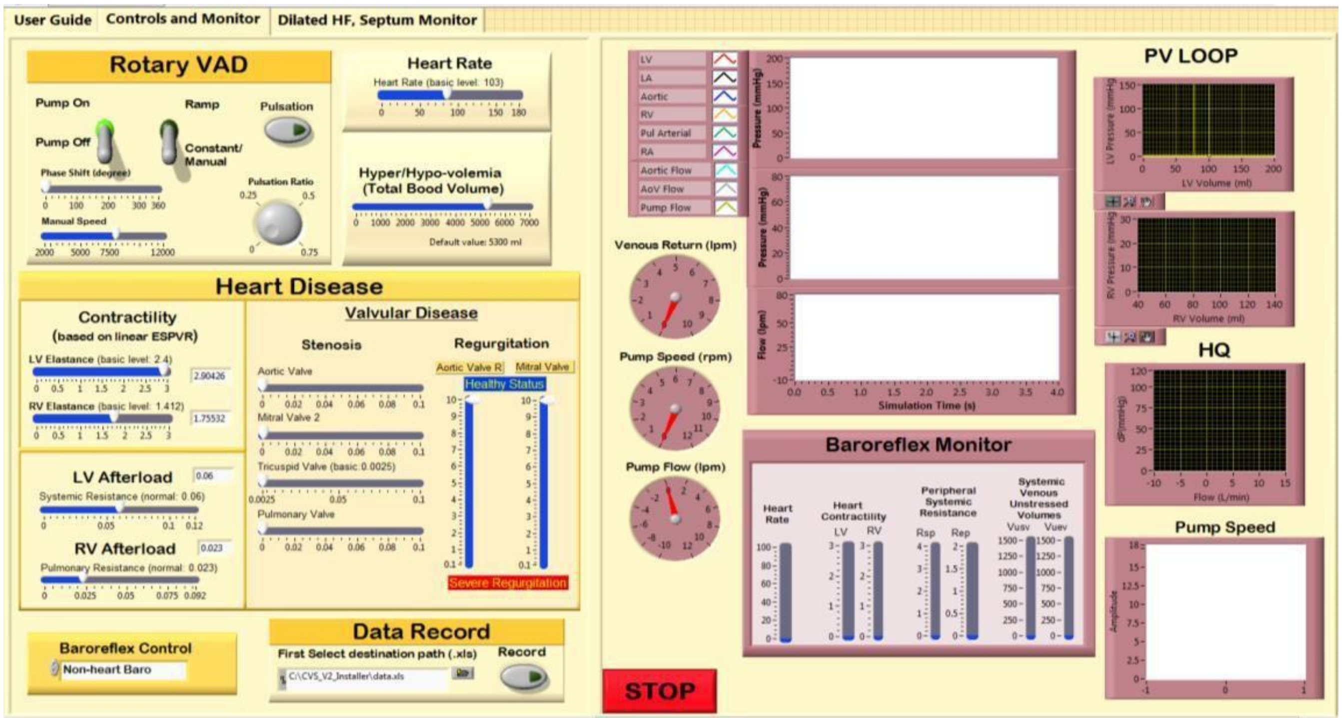


Figure 2: Controls and Monitor Tab

Dilated HF and Septum Monitor (Figure 3): Dilated Heart Failure controls, Mean value for certain parameters and instantaneous monitor for septum [4].

1. **Dilated Heart Failure (HF):** You could set the four heart failure conditions listed below or manipulate the parameters according to your needs.
    - CVS Setting: Here you can change the LV/RV ESPVR hypothesis - "linear" refers to traditional linear ESPVR settings (see the dotted line in Figure 4 labeled with normal); all the other "nonlinear" conveys the concept that when the cardiac myosin overstretches, the force produced by them will decrease (see the dotted line in Figure 3 labeled with depressed ESPVR.

The following are the equations to model LV and RV; Table 1 lists the settings for each of the nonlinear ESPVR hypothesis.

$$P_{\max.lv}(t) = e(t)\cdot P_{lv,es} + [1-e(t)]\cdot P_{ed,lv} \quad 0 \le e(t) \le 1 \qquad (1)$$

$$e(t) = \begin{cases} \sin^2(\pi \cdot T(t)\cdot u / T_{sys}) & 0 \le u \le T_{sys}/T \\ 0 & T_{sys}/T \le u \le 0 \end{cases} \qquad (2)$$

$$P_{es,lv} = \begin{cases} 0 & V_{lv} <= V_{u,lv} \\ E_{+,lv}(V_{lv} - V_{u,lv}) & V_{u,lv} < V_{lv} <= (E_{+,lv}V_{u,lv} + V_{b,lv})/(E_{+,lv} - E_{-,lv}) \\ E_{-,lv}V_{lv} + V_{b,lv} & V_{lv} > (E_{+,lv}\cdot V_{u,lv} + V_{b,lv})/(E_{+,lv} - E_{-,lv}) \end{cases} \qquad (3)$$

$$P_{ed,lv} = P_{0,lv}\cdot(e^{k_{E,lv}\cdot(V_{lv}-V_{u,lv})} - 1) \qquad (4)$$

$$P_{lv} = P_{\max.lv} - R_{lv}\cdot Q_{o.l} \qquad (5)$$

$$R_{lv} = k_{R.lv}\cdot P_{\max.lv} \qquad (6)$$

Table 1: Settings for each of the nonlinear ESPVR hypothesis

	$E_{+,lv}$	$V_{u,lv}$	$E_{-,lv}$	$V_{b,lv}$
Heart failure (nonlinear ESPVR1)	1.2	25	-0.6	240
Heart failure (nonlinear ESPVR2)	1	25	-0.6	215
Heart failure (nonlinear ESPVR3)	0.8	25	-0.6	190
RV failure (nonlinear ESPVR1)	9/8	40.8	-0.2	117.36
RV failure (nonlinear ESPVR2)	0.9	40.8	-0.1	73.28
RV failure (nonlinear ESPVR3)	13/8	40	-0.4	97
RV failure (nonlinear ESPVR4)	1.6	40.8	-0.2	204.72

LV/RV input provides the options to adjust the LV/RV diastolic functions.

You could also change the parameters in the systemic/pulmonary circulation to simulate different vascular diseases.

- Baroreflex Setting: This offers the opportunity to adjust the parameters in the baro-reflex system, including “unstressed volume”, “Vusv Baro Parameter” and “Vuev Baro Parameter”. More detailed definitions for each parameter are in Ursino’s study [1].

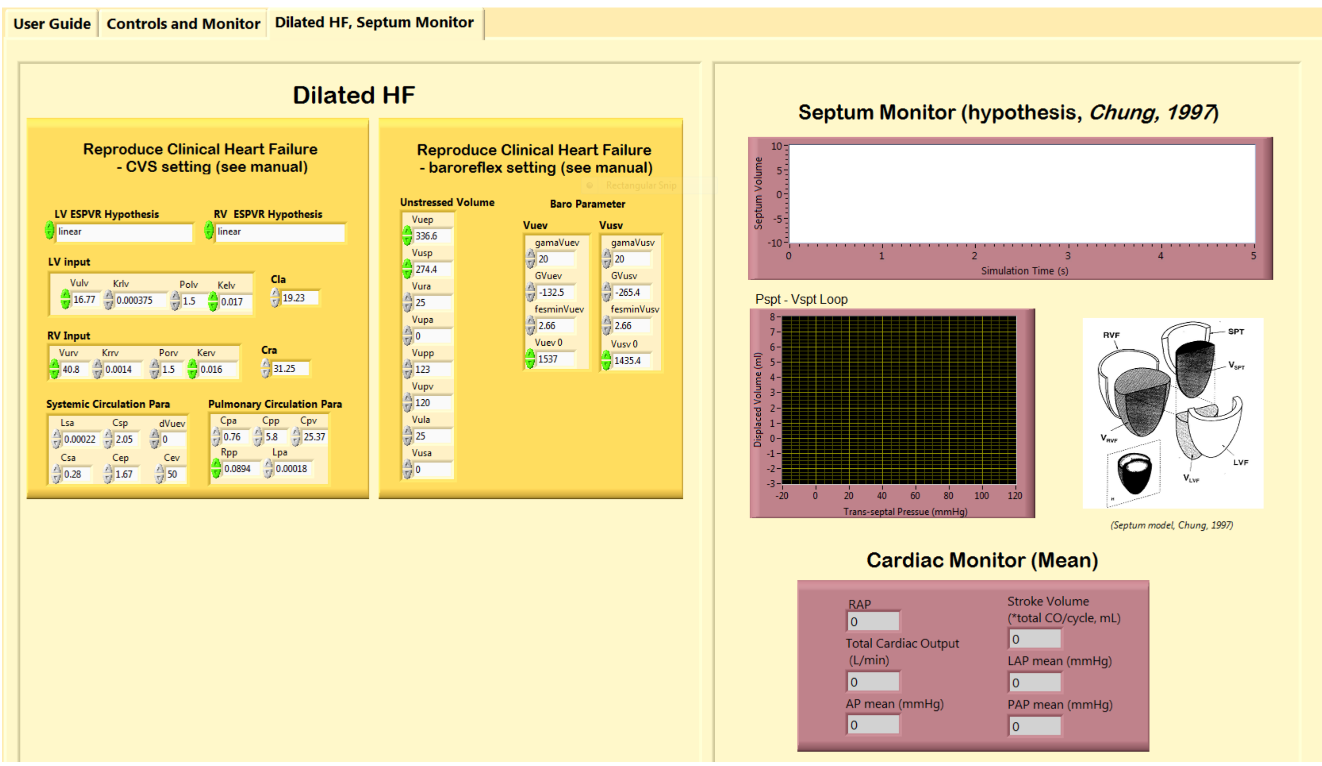
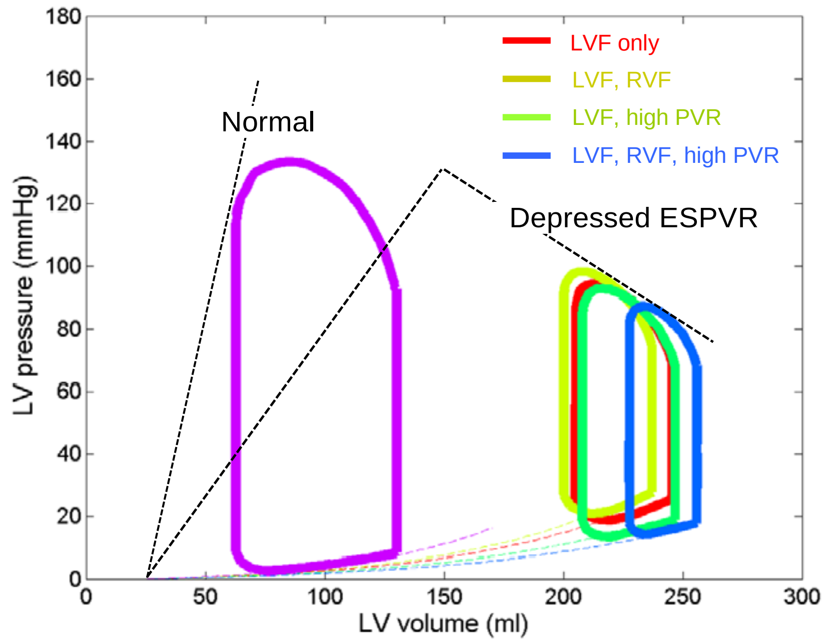
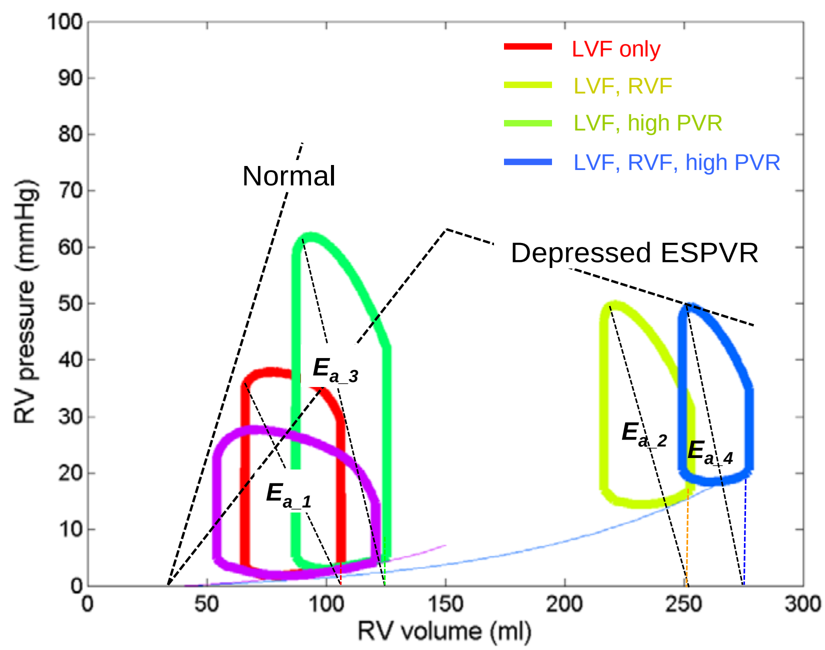


Figure 3: Dilated HF and Septum Monitor



(a)



(b)

Figure 4: Pressure-volume relationships for normal and four heart failure conditions: (a) left ventricle; (b) right ventricle.

Reference Set-Up: Here are the few suggested settings for your trial of simulation: -

1. For one normal cardiovascular system, we select "All Baro" baro-reflex control and turn off the Rotary VAD; set the parameters as the ones listed in the Table 2 (normal baseline condition). With the Baroreflex regulation, the real value of HR, LV free wall elastance and RV free wall elastance regulated in the program are displayed in the "Baroreflex monitoring" panel.
2. For another normal cardiovascular system, we select "Non-heart Baro" control and turn off the Rotary VAD; set the parameters as the one listed in the Table 4 (the default setting for this program is to simulate these conditions and the corresponding PV loop, the hemodynamic outputs are detailed in Table 7.)
3. For 4 heart failure conditions, we select "Non-heart Baro" control in the "Baroreflex" tab; set all the parameters listed in Table 6 to the indicated values in each condition.
4. Table 7 demonstrates the corresponding hemodynamic output under each of the four conditions.

   - LV failure: LV ESPVR hypothesis "heart failure (nonlinear ESPVR1)"; RV ESPVR hypothesis "linear" or "RV normal (nonlinear ESPVR)".
   - Bi-ventricular failure: LV ESPVR hypothesis "heart failure (nonlinear ESPVR1)"; RV ESPVR hypothesis "RV failure (nonlinear ESPVR1)".
   - LV failure with PVR+: LV ESPVR hypothesis "heart failure (nonlinear ESPVR1)"; RV ESPVR hypothesis "linear" or "RV normal (nonlinear ESPVR)".
   - Bi-ventricular failure with PVR+: LV ESPVR hypothesis "heart failure (nonlinear ESPVR1)"; RV ESPVR hypothesis "RV failure (nonlinear ESPVR1)".

Table 2: Reference set up for normal conditions with linear ESPVR hypothesis (default).

"Heart Disease" Tab	**Normal baseline**
LV Elastance (Elvmax: mmHg/ml)	**2.4**
RV Elastance (Ervmax: mmHg/ml)	1.412
Heart Rate (HR: bpm)	**103**
Stenosis (AV, MV, TV, PV: mmHg•s•ml-1)	0
LV afterload (SVR: mmHg•s•ml-1)	0.06
RV afterload (PVR: mmHg•s•ml-1)	0.023
Total Blood Volume (TBV: ml)	5300
"Dilated HF" Tab	**Normal baseline**
Csv (ml/mmHg)	61.11
Cev (ml/mmHg)	50
Cpa (ml/mmHg)	0.76
Cpp (ml/mmHg)	5.8
Polv (mmHg)	**1.5**
Porv (mmHg)	1.5
Vulv (ml)	**16.77**
Vurv (ml)	46.8

Table 3: The normal Parameters for the Vascular System

Parameter Group Name	Symbol	Units	Values
Compliance			
Systemic arterial circulation	C_{sa}	ml/mmHg	0.28
Splanchnic peripheral circulation	C_{sp}	ml/mmHg	2.05
Extra splanchnic peripheral circulation	C_{ep}	ml/mmHg	1.67
Splanchnic venous circulation	C_{sv}	ml/mmHg	61.11
Extra splanchnic venous circulation	C_{ev}	ml/mmHg	50.0
Pulmonary arterial circulation	C_{pa}	ml/mmHg	0.76
Pulmonary peripheral circulation	C_{pp}	ml/mmHg	5.80
Pulmonary venous circulation	C_{pv}	ml/mmHg	25.37
Unstressed Volume			
Systemic arterial circulation	$V_{u,sa}$	ml	0
Splanchnic peripheral circulation	$V_{u,sp}$	ml	274.4
Extra splanchnic peripheral circulation	$V_{u,ep}$	ml	336.6
Splanchnic venous circulation	$V_{u,sv}$	ml	1121
Extra splanchnic venous circulation	$V_{u,ev}$	ml	1375
Pulmonary arterial circulation	$V_{u,pa}$	ml	0
Pulmonary peripheral circulation	$V_{u,pp}$	ml	123
Pulmonary venous circulation	$V_{u,pv}$	ml	120
Hydraulic Resistance			
Systemic arterial circulation	R_{sa}	$mmHg*s*ml^{-1}$	0.06
Splanchnic peripheral circulation	R_{sp}	$mmHg*s*ml^{-1}$	3.307
Extra splanchnic peripheral circulation	R_{ep}	$mmHg*s*ml^{-1}$	1.407
Splanchnic venous circulation	R_{sv}	$mmHg*s*ml^{-1}$	0.038
Extra splanchnic venous circulation	R_{ev}	$mmHg*s*ml^{-1}$	0.016
Pulmonary arterial circulation	R_{pa}	$mmHg*s*ml^{-1}$	0.023
Pulmonary peripheral circulation	R_{pp}	$mmHg*s*ml^{-1}$	0.0894
Pulmonary venous circulation	R_{pv}	$mmHg*s*ml^{-1}$	0.0056
Inertance			
Systemic arterial circulation	L_{sa}	$mmHg*ml*s^{-2}$	$0.22*10^{-3}$
Pulmonary arterial circulation	L_{pa}	$mmHg*ml*s^{-2}$	$0.18*10^{-3}$
Total Blood Volume	TBV	ml	5300

Table 4: The normal Parameters for left and right heart

Parameter Group Name	Symbol	Units	Values
Left Heart			
Left atrial compliance	C_{la}	ml/mmHg	19.23
Left atrial unstressed blood volume	$V_{u,la}$	ml	16.7
Left atrial resistance	R_{la}	mmHg*s*ml^{-1}	2.5*10^{-3}
Scaling factor for LV EDPVR	$P_{0,lv}$	mmHg	1.5
Exponent for LV EDPVR	$K_{E,lv}$	ml^{-1}	0.017
LV unstressed blood volume	$V_{u,lv}$	ml	16.7
Ascending slope for LV ESPVR	$E_{+,lv}$	mmHg/ml	2.9
Descending slope for LV ESPVR	$E_{-,lv}$	mmHg/ml	--
Descending LV ESPVR pressure axis intercept	$V_{b,lv}$	ml	--
Scaling factor for LV viscous resistance	$K_{R,lv}$	s/ml	3.75*10^{-4}
Right Heart			
Right atrial compliance	C_{ra}	Ml/mmHg	31.25
Right atrial unstressed blood volume	$V_{u,la}$	ml	25
Right atrial resistance	R_{la}	mmHg*s*ml^{-1}	2.5*10^{-3}
Scaling factor for RV EDPVR	$P_{0,rv}$	mmHg	1.5
Exponent for RV EDPVR	$K_{E,rv}$	ml^{-1}	0.016
RV unstressed blood volume	$V_{u,rv}$	ml	40.8
Ascending slope for RV ESPVR	$E_{+,rv}$	mmHg/ml	1.75
Descending slope for RV ESPVR	$E_{-,rv}$	mmHg/ml	--
Descending RV ESPVR pressure axis intercept	$V_{b,rv}$	ml	--
Scaling factor for RV viscous resistance	R_{sa}	s/ml	1.4*10^{-3}

* LV: left ventricle; RV: right ventricle; ESPVR: End-systolic pressure and volume relationship; EDPVR: End-diastolic pressure and volume relationship

Table 5: The parameters for baroreflex control

Parameter name/description	Symbol	Units	Values
Carotid sinus afferent pathway			
Intrasinus pressure at the central point of sigmoidal function	P_n	mmHg	92
Lower saturation of frequency discharge in afferent fibers	f_{min}	spikes/s	2.52
Upper saturation of frequency discharge in afferent fibers	f_{max}	spikes/s	47.78
Relate to the slope of the static function at the central point	k_a	mmHg	11.758
Time constant for real zero in the linear dynamic block	τ_z	s	6.37
Sympathetic efferent pathway			
Frequency constant of spikes in the efferent sympathetic nerves	$f_{es,oo}$	spikes/s	2.10
Frequency constant of spikes in the efferent sympathetic nerves	$f_{es,0}$	spikes/s	16.11
Minimum sympathetic stimulation	$f_{es,min}$	spikes/s	2.66
Constant in the exponential frequency trend	k_{es}	spikes/s	0.0675
Vagal efferent pathway			
Frequency constant of spikes in the efferent vagal nerves	$f_{ev,oo}$	spikes/s	6.3
Frequency constant of spikes in the efferent vagal nerves	$f_{ev,0}$	spikes/s	3.2
Constant in the exponential frequency trend	k_{ev}	spikes/s	7.06
Central value for the frequency of spikes in the afferent fibers	$f_{cs,0}$	spikes/s	25
Effectors			
Mechanism strength for splanchnic peripheral resistance	$G_{R,sp}$	mmHg•ml^{-1}•υ^{-1}	0.0695
Mechanism strength for Extrasplanchnic peripheral resistance	$G_{R,ep}$	mmHg•ml^{-1}•υ^{-1}	0.53
Mechanism strength for unstressed splanchnic venous volume	$G_{Vu,sv}$	ml•υ -1	-265.4
Mechanism strength for unstressed Extrasplanchnic venous volume	$G_{Vu,ev}$	ml•υ -1	-132.5
Time constant for splanchnic peripheral resistance	$\tau_{R,sp}$	s	6
Time constant for Extrasplanchnic peripheral resistance	$\tau_{R,sp}$	s	6
Time constant for unstressed splanchnic venous volume	$\tau_{Vu,sv}$	s	20
Time constant for unstressed Extrasplanchnic venous volume	$\tau_{Vu,sv}$	s	20
Time delay for splanchnic peripheral resistance	$D_{R,sp}$	s	6
Time delay for Extrasplanchnic peripheral resistance	$D_{R,ep}$	s	2
Time delay for unstressed splanchnic venous volume	$D_{Vu,sv}$	s	5
Time delay for unstressed Extrasplanchnic venous volume	$D_{Vu,sv}$	s	5
Splanchnic peripheral resistance in absence of innervation	$R_{sp,0}$	mmHg•s•ml-1	2.49
Extrasplanchnic peripheral resistance in absence of innervation	$R_{ep,0}$	mmHg•s•ml-1	0.78
Unstressed splanchnic venous volume in absence of innervation	$V_{usv,0}$	ml	1435.4
Unstressed Extrasplanchnic venous volume in absence of innervation	$V_{usv,0}$	ml	1537

Table 6: Parameter values to simulate four pathological conditions

	LVF	***Bi-F***	***LVF, PVR+***	***Bi-F, PVR+***
Left Ventricle				
$K_{E.lv}$	0.0136	0.0144	0.0121	0.0109
$V_{u.lv}$	25	25	25	25
$E_{+.lv}$	1.2	1.2	1.2	1.2
$E_{-.lv}$	-0.6	-0.6	-0.6	-0.6
$V_{b,lv}$	240	240	240	240
Right Ventricle				
$K_{E.rv}$	0.016	0.0115	0.016	0.0115
$E_{+.rv}$	1.6	0.8	1.6	0.8
$E_{-.rv}$	-0.2	-0.2	-0.2	-0.2
$V_{b,rv}$	204.72	117.36	204.72	117.36
Vascular System				
R_{pa}	0.023	0.092	0.092	0.092
R_{pp}	0.0894	0.0894	0.44	0.44
$V_{u.sp}$	274.4	94.4	274.4	94.4
$V_{u.ep}$	336.6	66.6	336.6	66.6
$V_{u.sv}$	1435.4	735.4	1435.4	735.4
$V_{u.ev}$	1537	467	1537	467
TBV	5700	5700	5700	5700

Note that model parameter value not shown in this table retained normal values, as specified in Appendix 4. See Appendix 4 for definitions of abbreviations.

LVF: left ventricular failure; Bi-F: biventricular failure, including LVF and right ventricular failure (RVF); PVR+: high pulmonary vascular resistance.

Table 7: Simulation variables at normal and four pathological heart failure conditions.

Parameters	*Units*	*Normal*	*LVF*	*Bi-F*	*LVF,PVR+*	*PVR+*
Cardiac output	L/min	5.8	4.5	3.2	3.3	2.4
Stroke volume	mL	68.0	41.1	37.1	39.2	28.6
Left atrial pressure (mean)	mmHg	8.7	26.0	28.0	19.1	18.0
Right atrial pressure (mean)	mmHg	4.4	3.5	17.1	5.1	20.7
Arterial pressure						
Systolic	mmHg	133.0	95.2	98.4	93.0	87.6
Diastolic	mmHg	93.0	69.4	74.8	68.3	68.0
Mean	mmHg	106.0	77.3	82.1	75.9	73.8
Pulmonary arterial pressure						
Systolic	mmHg	28.0	37.9	49.8	61.9	49.4
Diastolic	mmHg	15.0	29.3	31.7	42.3	35.0
Mean	mmHg	20.1	32.9	37.8	48.9	39.8
LV end-diastolic pressure	mmHg	10.0	25.6	27.6	18.8	17.8
LV end-diastolic volume	mL	130.0	245.6	237.1	246.8	256.0
RV end-diastolic pressure	mmHg	4.0	3.3	16.8	4.8	20.5
RV end-diastolic volume	mL	121.0	106.4	252.8	125.6	277.5
LV ejection fraction	%	52	17	16	16	11
RV ejection fraction	%	56	39	15	31	10
Pulmonary vascular resistance	Wood Units	2.0	2.0	3.1	9.0	9.0

* The approximate calculation: pulmonary vascular resistance = (mean pulmonary arterial pressure – mean left atrial pressure)/cardiac output; LV: left ventricle; RV: right ventricle.

References:

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