## **Analysis of Physiological Systems**

## Assignment on analysis of cardiac physiology

In this assignment, you will use CircAdapt simulation software to simulate normal cardiac rhythm and cardiac rhythm during aortic valve stenosis. Prepare a report explaining the answers and including the relevant plots.

You may refer to articles on 'Wiggers diagram' as a starting point to this assignment.
You can download the CircAdapt Simulator v1.1.0 at: <a href="http://www.circadapt.org/downloads/files">http://www.circadapt.org/downloads/files</a>
You can also refer to the manual of the software for basic functionality by clicking the link below.
[LINK]

## 1. Normal Sinus Rhythm

Open the simulation software and display left ventricular pressure, left atrial pressure and the aortic pressure. (Right click on the top left graph (Pressure vs time graph) and select aorta, left\_atrium, left\_ventricle)

Also display the left ventricular volume. (Right click on the volume-time graph and select left\_ventricle).

Display blood flow velocities in the aortic and mitral valves (lower panel row) and the pressure-volume relation of the left ventricle in the pressure-volume graph on the right side of the user interface.

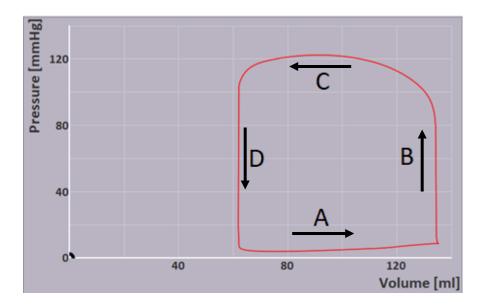
You can place your cursor on any given graph and scroll to zoom in or zoom out. Scrolling while pressing down the CTRL button on your keyboard will zoom the graphs horizontally. Hovering the mouse over any point on the graph gives the time and amplitude at that point.

Try to understand the graphs you see in the simulation, comparing them with the Wiggers diagram.

The Mitral valve opens only in the direction of the left ventricle. This is a passive process and occurs when the left atrial pressure is greater than that of the left ventricular pressure. The aortic semilunar valve on the other hand opens only in the direction of the aorta when the left ventricular pressure is greater than the aortic pressure.

- a. Check left ventricular and aortic blood pressure signals in the REFERENCE column and determine when the aortic valve is open and when the aortic valve is closed. Also check whether this corresponds with the change of left ventricular volume. Click on the appropriate point of time on the REFERENCE column to place a vertical line at that point to mark the opening and closing points of the aortic valve. Take a screenshot of the graphs displayed in the software and attach them in your report.
- b. Check left ventricular and left atrial blood pressure signals in the REFERENCE state and determine when the mitral valve is open and when the mitral valve is closed. Also check whether this corresponds with the change of left ventricular volume. Click on the appropriate point of time on the REFERENCE column to place a vertical line at that point to mark the opening and closing points of the mitral valve.

- Take a screenshot of the graphs displayed in the software and attach them in your report. You may zoom into a given graph to clearly identify the points of interest.
- c. Identify which points of the pressure-volume relation correspond to the closing and opening of the aortic and mitral valves and place the numbers 1, 2, 3 and 4 in the right place on the figure below. (1-aortic opening, 2-aortic closing, 3-mitral opening, 4-mitral closing)



- d. The pressure-volume relation can be regarded as a rectangle with each of its four sides corresponding to a phase of the cardiac cycle. Name the phases (A, B, C, and D) indicated in the figure below by choosing one of the following phases: isovolumic relaxation, ejection, filling and isovolumic contraction.
- e. Explain why the flow velocity pattern in the aortic valve has one hump and the pattern in the mitral valve has two. You may refer to the description in blue color above to answer this question.
- f. Check the atrial pressure in detail by adjusting the scale of the y-axis (scrolling). One can identify one fast (steep) and one slow increase in atrial pressure during a single cardiac cycle. Explain what causes these two atrial pressure rises. Also state the ECG waveform (choose from P-wave, QRS complex, T Wave) that corresponds to the sharp rise of pressure mentioned above.

Under normal circumstances, diastolic filling of the left ventricle is characterized by an early passive filling phase (E-wave) and a late active filling phase (A-wave) that results from atrial contraction. Keep in mind that the 'E' of E-wave stands for 'early' / 'elastic' and that the 'A' of A-wave refers to 'atrial' / 'active'. Understand how the E-wave corresponds to blood flowing from the atria to ventricles passively without any contraction of atrial muscles. Understand how the contraction of atrial muscles actively fill the ventricles subsequently.

- g. Identify the E- and A-waves of the mitral blood flow velocity signal in the simulation. (Attach a labeled screenshot). The E/A-ratio (amplitude of the E-wave divided by that of the A-wave) is often used as a measure of ventricular diastolic function. In general, diastolic function is considered to be good when the E/A ratio is above 1.
- h. Calculate the E/A-ratio of the current simulation (use the mouse to determine peak velocities in the REFERENCE column).
- i. Estimate the relative amount of left ventricular filling that is due to passive filling and how much due to active filling in this normal heart during rest.
- j. Blood flow velocity ( $V_{valve}$ ) in a valve is related to flow rate ( $Q_{valve}$ ) through the valve. What geometrical/anatomical property of the valve do you need to know in order to convert  $V_{valve}$  into  $Q_{valve}$ ? Consider the units of both quantities.

## 2. Aortic Valve Stenosis

Return to the normal REFERENCE simulation by clicking the reset-button and display all signals discussed in Exercise 1.

The opening area ( $A_{valve}$ ) of a normal aortic valve is approximately 4 cm<sup>2</sup> during the ejection phase. In case of an aortic valve stenosis (AS), the opening area is reduced. In this practical, a stenosis is expressed in percentage of  $A_{valve}$ . In the clinic, an AS of >75% (and 50 mmHg pressure drop across the valve) is considered to be critical.

- a. Explain the terms "preload" and "afterload"
- b. Simulate an AS of 80% by gradually increasing the percentage of stenosis with steps of 5% ("valves" tab). Evaluate the hemodynamic changes per step increase of AS. In particular, pay attention to the left ventricular pressure-volume relation. Determine maximal left ventricular pressure.
- c. Explain what aortic valve stenosis does to the preload of the left ventricle and the afterload of the left ventricle. Explain what happens to the cardiac output as a result of this change.
- d. Determine aortic blood pressure at the moment of maximal left ventricular pressure and calculate the pressure drop across the stenotic aortic valve at that same moment.

For a blood vessel with a stenosis, according to Bernoulli's equation it holds:  $\frac{1}{2}pv^2 + pgh + p = constant$ . This relation can be simplified so that it can be used to estimate the maximal pressure drop across a stenotic valve from the maximal blood flow velocity in the valve. For this purpose, we assume that blood flow velocity proximal to the stenotic valve is much smaller than that in the valve and that all the kinetic energy is converted into heat due to turbulence/friction, and that there is no height difference to be bridged). When p is expressed in mmHg, the relation can be approximated by:  $\Delta p \approx 4v^2$  (since 1 mmHg equals 133 Pa and  $\rho_{blood}$ =1060kgm<sup>-3</sup> so that  $\frac{1}{2}p/133 = \frac{1}{2}*1060/133 \approx 4$ ). In the clinical setting, this formula (simplified Bernoulli equation) is commonly used to noninvasively determine the severity of a stenosis.

- e. Use the formula  $\Delta p \approx 4v^2$  as well as the blood flow velocity signal in the stenotic aortic valve to estimate the maximal pressure drop across the valve. Compare the answer with the outcome of exercise 2) part d).
- f. Use the blood flow velocity signal in the aortic valve to determine the duration of ejection.
- g. The surface area enclosed by the pressure-volume relation is a measure of the external pump work generated by the left ventricle. Estimate the increase in external pump work generated by the left ventricle due to 80% AS. You may count the effective number of squares enclosed by the pressure-volume curve to estimate the area.
- h. How will the myocardial tissue of the left ventricle adapt in order to be able to generate the chronically increased pump work? What is the effect of this adaptation on afterload?

You may refer to the following link on 'Tricuspid Regurgitation' to see another example of how Bernoulli's equation is applied to the circulatory system. Start viewing from 3:20 seconds in the video.

https://www.youtube.com/watch?v=cO6B9Q3At1Y