EXAMPLE TUTORIAL
WITH THE CIRCADAPT SIMULATOR

“ACUTE VALVULAR PROBLEMS”

Visit www.circadapt.org for free download of the CircAdapt Simulator software (available for both Windows and OS X) as well as the user manual.

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INTRODUCTION

This tutorial aims at improving the students’ understanding of the pathophysiology of valvular diseases (valvulopathies). The hemodynamic consequences of two different valvular diseases of the left heart (i.e., mitral valve insufficiency and aortic valve stenosis) are simulated by the student using a computer model of the cardiovascular system (CircAdapt Simulator). With each valvular heart disease, cardiac pump function is evaluated by assessing 1) blood pressures in the left ventricle, left atrium, and aorta, 2) left ventricular pressure-volume relation (pressure-volume loop), and 3) blood flow velocities in the valves. Simulations are also used to improve understanding of the concepts “preload” and “afterload” and their relationship with cardiac pump function.

Exercise 1: Normal cardiac function

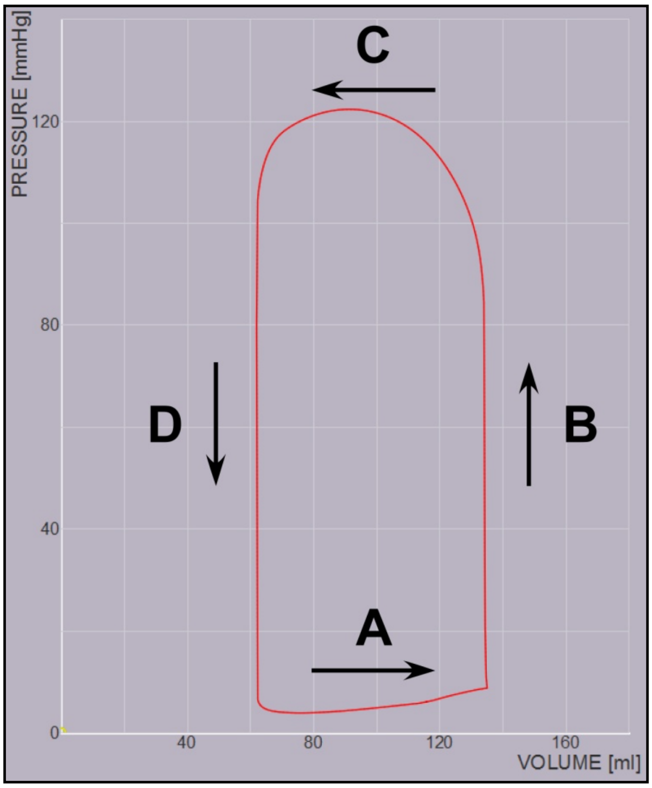
Start the CircAdapt Simulator. In addition to aortic pressure, which is the only signal shown in default mode, also display left ventricular and atrial pressure as well as left ventricular volume (click right mouse button in one of the upper pressure panels and middle volume panels, respectively). Remember that blood generally flows from high to low pressure. However, flowing blood does not stop instantly. Due to mass inertia, decelerating blood shortly flows from low to high pressure.

a. Check left ventricular and aortic blood pressure signals in the *REFERENCE* state and determine when the aortic valve is open. Also check whether this corresponds with the change of left ventricular volume.

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 left side of the user interface.

b. Use the time marker in the *REFERENCE* column (vertical black line) to determine which points of the pressure-volume relation correspond to the closing and opening of the aortic valve and the mitral valve and **place the numbers 1, 2, 3 and 4 in the right place on the figure below**.

c. 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.



Opening/closure of valves:

1. Aortic valve closure
2. Mitral valve closure
3. Mitral valve opening
4. Aortic valve opening

Phases of the cardiac cycle:

A. ……………………………………

B. ……………………………………

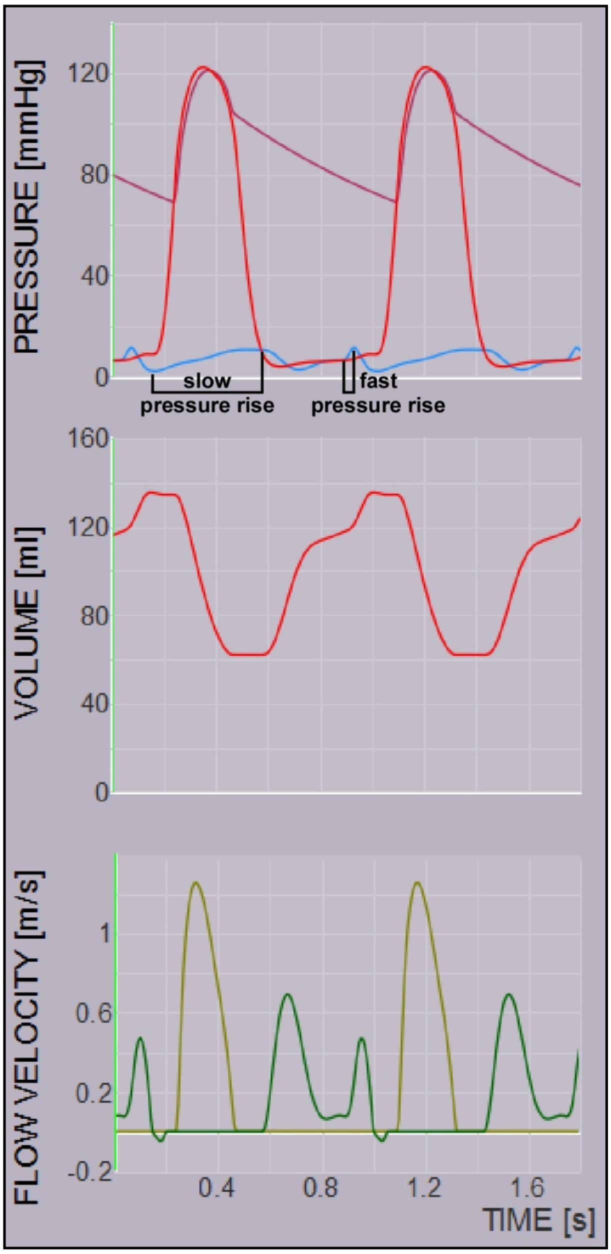
C. ……………………………………

D. ……………………………………

d. Explain why the flow velocity pattern in the aortic valve has one hump and the pattern in the mitral valve has two.

e. Check the atrial pressure in detail by adjusting the scale of the y-axis (scrolling). One can identify one fast and one slow increase in atrial pressure during a single cardiac cycle (see figure below). Explain what causes these two atrial pressure rises.

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'.



f. Identify the E- and A-waves of the mitral blood flow velocity signal in the figure alongside.

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.

g. Calculate the E/A-ratio of the current simulation (use the mouse to determine peak velocities in the REFERENCE column).

h. 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.

Blood flow velocity (**v_{valve}**) in a valve is related to flow rate (**Q_{valve}**) through the valve.

i. 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.

Exercise 2: Mitral valve insufficiency

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

The opening area ($\mathbf{A}_{valve}$) of a normal mitral valve is approximately 6 cm^2 during the diastolic filling phase and the valve is fully closed during systole (leakage area = 0%). In case of a mitral valve insufficiency (MI), the valve does not completely close during systole. In this practical, leakage size is expressed in percentage of $\mathbf{A}_{valve}$.

a. Simulate an MI of 10% by gradually increasing the leakage size with steps of 1% ("valves" tab). Evaluate the hemodynamic changes per step increase of MI. Describe in your own words how an acute MI affects left ventricular filling and output.

Store the current simulation by clicking the *snapshot-button*.

b. Determine the left ventricular stroke volume on the basis of the pressure-volume relation. Is stroke volume increased or decreased relative to the normal *REFERENCE* condition?

c. Check what happened with the maximum blood flow velocity ($\mathbf{v}_{max}$) through the aortic valve. Explain the differences in behavior of $\mathbf{v}_{max}$ and stroke volume. Where goes the blood that is ejected by the left ventricle during systole? Verify your answer by examining the pattern of blood flow velocity in the mitral valve.

d. Adjust the scaling of the y-axis of the pressure signals (using the scroll function) so that the atrial pressure signal can be evaluated in detail. Explain the difference in atrial pressure between the normal *REFERENCE* simulation and the *CURRENT* simulation with MI.

e. What happened to the mean aortic pressure? Explain the change of mean aortic pressure. How will the body respond to this change of **mean arterial pressure**?

Turn on homeostatic control of **mean arterial pressure** and **venous return** of blood to the heart (right atrium) by checking the **pressure/flow regulation** box ("general" tab). By doing so, peripheral systemic flow resistance and total blood volume are regulated so that **mean arterial pressure** and **venous return** equal the desired values entered (see the user manual for more information about the **pressure/flow regulation** function).

f. Examine the hemodynamic differences between the *SNAPSHOT* and the *CURRENT* (after enabling **pressure/flow regulation**) simulation. What do you notice when examining left atrial pressure and volume?

The terms **preload** and **afterload** are often used in the clinic to characterize cardiac pump function. For proper understanding, it is of utmost importance to consider **preload** and **afterload** as qualitative concepts instead of measurable variables.

The concept **preload** can be defined as mechanical load of the myocardial tissue at the end of diastole (end-diastolic wall stress). Preload increases with end-diastolic pressure and volume, but decreases with wall thickness (Laplace's Law on wall tension). Thus, end-diastolic ventricular pressure and volume can be considered indirect measures of **preload**. On their own, they provide a rather incomplete representation of **preload**.

The concept **afterload** can be defined as mechanical load of the myocardial tissue during ejection. Any condition that requires a greater ventricular pressure to be generated by the ventricular myocardium for ejection will cause an increase in **afterload**. Also, if the chamber volume is increased as the result of increased filling during diastole (increased preload) or ventricular dilation in response to chronic increases in filling pressures, **afterload** will be increased even if arterial pressure is normal. Also for **afterload** it holds that variables such as arterial pressure and total peripheral resistance contribute to **afterload** but are not the same as **afterload**.

g. Strike out as appropriate:

   "Acute mitral valve insufficiency **increases / decreases / hardly changes** preload of the left ventricle."

   "Acute mitral valve insufficiency **increases / decreases / hardly changes** afterload of the left ventricle."

   "Acute mitral valve insufficiency increases **pressure/volume** load of the left atrium."

h. Patients with chronic MI are often treated with angiotensin-converting enzyme inhibitors (ACE inhibitors) and diuretics. Explain why this treatment is considered taking into account the observations in exercise 2f?

Exercise 3: 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 ($\mathbf{A_{valve}}$) of a normal aortic valve is approximately 4 cm^2 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 $\mathbf{A_{valve}}$. In the clinic, an AS of >75% (and 50 mmHg pressure drop across the valve) is considered to be critical.

a. 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.

b. Strike out as appropriate:

   "Aortic valve stenosis primarily **increases / decreases / hardly changes** preload of the left ventricle."

   "Aortic valve stenosis primarily **increases / decreases / hardly changes** afterload of the left ventricle."

c. 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.

The **conservation of energy law** states that the total amount of energy in an isolated system always remains constant. In such a system, energy can be converted from one form to another (e.g., from kinetic to potential energy). Remember that, when you are using a garden hose to spray water straight up in the air, the water will reach a certain height. When the water is leaving the hose, energy in the form of hydrostatic pressure (**p**) in the hose is converted into kinetic energy ($\frac{1}{2}\rho v^2$ with velocity **v** and water density ρ). During the upward motion of the water in the air, kinetic energy is converted into potential energy (**ρgh** with gravitational acceleration **g** and height **h**). At the highest point, the kinetic energy is shortly zero and the potential energy reached its maximal value. Then, the water falls down again and the potential energy is converted into kinetic energy. When you squeeze the end of the hose the water will reach up higher since you built up a higher hydrostatic pressure in the hose and, thereby, generate more kinetic energy of the water after leaving the hose.

For such a system (also for a blood vessel with a stenosis) it holds: $\frac{1}{2}\rho v^2 + \rho gh + p = \text{constant}$. 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 (it is assumed that blood flow velocity proximal to the stenotic valve is much smaller than that in the valve, 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 so that $\frac{1}{2}\rho/133 = \frac{1}{2}*1060/133 \approx 4$). In the clinical setting, this formula (simplified Bernoulli equation) is commonly used to noninvasively determine the severity of a stenosis.

d. 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 3c.

e. Use the blood flow velocity signal in the aortic valve to determine the duration of ejection.

f. Is it possible to obtain the duration of ejection from the pressure-volume relation of the left ventricle?

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.

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?