



Graduada en Ingeniería de la Salud

Modelado Físico del Sistema

Cardiorrespiratorio y sus Interacciones

usando SIMSCAPE

Physical Model of the Cardiopulmonary

System and his Interactions using SIMSCAPE

Realizado por

Maryana Pyzh

Tutorizado por Francisco Javier Fernández de Cañete Rodríguez

Departamento

Ingeniería de Sistemas y Automática

MÁLAGA, julio de 2022





## ESCUELA TÉCNICA SUPERIOR DE INGENIERÍA INFORMÁTICA GRADUADA EN INGENIERÍA DE LA SALUD

#### Modelado Físico del Sistema Cardiorrespiratorio y sus Interacciones usando SIMSCAPE

#### Physical Model of the Cardiopulmonary System and his Interactions using SIMSCAPE

Realizado por **Maryana Pyzh** 

Tutorizado por **Francisco Javier Fernández de Cañete Rodríguez** 

Departamento
Ingeniería de Sistemas y Automática

UNIVERSIDAD DE MÁLAGA MÁLAGA, JULIO DE 2022

Fecha defensa: julio de 2022

## **Abstract**

This Final Degree Project aims to implement the cardiorespiratory system through Object-Oriented Programming and use a double electrical analogy to facilitate its implementation and interpretation.

First, an introductory study of the physiology and anatomy of the cardiorespiratory system is carried out, both the respiratory and cardiac parts, as well as the relationship between the two systems.

Subsequently, a mathematical model sased on differential equations that represent the cardiovascular and respiratory parts separately is presented, allowing for a subsequent interconnection between the two models. In turn, the cardiopulmonary system, which will already be formed by the connection between the two systems, will be subjected to functional tests under normal conditions during rest and exercise and pathological conditions such as pulmonary obstruction and aortic regurgitation.

The main advantage of subjecting the pulmonary and cardiovascular systems to pathology is to show how these systems affect one to another and their consequences.

Finally, the model can be employed in research and by specialists to comprehend the cardiorespiratory function and their tight relationship.

**Keywords:** Cardiovascular system, Pulmonary system, Electric analogies, Block diagram, Object Oriented Programming

### Resumen

Este Proyecto Fin de Grado pretende implementar el sistema cardiorrespiratorio a través de la Programación Orientada a Objetos y utilizar una doble analogía eléctrica para facilitar su implementación e interpretación.

En primer lugar, se realiza un estudio introductorio de la fisiología y anatomía del sistema cardiorrespiratorio, tanto de la parte respiratoria como de la cardíaca, así como de la relación entre ambos sistemas.

Posteriormente, se presenta un modelo matemático basado en ecuaciones diferenciales que representan las partes cardiovascular y respiratoria por separado, lo que permite una posterior interconexión entre ambos modelos. A su vez, el sistema cardiopulmonar, que ya estará formado por la conexión entre los dos sistemas, será sometido a pruebas funcionales en condiciones normales durante el reposo y el ejercicio, y en condiciones patológicas como la obstrucción pulmonar y la regurgitación aórtica.

La principal ventaja de someter a los sistemas pulmonar y cardiovascular a una patología es mostrar cómo estos sistemas se afectan mutuamente y sus consecuencias.

Por último, el modelo puede ser utilizado en la investigación y por los especialistas para comprender la función cardiorrespiratoria y su estrecha relación.

Palabras Clave: Sistema cardiovascular, Sistema respiratorio, Analogías eléctricas, Diagrama de bloques, Programación Orientada a Objetos

To my mom Iryna for being the support, love and strength I need,
because you showed me what is hard work and family.

To my grandma Mariya for being the angel in my life
and make me the person I am.

To my teacher, F.J. Fernández de Cañete Rodríguez,
for being my mentor.

And last but not least, to my whole family
because without you, I am nothing.

## **Table of Contents**

I	Intr	oauctio	on a second control of the second control of	1
	1.1	Motiva	ation	1
	1.2	Object	ives	2
	1.3	State o	of the art	2
	1.4	Structu	are of the document	3
	1.5	Techno	ologies used	3
2	Car	diopuln	nonary physiology	5
	2.1	Cardio	vascular system	5
		2.1.1	Blood circulation and heart contraction	6
	2.2	Respira	atory system	7
		2.2.1	The process of breathing	9
	2.3	Relatio	on between cardiovascular and respiratory system	10
		2.3.1	Gas exchange	10
		2.3.2	Oxygen transport in the blood	11
		2.3.3	Interactions between the two systems	12
3	Usa	ge of ar	nalogies in systems modelling	15
	3.1	The hy	draulic analogy	15
	3.2	The me	echanical-electrical analogy	17
	3.3	Windk	tessel Model	18
4	Sim	ulation	environment	21
	4.1	The SI	MULINK environment	21
	4.2	The SI	MSCAPE environment	22
5	Mod	delling	of the cardiopulmonary system	25
	5.1	Model	ling of the Cardiovascular System	25
	5.2	Model	ling of the Pulmonary System	28
	5.3	Model	ling of the Cardiopulmonary Interactions	29

		5.3.1	Exercise mode	29
		5.3.2	Pulmonary obstruction	31
		5.3.3	Aortic regurgitation	32
	5.4	Block-	diagram Model of Cardiopulmonary System in SIMULINK	34
		5.4.1	Cardiovascular block model	34
		5.4.2	Pulmonary block model	36
	5.5	Orient	ed Object Model of Cardiopulmonary System in SIMSCAPE	38
		5.5.1	Cardiovascular System	38
		5.5.2	Pulmonary System	41
	5.6	Orient	ed Object Model of Cardiopulmonary Interactions in SIMSCAPE	44
		5.6.1	Exercise model	44
		5.6.2	Pulmonary obstruction	46
		5.6.3	Aortic regurgitation	47
6	Exp	erience	es and results	49
	6.1	Results	s in physiological conditions	49
		6.1.1	Normal conditions	49
		6.1.2	Exercise conditions	53
	6.2	Results	s in pathological conditions	56
		6.2.1	Aortic valve regurgitation	56
		6.2.2	Chronic Obstructive Pulmonary Disease	58
7	Con	clusion	ns and future lines of study	63
	7.1	Conclu	asions	63
	7.2	Future	lines of study	63
8	Con	clusion	nes y líneas futuras	65
	8.1	Conclu	usiones	65
	8.2		futuras	65

## List of Figures

Figure 2.1	Representation of the heart location in the human body	5
Figure 2.2	Representation of the heart parts	6
Figure 2.3	Cardiac cycle	7
Figure 2.4	Parts of the respiratory system	8
Figure 2.5	The process of inhalation and exhalation	9
Figure 2.6	Lung volumes and capacities	10
Figure 2.7	Exchange and transport of $O_2$ and $CO_2$	11
Figure 2.8	Aortic pressure wave for different ranges of EF	14
Figure 2.9	Quantitative results of the data obtained of the dogs	14
Figure 3.1	Comparison between Poiseuille and Ohm law	17
Figure 3.2	The damper mass spring model and the RCL circuit	18
Figure 3.3	Three different Windkessel models	19
Figure 3.4	Inductance implemented in three-element windkessel	19
Figure 4.1	Simulink Library Browser	22
Figure 4.2	Different essential blocks of Simscape to model the Cardiopulmonary	
Syste	m	23
Figure 5.1	Representation of the cardiovascular circuit	26
Figure 5.2	Representation of the respiratory circuit	28
Figure 5.3	SIMULINK block diagram of the cardiovascular system using the dif-	
ferent	tial equations	34
Figure 5.4	Differentiation of the different sections of the SIMULINK block diagram	
of Ca	rdiovascular System	34
Figure 5.5	Representation of all the blocks of the cardiovascular system	36
Figure 5.6	SIMULINK block diagram of the pulmonary system using the differen-	
tial ed	quations	36
Figure 5.7	Differentiation of the different sections of the SIMULINK block diagram	
of Pul	monary System	37
Figure 5.8	Representation of all the blocks of the pulmonary system in SIMULINK	38

Figure 5.9	Block diagram of the pulmonary system	38
Figure 5.10	Block - Driving force of the left ventricle	39
Figure 5.11	Left ventricle pressure	39
Figure 5.12	Aortic valve	40
Figure 5.13	Blood flow rate	40
Figure 5.14	Electric analogy of the Windkessel model	41
Figure 5.15	Aortic pressure and Peripheral pressure	41
Figure 5.16	Block diagram of the pulmonary system	42
Figure 5.17	SIMSCAPE - Driving force of the respiratory cycle	42
Figure 5.18	SIMSCAPE - Air volume flow rate	43
Figure 5.19	Electric analogy connected of the pulmonary system	43
Figure 5.20	SIMSCAPE - Pulmonary pressure	43
Figure 5.21	Cardiovascular model in exercise conditions	44
Figure 5.22	Exercise interconnecting elements	44
Figure 5.23	Variable impedance in the cardiovascular system	45
Figure 5.24	Pulmonary model in exercise conditions	46
Figure 5.25	Driving force of the alveoli depending on workload module	46
Figure 5.26	Pulmonary obstruction cardiovascular system	47
Figure 5.27	Left ventricle driving force in pulmonary obstruction	47
Figure 5.28	Aortic regurgitation in pulmonary system	48
Figure 5.29	Decrease in the muscle blood flow module	48
Figure 5.30	Increase of the muscle stiffness module	48
Figure 6.1	Pressures evolution in normal conditions	49
Figure 6.2	Blood flow rate in normal conditions	50
Figure 6.3	Left ventricle pressure in normal conditions	51
Figure 6.4	Aortic pressure in normal conditions	51
Figure 6.5	Normal condition peripheral pressure	52
Figure 6.6	Air volume flow rate in normal conditions	52
Figure 6.7	Air volume inside the lung in normal conditions	53
Figure 6.8	Exercise conditions for the left ventricle pressure	53
Figure 6.9	Exercise conditions for the aortic pressure	54

Figure 6.10	Exercise conditions for the blood flow rate	54
Figure 6.11	Exercise conditions for the air volume flow rate	55
Figure 6.12	Exercise conditions for the air volume within the lung	55
Figure 6.13	Blood flow rate in the aortic valve regurgitation	57
Figure 6.14	Aortic pressure in the aortic valve regurgitation	57
Figure 6.15	Air volume flow rate in the aortic valve regurgitation	58
Figure 6.16	Air volume in the aortic valve regurgitation	58
Figure 6.17	Air volume flow rate in the chronic obstructive pulmonary disease	59
Figure 6.18	Air volume in the chronic obstructive pulmonary disease	59
Figure 6.19	Aortic pressure in the aortic chronic obstructive pulmonary disease   .   .	60
Figure 6.20	Blood flow rate in the chronic obstructive pulmonary disease	60

## List of Tables

Table 3.1	Electric-hydraulic components and physical quantities comparison	16
Table 3.2	Similarities between electric and hydraulic systems	16
Table 3.3	Mechanical-electrical variables	17
Table 3.4	Electric-Mechanic equations	18
Table 5.1	Values of the components of the cardiovascular system	27
Table 5.2	Values of the components of the pulmonary system	29
Table 5.3	Impedance parameters for the exercise	30
Table 5.4	Values obtained for different exercise modes	31
Table 5.5	Amplitude parameters that define the change in the driving force by the	
left v	ventricle	32
Table 5.6	Values obtained for different pulmonary obstruction levels	32
Table 5.7	Values obtained for different degrees of aortic regurgitation	33

1

## Introduction

#### 1.1 Motivation

In the 21st century, non-communicable diseases, including cardiovascular diseases, chronic respiratory diseases, cancers and diabetes, are the leading cause of death. Cardiovascular diseases alone accounted for 17.7 million deaths in 2015, representing 31% of all deaths worldwide [WHO, 2017]. In addition, in terms of respiratory diseases, the chronic obstructive pulmonary disease cause the death of 3 million people in 2016, the third most lethal disease, among others [Forum, 2017].

On a physiological level, the cardiovascular and respiratory systems are closely related as the heart and lungs are responsible for providing oxygen to the body and removing waste substances. Therefore, according to recent studies, patients with respiratory diseases such as chronic obstructive pulmonary disease tend to develop cardiovascular diseases [Carter et al., 2019].

Moreover, with the emergence of new tobacco products such as e-cigarettes, the possibility of getting cardiopulmonary diseases has incremented. Just in Spain, 54 thousand death were related to people over 34 years of age who died because of this disease in particular. This numbers represent the 13.7% of total mortality in 2016 [Pérez-Ríos et al., 2020]. That is just a mere example of why it is still necessary to continuously gain knowledge in this area, in order to develop better therapies.

The use of mathematical models has contributed to a greater extent to gain an insight of the internal process that take place at cardiovascular and pulmonary level. That is why a mathematical model based approach has been followed in this Final Degree Project.

#### 1.2 Objectives

The Final Degree Project aims to use an electro-hydraulic and mechanic-electrical analoges to model the cardiovascular and respiratory systems [Tsai and Lee, 2011; Lee and Tsai, 2013] using the SIMSCAPE physical modelling environment.

It should be noted that this project is in the same line of study of David Cuesta Merino Final Degree Project [Cuesta Merino, 2016], which fundamentally contributes to the use of the electrical analogies mentioned before. Moreover, the design will be subjected to different respiratory and cardiovascular pathologies, which will be analyzed and studied in-depth.

The objective here is to provide the clinician with a piece of key information by designing a simple mathematical model of the cardiorespiratory system also by facilitating the testing of severe pathological circumstances. This will enable the clinicians with and easy-to-use computational tool to get insight of the cardiorespiratory performance.

#### 1.3 State of the art

Different interpreted mathematical models of cardiorespiratory system can be found in literature as [Albanese et al., 2016],[Tsai and Lee, 2011] and software simulations packages have been employed to show the performance in physiologic and pathological.

Another studies that integrate mathematical models of cardiorespiratory control have showed to test the consequences of variable exercise load in patients [Barzel et al., 2015] and also under cardiac insufficiency [Batzel et al., 2005].

To conclude this section, it is noteworthy to mention that many mathematical lumped models have been developed in literature [Kappel, 2012].

The simplicity shown in our particular analogy-based application permits the clinicians to

asses different cardiopulmonary conditions and help them to take better decisions.

#### 1.4 Structure of the document

The following document is organized to be as straightforward as possible to comprehend his structure. It is divided into the next parts:

- **Chapter 1**: Presents an introduction states the justification and motivation of this Final Degree Project.
- **Chapter 2**: An anatomical-physiological description of the cardiovascular and pulmonary system is given, and physiological links these two systems.
- **Chapter 3**: This section consists of the use of electrical analogies to express system dynamics.
- **Chapter 4**: This section consists of a brief description of the modelling tools.
- Chapter 5: This chapter consists of the description and understanding of the differential equations that make up cardiopulmonary system as well as their implementations in SIMULINK and SIMSCAPE.
- **Chapter 6**: In this section, the system is subjected to various types of simulated physiopathologic situations and a performance analysis.
- **Chapter 7 and 8**: A discussion of the results obtained in the previous section is given, as well as possible future lines of research.

#### 1.5 Technologies used

The primary technology used in this project is MATLAB, specifically SIMULINK and SIM-SCAPE.

SIMULINK is a block diagram environment used to design systems with multidomain models. While SIMULINK allows the creation of physical models ["Simscape", n.d.].

In this work, the Electrical Library has been the one that has been employed together with the Physical Signal Library to connect with SIMULINK.

2

## Cardiopulmonary physiology

#### 2.1 Cardiovascular system

The heart is one of the essential organs in the human body and is the centre of the cardiovascular system; without it, humans could not be able to be alive. A simple way of seeing the heart is as a ball inside the chest that contracts from the top until the bottom, repeating itself a billion times. Thus, in reality, it is more complex than that.

It is placed in the thoracic cavity, also known as the chest, in the mediastinum (the space between the lungs), behind and to the left of the sternum (Figure 2.1). As a result, the heart lies on the diaphragm in the thoracic cavity, which is encircled by the pericardium [Peate, 2015].

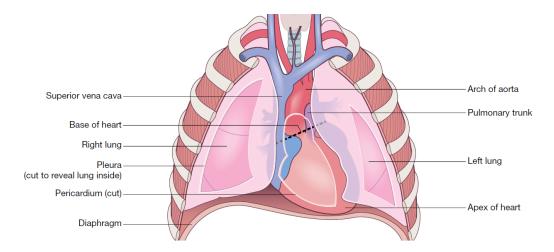


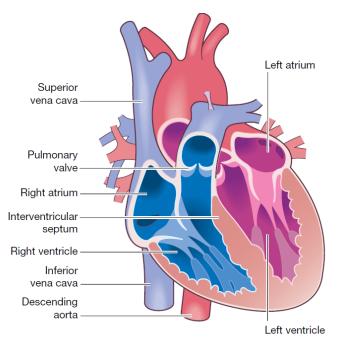
Figure 2.1: Representation of the heart location in the human body

Source: Peate I, Wild K & Nair M (eds) Nursing Practice: Knowledge and Care (2014)

The heart is made up of four chambers (Figure 2.2) whose primary functions are to supply

the rest of the body with oxygen and clean all the waste produced by the cells, specifically:

- Left atrium is responsible for receiving the oxygenated blood from the lungs and pumping it inside the left ventricle.
- Right atrium is responsible for receiving the deoxygenated blood from the body and pumping it inside the right ventricle.
- Left ventricle pumps the deoxygenated blood to the rest of the body.
- Right ventricle pumps the oxygenated blood to the lungs.



Source: Peate I, Wild K & Nair M (eds) Nursing Practice: Knowledge and Care (2014)

Figure 2.2: Representation of the heart parts

#### 2.1.1 Blood circulation and heart contraction

It is essential to mention the blood circulation of the heart and its contraction mechanism to comprehend this complex machine's operation better.

The process starts when the oxygenated blood (blood high in  $O_2$  content) that comes from the lungs is being emptied from the pulmonary veins into the left atrium; meanwhile, at the

same time, the deoxygenated blood (blood low in  $CO_2$  content) enters the heart through the inferior and superior vena cava into the right atrium. Once the atria are full, the atrial systole (contraction of the heart chambers) forces the tricuspid valve (connecting the right atrium with the right ventricle) and the mitral valve (connecting the left atrium with the left ventricle) to open, then when the ventricles are full both valves shut, this prevents blood from flowing backwards into the atria [Luisada and MacCanon, 1972].

The next step is the contraction of the ventricles creating the ventricular systole while the atria are in diastole (relaxation of the heart chambers while they are being filled with blood), this forces the opening of the pulmonary and aortic valves pumping the blood to the lungs and the body respectively (Figure 2.3).

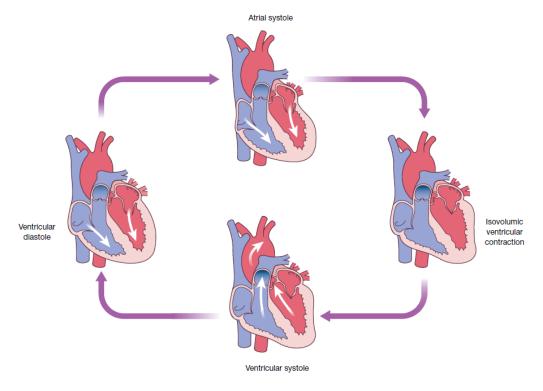


Figure 2.3: Cardiac cycle [Peate, 2015]

#### 2.2 Respiratory system

This system contains another of the most critical organs in the human body: the lungs; without them, human beings can not breathe. In this case, there are two good defined sections: the upper respiratory tract and the lower respiratory tract.

The upper respiratory tract includes the mouth, nose, nasal cavity, and throat. This component of the system warms, filters, and moistens the air that is inhaled [Peate, 2015]. The larynx, trachea, right and left main bronchi, and all the elements of both lungs constitute the lower respiratory tract (Figure 2.4).

In an anathomical level, the lungs are divided into different regions called lobes; in the right lung, there are three lobes, and in the left one, there are two because the heart is occupying the space of the third one. Each lung is surrounded by a parietal and visceral membrane. Moreover, they are located on either side of the heart in the chest cavity; simultaneously, they are encircled and protected by the rib cage.

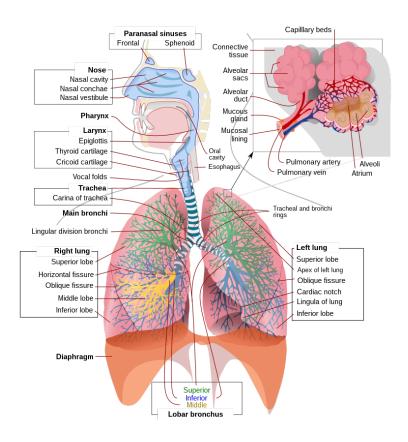


Figure 2.4: Parts of the respiratory system [Wikipedia, 2022d]

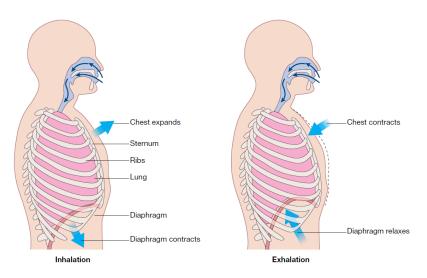
From the nasal cavity, air passes through the pharynx and the larynx as it makes its way to the trachea, which is later divided into the two primary bronchi: the right and left lung. In the lungs, the air is split into the bronchi, each one of the two bronchi divides into secondary bronchi, then into tertiary bronchi, and these keep dividing and creating smaller and smaller

diameter bronchioles. The terminal bronchioles keep dividing themselves into respiratory bronchioles, and these subdivide into several alveolar ducts.

At the end of each duct, there are approximately 100 alveolar sacs, each of them containing 20 to 30 alveoli [Molnar, 2015]. The lungs alveoli are their functional units; moreover, a network of pulmonary capillaries surrounds each alveolus, and each alveolus is lined with a thin layer of tissue, which is essential for the diffusion of gases [Scanlon and Sanders, 2006].

#### 2.2.1 The process of breathing

Pulmonary ventilation is commonly known as breathing, which takes place during the process of inspiration through which atmospheric air is drawn in, and exhalation by which the alveolar air is released out (Figure 2.5).



Source: Peate I & Nair M Fundamentals of Anatomy and Physiology for Student Nurses (2011)

Figure 2.5: The process of inhalation and exhalation

The gradient pressure between the lungs and the atmosphere is responsible for moving air into the lungs, and the same is valid for moving air from the lungs into the atmosphere. When the pressure inside the lungs is below the ambient pressure, inspiration occurs. At the same time, expiration occurs when the intra-pulmonary pressure exceeds the ambient pressure.

Inspiration starts with the contraction of the diaphragm, helping to increase the pulmonary volume. As the pulmonary volume rises, the intra-pulmonary pressure decreases below atmospheric pressure, forcing air to pass through the lungs. The thoracic volume and, thus, the pulmonary volume are reduced when the diaphragm relaxes. The same process re-

peats cyclically.

#### 2.3 Relation between cardiovascular and respiratory system

The relationship between the respiratory and pulmonary system can be related through two processes: gas exchange and blood gas transport [Tortora and Derrickson, 2013], these processes themselves represent respiration and oxygen transport in the blood.

#### 2.3.1 Gas exchange

The gas exchange takes place in the lungs between the air coming to the alveoli and the pulmonary capillaries through the alveolocapillary membrane. To do so, the diffusion of the gases has to happen which is carried our passively, depending on the partial pressure of oxygen  $(O_2)$  and carbon dioxide  $(CO_2)$ . As the partial pressure of  $O_2$  is greater than that of the pulmonary capillaries, the  $O_2$  passes into the capillaries until the partial pressure of the  $O_2$  is equalised on both sides of the alveolocapillary membrane [Pérez de la Plaza and Fernández Espinosa, 2018].

Diffusion of  $CO_2$  takes place in the opposite direction. As the partial pressure of  $CO_2$  in the capillaries is higher than in the alveoli, it diffuses into the alveoli until the pressures equalise on both sides of the alveolocapillary membrane (Figure 2.6).

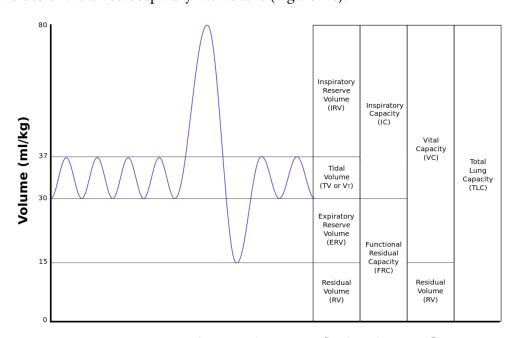


Figure 2.6: Lung volumes and capacities [Wikipedia, 2022b]

#### 2.3.2 Oxygen transport in the blood

Once gases enter the bloodstream they dissolve in plasma, from which 97% of  $\rm O_2$  is transported by haemoglobin (Hb) forming oxyhaemoglobin, the remaining 3% of oxygen is transported dissolved in the plasma, and from here it is distributed through the bloodstream to all the cells of the organism (Figure 2.7).

The partial pressure of  $O_2$  is higher in the blood cells than in the tissue cells, which facilitates its diffusion. The affinity of haemoglobin to bind with oxygen increases when there is an increase in the partial pressure of  $O_2$  and a decrease in the partial pressure of  $O_2$ .

Most  $CO_2$  is transported bound to Hb, forming carboxyhaemoglobin. A small part is dissolved in the plasma as a solute or in the form of ions. The  $CO_2$  exchange process is carried out in the same way as  $O_2$  exchange, but in reverse. The partial pressure of  $CO_2$  in tissues is higher than in blood cells, which facilitates its diffusion into the bloodstream until it reaches the capillaries [Pérez de la Plaza and Fernández Espinosa, 2018].

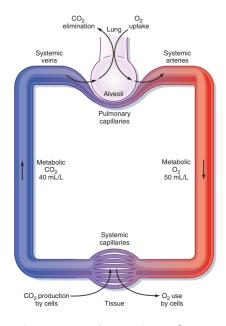


Figure 2.7: Exchange and transport of  $O_2$  and  $CO_2$  [Koeppen and Stanton, 2017]

#### 2.3.3 Interactions between the two systems

Cardiovascular and respiratory systems are tightly related to each other so that certain pathologies present in one of these systems affect the other.

#### 1. Exercise

Aerobic exercise training leads to cardiovascular changes increasing the hear beat and breathing frequency. The most important adaptation is the improvement in maximal cardiac output which is the result of an enlargement in cardiac dimension (meaning that the resistance of the vessels drops because of the need to supply the organism with nutrient) and an increase in blood volume, allowing for greater filling of the ventricles and a consequent larger stroke volume. In parallel with the greater maximal cardiac output, the perfusion capacity of the muscle is increased, permitting for greater oxygen delivery [Hellsten and Nyberg, 2016].

#### 2. Aortic valve regurgitation

Also known as a ortic insufficiency, this problem occurs when the mitral valve does not close entirely but remains slightly open, causing a backflow of blood into the left ventricle.

Aortic regurgitation characterizes by a sudden exposure of the left ventricle provoking an increased level of blood it should contain, causing an acute rise in the left ventricle end-diastolic pressure (LVEDP) leading to a pulmonary capillaries wedge and left atrial pressure increase that cause pulmonary edema. Moreover, it is likely the appearance of mitral valve regurgitation after submitting the left ventricle continuous stress increasing the chances of pulmonary edema [Soltesz and Carabello, 2017].

Pulmonary edema is: "A buildup of fluid in the alveoli (air spaces) in the lungs. This keeps oxygen from getting into the blood. Pulmonary edema is usually caused by heart problems, but it can also be caused by high blood pressure, pneumonia, certain toxins and medicines, or living at a high altitude. Symptoms include coughing, shortness of breath, and trouble exercising." [National Cancer Institute, n.d.].

Mital valve regurgitation is prone to the generation of pulmonary hypertension. Pulmonary hypertension [PH] implies a high pressure in the pulmonary arteries leading to the reduction of the total lung capacity (TLC) and forced vital capacity (FVC) (Figure 2.6).

TLC is the amount of air the lung can hold, while FVC is the maximum volume of air a person can exhale after completely inhaling it inside the lungs. Furthermore, a decrease in the volume the lungs can hold may occur because of the displacement of lung tissue [Low et al., 2015].

#### 3. Pulmonary obstruction

There are several pulmonary diseases but relative to the pulmonary obstruction there is a chronic pulmonary disease called COPD, the acronym for Chronic Obstructive Pulmonary Disease. COPD is characterized by a limitation of the airflow that is not wholly regressive and, due to an unusual inflammatory response of the system, it is frequently progressive [Han et al., 2007].

First of all, there is a need to explain what is ejection fraction: "Ejection fraction (EF) is a measurement, expressed as a percentage, of how much blood the left ventricle pumps out with each contraction" [American Health Association, 2022]. It is considered a normal EF for a heart between 50-70%, between 41-49% it is considered to be in the margin while <40% then a heart failure or cardiomyopathy can be established.

According to the study conducted by [Rutten et al., 2006] about the prevalence of heart failure or left ventricular ejection fraction (LVEF) in patients with COPD, the percentage of LVEF is lower than 40-50% even in some cases, reaching a range of 18-25%.

With the information provided in the previous articles, the [Swamy et al., 2009] study can be better interpreted. In this article, the author performs a series of monitorings on dogs to collect how aortic pressure changes with varying LVEF. Although not directly related to humans, it gives a good insight into the relationship between LVEF and aortic

pressure.

The conclusion shown in Figure 2.8 and Figure 2.9 is when the EF percentage is high the aortic pressure increases as well. It can be said it is a directly proportional relationship.

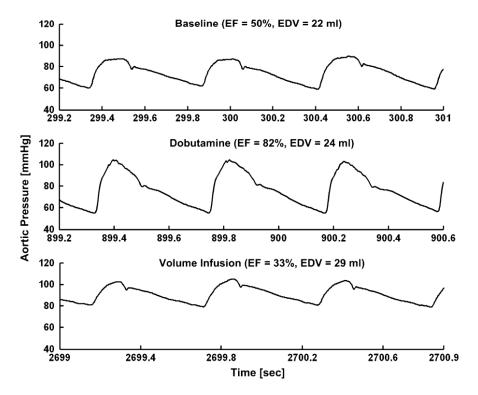


Figure 2.8: Aortic pressure wave for different ranges of EF [Swamy et al., 2009]

Dog	Number of comparisons	EF range (%)	EDV range (mL)	HR range (beats/min)	MAP range (mmHg)	EF RMSE (%)	EDV RMSE (mL)
1	7	53–90	28–46	103-132	67–156	8.5	8.6
2	9	33-84	17-29	94-174	60-94	6.1	1.9
3	10	56-74	21-25	147-179	58-118	4.1	4.5
4	10	52-69	18-23	107-144	42-82	3.4	4.3
5	17	37–74	10-15	60-172	36-116	5.5	1.4
6	9	43-74	13-18	80-140	53-128	5.8	3.3
Total	62	33-90	10-46	60-179	36-156	5.6	4.1

EF is left ventricular ejection fraction; EDV, left ventricular end-diastolic volume; HR, heart rate; MAP, mean aortic pressure; and RMSE, root-mean-squared-error. The EF and EDV ranges were established with the reference echocardiographic measurements.

Figure 2.9: Quantitative results of the data obtained of the dogs [Swamy et al., 2009]

3

# Usage of analogies in systems modelling

Conserning the cardiovascular system, the heart at mechanical level would represent a pump pushing blood to the rest of the arteries and veins; meanwhile, the veins and arteries would be branching pipelines. Having this in mind, a basic formulation of an equivalent hydraulic model would be direct.

Following the same reasoning, lungs perform as mechanical system that push the air in and out during inspiration and expiration provoking the air displacement. Thus, both, could be modelled as mechanical systems, and from here, by using analogies, an electric circuit is easier to be implemented. Therefore, it is said that two systems are analogous to each other when even though the systems are physically different and their mathematical model are represented by the same type of differential equations.

#### 3.1 The hydraulic analogy

The hydraulic analogy consists of implementing electric circuits applying hydraulic components or the other way around. The idea behind this concept is that electricity, which essentially is the flow of the electrons, can be seen as a fluid flowing through a wire. Nevertheless, it must be applied carefully and keep the fact that electricity and water must behave similarly. If this feature does not occur, it might lead to the wrong analogous implementation and posterior conclusion of the results[Akers et al., 2006].

Table 3.1 summarizes the analogy between hydraulic circuits and electric circuits.

Electric	Hydraulic
Wires	A pipe with water
Electric potential	Pressure
Voltage	Potential difference
Current	Volume flow rate
Ideal voltage source	Dynamic pump
Resistor	A constriction in the middle of the pipe
Capacitor	A thick-walled balloon at each end of the pipe
Inductor	A heavy paddle wheel in the current
Diode	One-way check valve

Table 3.1: Electric-hydraulic components and physical quantities comparison

All the information provided in the Table 3.2 represents the equivalence between the equations of the hydraulic and electric systems.

Electric equations	Hydraulic equations
Voltage $\phi[V]$	Pressure p [Pa]
Charge q [C]	Volume V [m <sup>3</sup> ]
Current I [A=C/s]	Flow rate $\phi_V[m^3/s]$
Current density <i>j</i> [A/m <sup>2</sup> ]	Velocity v [m/s]
Electric resistance $R[\Omega]$	Hydraulic resistance $R[\Omega]$

Table 3.2: Similarities between electric and hydraulic systems

In fluid mechanics, the *Poiseuille's law* describes how pressure and driven flow behave hydraulically in a circular channel. In the same way, *Ohm's law* characterizes the voltage drop and electric current in a resistive conductor in an electric circuit. When the pressure drop is equivalent to the voltage drop, the volumetric flow rate to the current, and the hydraulic resistance to the electric resistance, these two laws correlate[Oh et al., 2012] (Figure 3.1).

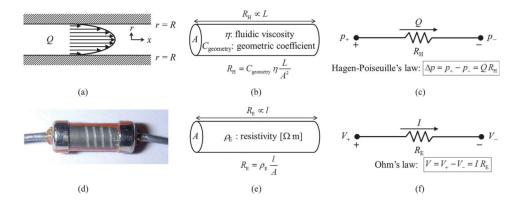


Figure 3.1: Comparison between Poiseuille and Ohm law [Oh et al., 2012]

#### 3.2 The mechanical-electrical analogy

The mechanical-electrical analogy helps with the implementation of the mechanical system through the use of an equivalent electrical circuit.

The advantage of employing electro-mechanical analogies is that analytical modelling is significantly simplified when a network of electrical elements is considered, and mechanical values are directly incorporated into the electrical model by applying the analogy [Zagrai, 2007].

From all the elements listed in the Table 3.3, which are comparable variables from one system to another one, three of them define a distinct activity in the circuit: resistance, inductance and capacitor [Olson, 1958] whose analogous equations can be seen in the Table 3.4.

Electric variables	Mechanical variables
Voltage e [v]	Force $f_M[dyn]$
Current i [A]	Linear velocity $\dot{m{x}}$ [cm/s]
Charge q [C]	Displacement x [cm]
Electrical Resistance $r_E[\Omega]$	Mechanical Resistance $r_M[\Omega]$
Electrical Capacitance $C_E[F]$	Compliance $C_M[cm \cdot dyn]$
Inductance L [H]	Mass m [g]
Electrical Impedance $\mathfrak{s}_E[\Omega]$	Mechanical Impedance $z_M[\Omega]$

Table 3.3: Mechanical-electrical variables

Element	Electric equation	Mechanical equation
Resistance	Ri(t)	$m rac{d^2 x}{dt^2}$
Inductance	$L\frac{di(t)}{dt}$	$b\frac{dx}{dt}$
Capacitance	$\frac{1}{C}\int i(t)dt$	kx

Table 3.4: Electric-Mechanic equations [Olson, 1958]

In the Figure 3.2 it is shown an example of how a the mechanical system can be built as an RLC circuit using the analogy. In this specific example all the components get changed as mass/inductor, spring/resistor and dumper/capacitor.

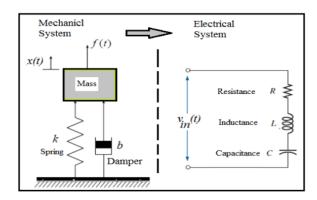


Figure 3.2: The damper mass spring model and the RCL circuit [Badr, 2017]

#### 3.3 Windkessel Model

The Windkessel Model [Catanho et al., 2012] represents the heart and systemic arterial system as a closed hydraulic system where the pump compresses the water out of the chamber thanks to the air of its inside.

Exist three different basic Windkessel models, which are created by a combination of Resistor (R), Capacitor (C), Resistor (R) and Inductor (L) elements with two, three or four elements (Figure 3.3). Besides, there are two variable components, the input function i(t) which is the blood flow and output function u(t) that is the blood pressure [Hauser et al., 2012]. Here R refers to the total peripheral resistance, C is the compliance of veins, r can represent the pulmonary or a ortic valve.

From the three models in Figure 3.3, where 2WM, 3WM and 4WM represent the number

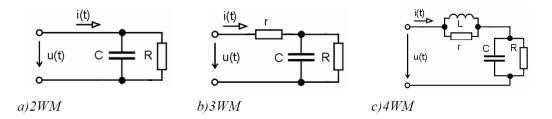


Figure 3.3: Three different Windkessel models [Hlaváč, 2004]

of components that constitutes the circuit, the one that allows to get the most realistic biological response is the third one (Figure 1c). The fact that makes him give a better response is the precede of the inductance (L) whose function is to works as the inertia of blood flow, meanwhile the other two neglected its presence [Hlaváč, 2004].

Taking the previous section as a premise, some models implement the inductance in series or in parallel for the case of three-element windkessel, which are transformed into four-element windkessel with some adjustments (Figure 3.4). The W4S has the  $R_C$ , aortic resistance, and L connected in series in comparison to the 4MW, meanwhile, in IVW, the series connection for C and  $R_d$  stands for atrial viscoelasticity, and their connection in parallel with  $R_p$  creates the viscoelastic windkessel.

It is proven that W4S and IVW give better data information than 4WM, especially for kids. The difference between them is the interpretation of the impedance in terms of the elastic and resistive properties [Burattini and Bini, 2011].

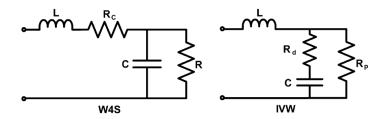


Figure 3.4: Inductance implemented in three-element windkessel[Burattini and Bini, 2011]

4

# Simulation environment

MATLAB is a numerical computing system that offers an integrated development environment with its own programming language. Moreover, this project will make use of one of the essential tools in MATLAB, known as Simulink, and within Simulink, the library of Simscape will be utilized to create the electric circuits.

In industry and academia, MATLAB is used by millions of engineers and scientists for a variety of applications, including deep learning and machine learning, signal processing and communications, image and video processing, control systems, test and measurement, computational finance, and computational biology [MathWorks, n.d.].

### 4.1 The SIMULINK environment

Simulink is a multidomain simulation and Model-Based Design block diagram environment. It helps with embedded system design, simulation, automatic code creation, and continuous testing and verification. It is compatible with MATLAB, so it allows to use of MATLAB techniques in the models and export simulation results to MATLAB for further analysis [The MathWorks, 2013]. Furthermore, Simulink is a dynamic systems graphical modelling and simulation platform. It enables making block diagrams, in which blocks represent system components. A block might be a physical part, a tiny system, or a function.

Simulink provides a set of block libraries, organized by functionality in the Library Browser (Figure 4.1). In this case, the libraries used are the, Commonly Used Blocks, Continuous, Math Operations, Sources and Sink to visualize the results.

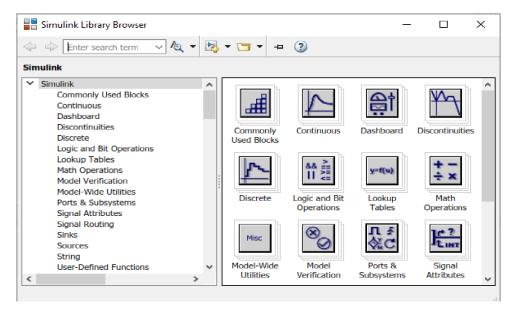


Figure 4.1: Simulink Library Browser [The MathWorks, 2013]

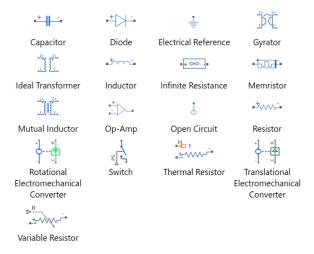
# 4.2 The SIMSCAPE environment

Simscape allows to create physical component models based on physical connections that work with block diagrams and other modelling elements. By arranging key components the system permit to create electric motors, bridge rectifiers, hydraulic actuators, and refrigeration systems [Mathworks and Drive, 2020].

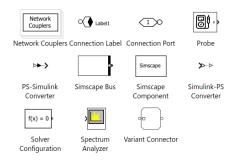
Simscape contains the Foundation Library from where it is easy to implement the electric representation of the system; it will be necessary to use the Electrical part of the Library. This subsection has three main components, the Electrical Elements, Electrical Sensors and Electrical Sources (Figure 4.2a). The Electrical Elements enable to use of resistors, indicators, capacitors, diodes, variable resistors, et cetera. Electrical Sensors help to measure the electric current in a specific point of the circuit, same as the voltage; finally, the Electrical Sources supply, for example, controlled voltage or current.

Moreover, as well as in Simulink, the program, through a Physical Signals Library, helps in creating mathematical operations like add, divide, product, et cetera (Figure 4.2c). Besides these elements, some blocks allow the connection of different components of Simulink and Simscape and vice versa (Figure 4.2b).

It is crucial to note that the system will not work if it is not connected to an appropriated solver because without that one, Simscape could not carry out the mathematical operations that constitute the circuit.



(a) Electrical Elements of the Simscape/Foundation Library/Electrical



(b) Representation of the utilities of Simscape



(c) Mathematical blocks of the Physical Signal of Simulink

Figure 4.2: Different essential blocks of Simscape to model the Cardiopulmonary System

5

# Modelling of the cardiopulmonary system

The following sections will show object-oriented and diagram block modelling of the cardiovascular and pulmonary system using the analogy system explained in section 3 and the simulation tools in the section 4.

# 5.1 Modelling of the Cardiovascular System

The dynamics of the blood circulation through the heart and the rest of the body can be represented as an electric analogous circuit (Figure 5.1). The circuit used is described in [Tsai and Lee, 2011] and consists of a simplified arrangement of several components:

- AC power supply  $(P_v(t))$ : The driving force by the left ventricle.
- **Diode** (*D*): The function of aortic semilunar valve.
- **Resistor**  $R_1$ : The resistance of the aorta.
- **Resistor**  $R_2$ : The overall peripheral resistance.
- **Inductance** L : The overall inertia of blood.
- Capacitor C: The overall compliance of the arterial system.

#### where:

•  $P_{art}(t)$ : The blood pressure of the aorta.

- $P_{per}(t)$  : The blood pressure of peripheral artery.
- $Q_{art}(t)$  : The overall blood flow rate.
- $Q_{R_1}(t)$ : Blood flow through  $R_1$ .
- $Q_L(t)$  : Blood flow through L.
- $Q_{R_2}(t)$ : Blood flow through  $R_2$ .
- $Q_C(t)$ : Blood flow through C.

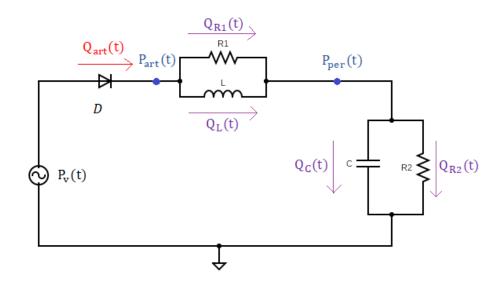


Figure 5.1: Representation of the cardiovascular circuit

The first step to get the equations of our system is to establish the *Kirchhoff's Current Law* (Equation 5.1), which states the current entering a node is the sum of the currents leaving it, that stands for this summation, from there it is extrapolated to the equation of  $Q_{art}$  (Equation 5.2).

$$\sum_{i=1}^{n} = I_1 + I_2 + \dots + I_n = 0 \tag{5.1}$$

$$Q_{art}(t) = Q_{R_1}(t) + Q_L(t) = Q_{R_2}(t) + Q_C(t)$$
(5.2)

Following the previous premise, it is necessary to apply the *Ohm law* where  $I=\frac{V}{R}$  in case of the resistance,  $\frac{dI}{dt}=\frac{V}{L}$  for the inductance and  $I=C\frac{dV}{dt}$  for the capacitor, that is:

$$Q_{R_1}(t) = \frac{P_{art}(t) - P_{per}(t)}{R_1}$$
 (5.3)

$$\frac{dQ_L(t)}{dt} = \frac{1}{L}(P_{art}(t) - P_{per}(t)) \tag{5.4}$$

$$Q_{R_2}(t) = \frac{P_{per}(t)}{R_2} {(5.5)}$$

The whole set of equations of the system would be as follows:

$$Q_{art}(t) = Q_L(t) + Q_{R_1}(t) \longrightarrow Q_{art}(t) = Q_L(t) + \frac{P_{art}(t) - P_{per}(t)}{R_1}$$

$$(5.6)$$

$$P_{art}(t) = P_{per}(t) + R_1(Q_{art}(t) - Q_L(t))$$
(5.7)

$$\frac{dP_{per}(t)}{dt} = \frac{1}{C}(Q_{art}(t) - Q_{R_2}(t)) \longrightarrow \frac{dP_{per}(t)}{dt} = \frac{1}{C}\left(Q_{art}(t) - \frac{P_{per}(t)}{R_2}\right)$$
(5.8)

Besides, to simulate the behaviour of the diode that represents a ortic semilunar valve, a proper function will be implemented as the Equation 5.9 where  $V_f$ ,  $R_{on}$ ,  $R_{off}$  represent the forward voltage, on resistance and off resistance respectively.

$$Q_{art} = \begin{cases} \frac{v - V_f(1 - R_{on}R_{off})}{R_{on}} & \text{if } v > V_f; \\ vR_{off} & \text{if } v \le V_f. \end{cases}$$

$$(5.9)$$

Once the differential equations are well defined, it is necessary to give every circuit component a parametric value. The values can be seen in the Table 5.1.

Cardiovascular parameters		
$P_V(t) = 120(\sin(\pi f_{HR}t)^{10})$		
$f_{HR}$ (hear beat rate at rest)	1.25~[Hz]	
$R_1$	$0.03~[\Omega]$	
$\mid L \mid$	0.005~[H]	
$R_2$	$1.2~[\Omega]$	
C	1 [F]	

Table 5.1: Values of the components of the cardiovascular system

# 5.2 Modelling of the Pulmonary System

The air intake, air inlet and air outlet will be done through the circuit described in [Tsai and Lee, 2011] (Figure 5.2).

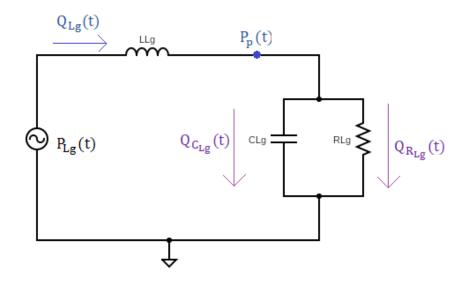


Figure 5.2: Representation of the respiratory circuit

The system is going to be composed of:

- AC power supply  $(P_{L_g}(t))$ : The driving force for the respiratory cycle formulated as the pressure at the lung .
- Inductance  $LL_g$ : The overall inertia of the airflow.
- Resistor  $RL_g$ : The overall resistance of the airflow.
- Capacitor  $CL_g$ : The overall compliance of the alveoli.

### where:

- $P_p(t)$  : The overall pulmonary pressure.
- $Q_{L_q}(t)$  : The overall air volume flow rate.
- $Q_{R_q}(t)$ : Air flow rate through  $R_{L_q}$ .
- $Q_{C_q}(t)$ : Air flow rate through  $C_{L_q}$ .

Taking the same approach as in the case of the cardiovascular system, the *Kirchhoff's Cur*rent Law will be applied as well as *Ohm law*. Now the equations of the circuit will be:

$$\frac{dQ_{L_g}(t)}{dt} = \frac{1}{LL_g}(P_{L_g}(t) - P_p(t))$$
 (5.10)

$$\frac{dP_p(t)}{dt} = \frac{1}{CL_g}(Q_{L_g}(t) - Q_{R_g}(t)) \longrightarrow \frac{dP_p(t)}{dt} = \frac{1}{CL_g}\left(Q_{L_g}(t) - \frac{P_p(t)}{RL_g}\right) \tag{5.11}$$

In Table 5.2 are represented the parametric values of the whole model.

Pulmonary parameters			
$P_{L_g}(t)$	$P_{L_g}(t) = (\sin(2\pi f_{BF}t))$		
$f_{HR}$ (breath frequency at rest)	0.25~[Hz]		
$LL_g$	$10^{-4}[H]$		
$RL_g$	$2.55 \times 10^{-3} [\Omega]$		
$CL_g$	$1.45 \times 10^{-4} [F]$		

Table 5.2: Values of the components of the pulmonary system

# 5.3 Modelling of the Cardiopulmonary Interactions

The interconnection between the two systems will be made on the basis of three conditions, the first involving progressive physical exercise, the second involving pulmonary obstruction and the third involving aortic regurgitation.

#### 5.3.1 Exercise mode

From walking to any task, physical exercise is mainly driven by the respiratory system, which takes in oxygen, and by the cardiovascular system as the heart that transports that oxygen to the muscles, allowing the body to move.

During exercise there is an increase in heart rate H(t) which is proportional to the oxygen demand required by the body, this correlation implies that  $H(t) = \alpha M R_{O_2}(t) + b$  where  $MR_{O_2}$ , in turn, is proportional to the workload  $MR_{O_2}(t) = MR_{O_2}^r + \rho W(t)$ . What it means to say is, the more physical activity that is being performed, the more work is needed to supply the organism, resulting in the work (W(t)) being the basis for implementing this particular experience.

Taking that for granted, when physical activity increases and with it the oxygen consumption, two key conditions are established [Kappel et al., 1997]:

- There is an increase in heart rate  $f_{HR}$
- A decrease in a rtic resistance  $R_1$

For the first condition, the increase of the heart rate can be expressed as:

$$f_{HRn}(W) = f_{HR} + 0.75W (5.12)$$

where the greater is the W higher is the frequency to accomplish that work.

The second condition is the decrease in the aortic resistance, so a variable resistance that allows this changes must be taken into account.

In the previous basic circuit without the interconnection relationships, the  $R_1$  is held constant since the heart is not stressed. Therefore, a variable resistance  $(R_{1n})$  is defined, where the more W is needed less is the aortic impedance [Kappel et al., 1997].

$$R_{1n} = (R_1 - R_{1min})e^{-aW} + R_{1min} (5.13)$$

Table 5.3 contain the corresponding values where  $R_{1min}$  is the minimum value the impedance can get and a is a constant.

New impedance parameters		
$R_{1min} [\Omega]$	0.03	
a	2	

Table 5.3: Impedance parameters for the exercise

As for the relation between cardiac and pulmonary function during normal condicions exercise, a proportional rate is set, that is:

$$\frac{f_{HR}}{f_{BF}} = 5 \longrightarrow f_{BFn} = \frac{f_{HRn}}{5} \tag{5.14}$$

Finally, simulation of different physical conditions such as walking and running can be implemented by increasing the value of the workload (W), measured as a percentage. Table 5.4 shows the different set for variable W values.

Exercise modes				
Resting $(W=0)$ Walking $(W=0.33)$ Running $(W=1)$				
$R_{1n}[\Omega]$	0.03	0.019	0.011	
$\int f_{HRn}[Hz]$	1.25	1.5	2	
$\int \mathbf{f}_{BFn}[Hz]$	0.25	0.3	0.4	

Table 5.4: Values obtained for different exercise modes

### 5.3.2 Pulmonary obstruction

As it was explained in section **2.3.3**, severe pulmonary obstruction (COPD) is characterized by the limitations of the airflow rate within the lungs. Specifically, COPD can cause pulmonary hypertension, which represents an increment of pressure in the pulmonary arteries, leading to hypertrophy dilatation and failure of the right ventricle [Álvarez et al., 2008].

Moreover, COPD can cause increased hypoxaemia, an abnormally low partial pressure of oxygen in arterial blood leading to heart rate variability. It is important to mention that the heart rate frequency has a saturation point caused by the fact that the heart reaches a maximum number of beats per minute [Diamantis et al., 2017].

With this information the key points to characterize this effect are:

- Cardiac insufficiency due to the failure of the left ventricle causing the drop of Pv
- Increase of the heart rate with a saturation limit

Furthermore, to represent different saturation levels, it is necessary to make changes in the resistance  $RL_g$ , assuming a mild or moderate pulmonary obstruction where  $RL_g$  is two or four times respectively the normal value [Álvarez et al., 2008].

First of all, the implementation of the cardiac insufficiency is represented in:

$$A_{vn} = 130 - K_{ob}RL_q (5.15)$$

where  $K_{ob}$  (Table 5.5) is a constant that depends on the level saturation of the lungs to reduce the ventricular pressure.

Amplitude parameter		
$K_{ob}$ 3846		

Table 5.5: Amplitude parameters that define the change in the driving force by the left ventricle

Second, the heart frequency also increases so the new frequency  $f_{HRobs}$ , the pulmonary obstruction is defined depending on a variable that same variable, presented as:

$$f_{HRobs} = f_{HRn}(W)K_{obs}(RL_q) \tag{5.16}$$

$$K_{obs} = 1.6(1 - e^{-377.2RL_g}) (5.17)$$

Now, the parametric values associated to the level of obstruction is defined in the Table 5.6.

Obstruction levels				
Normal Mild ( $2RL_g$ ) Moderate ( $4RL_g$ )				
$A_{vn}$	120	110	90	
$f_{HRobs}[Hz]$	1.24	1.7	1.96	

Table 5.6: Values obtained for different pulmonary obstruction levels

### 5.3.3 Aortic regurgitation

As explained before, aortic regurgitation results from blood flowing back into the left ventricle due to poor closure of the aortic valve and consequent heart failure, which causes a poor blood supply to the body. At the same time, this failure is the cause of respiratory dyspnoea [Kappel et al., 1997]. Dyspnoea is shortness of breath or breathlessness and is the most striking feature of heart failure.

Because there is not a good supply of nutrients to the rest of the body due to regurgitation, the muscles that are part of breathing, such as the diaphragm, do not receive enough energy to perform their function. In other words, there is a decrease in muscle blood flow and an increase in muscle stiffness. Therefore, the elements necessary for the characterizing of regurgitation are defined as follows [Batzel et al., 2005]:

- A reduction of  $P_{L_q}(t)$  causing the reduction of blood flow in the respiratory muscles
- An increase in respiratory resistance  $(RL_g)$  causing an additional obstructive effect due to muscle stiffness.

In order to implement this effect the variable amplitude for  $P_{L_q}(t)$  has been stated as:

$$P_{L_a}(t) = A_{L_a}(R_{off})sin(2\pi f_{BF}t)$$
 (5.18)

$$A_{L_q}(R_{off}) = 0.85 + 0.15(1 - e^{-R_{off}})$$
(5.19)

 $R_{off}$  refers to the aortic valve closure, so regurgitation will be analysed by changing the  $R_{off}$  values. It is worth mentioning that  $R_{off}$  presents a saturation curve where values above 100  $\Omega$  imply that the valve is completely closed. This is why the  $P_{L_g}(t)$  depends on this parameter, as it is a way to relate the valve opening to its effects at the pulmonary level.

The second element to be designed is the increase of the stiffness of the musculature through  $RL_g$ . For this purpose, a multiplicative factor  $K_{reg}$  is proposed, since the aortic valve opening increases so does the respiratory resistance due to muscle stiffness, that is:

$$RL_{greg} = RL_g K_{reg}(R_{off}) (5.20)$$

$$K_{reg}(R_{off}) = 1 + 2.02e^{-0.6R_{off}}$$
 (5.21)

Finally, the parametric values set to characterize the aortic regurgitation are shown in Table 5.7.

Grades of aortic regurgitation				
Normal Mild $(R_{off}=1)$ Moderate Severe				Severe
	$(R_{off}$ =100)		$(R_{off}$ =0.5)	$(R_{off} = 0.25)$
$A_{L_g}$	1	0.945	0.909	0.883
$\mathrm{RL}_{greg}[\Omega]$	0.00255	0.00538	0.00637	0.00698

Table 5.7: Values obtained for different degrees of aortic regurgitation

# 5.4 Block-diagram Model of Cardiopulmonary System in SIMULINK

This section will present the block diagram model of the two main systems in SIMULINK.

#### 5.4.1 Cardiovascular block model

Combining the equations (5.7) and (5.8) the data from the Table 5.1 the model can be implemented in SIMULINK. Thus, Figure 5.3 shows the cardiovascular system and Figure 5.4 each of its differentiated parts.

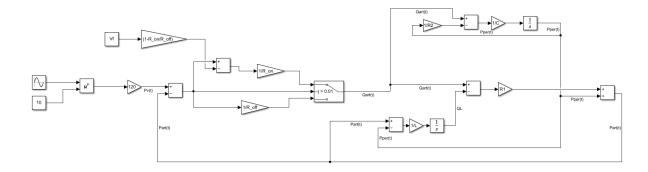


Figure 5.3: SIMULINK block diagram of the cardiovascular system using the differential equations

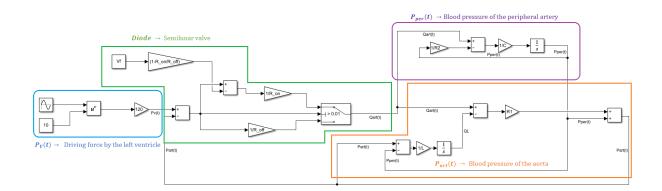


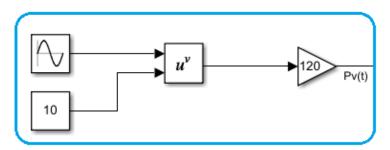
Figure 5.4: Differentiation of the different sections of the SIMULINK block diagram of Cardiovascular System

When the left atrium is filled with blood, the systole takes place forcing the mitral valve to open and starts the process of filling the left ventricle. By the time the filling process finished, the systole of the ventricle happens  $(P_v(t))$  forcing the semilunar valve (D) to open while the mitral valve is closed.

The sudden filling and subsequent emptying of the aorta causes the pressure in the aorta to vary  $(P_{art}(t))$ . In the meantime, the pressure drop in the peripheral artery, which is responsible for transporting blood to the body,  $(P_{per}(t))$ .

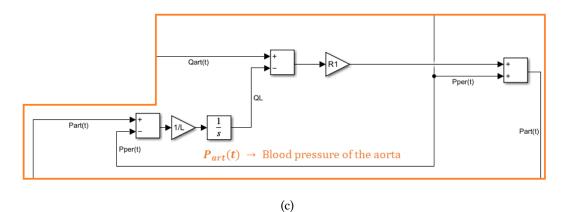
Figure 5.5 shows every single block separately. To be more precise, Figure 5.5a represents the building of the  $P_v(t)$  from the Table 5.1 using a *sine wave* block. Meanwhile Figure 5.5b constitutes the assembling of the code provided in the Equation 5.9.

Lastly, Figure 5.5c is the block model the representation of Equation 5.7 while Figure 5.5d is the implementation of the Equation 5.8.



 $P_V(t) o ext{ Driving force by the left ventricle}$ 

(a)



 $P_{per}(t) \rightarrow \text{Blood pressure of the peripheral artery}$ Qart(t)

Per(t)

Per(t)

Per(t)

Per(t)

Figure 5.5: Representation of all the blocks of the cardiovascular system

# 5.4.2 Pulmonary block model

Combining Equation 5.10, Equation 5.11 and Table 5.2 it results in the pulmonary system in SIMULINK as is shown in Figure 5.6.

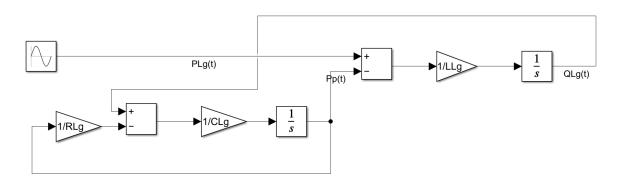


Figure 5.6: SIMULINK block diagram of the pulmonary system using the differential equations

Figure 5.7 represents each of its differentiated parts of the system separately.

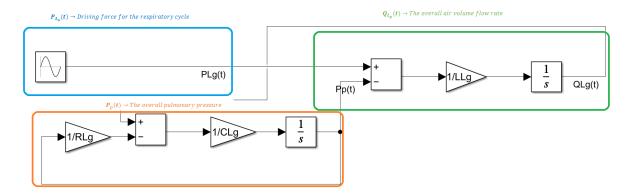
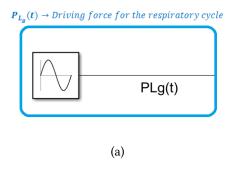


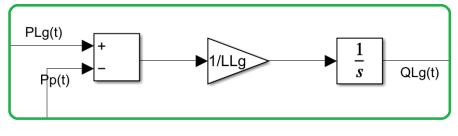
Figure 5.7: Differentiation of the different sections of the SIMULINK block diagram of Pulmonary System

The process begins when the alveolar pressure  $(P_{L_g}(t))$  is small making the air flow through the trachea and lungs  $(Q_{L_g}(t))$  creating a higher lung pressure  $(P_p(t))$  until the exhalation takes place, this process being repeated indefinitely.

Figure 5.8 represents the three blocks that constitute the system. The Figure 5.8a in implemented through data of Table 5.2 while Figure 5.8b and Figure 5.8c represent Equation 5.10 and Equation 5.11 respectively.



 $Q_{L_g}(t) o The \ overall \ air \ volume \ flow \ rate$ 



(b)

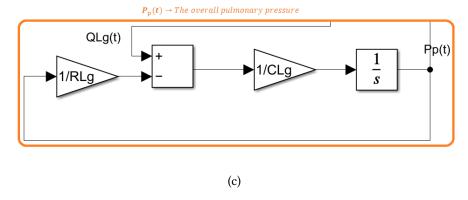


Figure 5.8: Representation of all the blocks of the pulmonary system in SIMULINK

# 5.5 Oriented Object Model of Cardiopulmonary System in SIMSCAPE

This part of the document deals with the representation of the cardiovascular system through the Object-Oriented Model.

# 5.5.1 Cardiovascular System

Through the implementation of the systems in SIMULINK, a block diagram has been created in SIMSCAPE, which will be explained step by step in the following section.

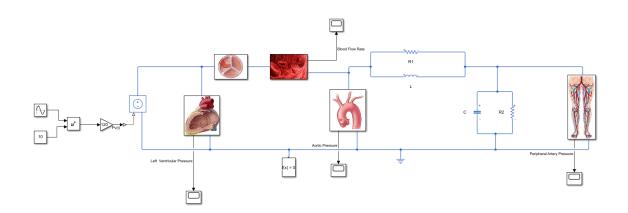


Figure 5.9: Block diagram of the pulmonary system

Clearly, several interconnected blocks can be distinguished from each other whose mission is the transport of the oxygenated blood from the left ventricle to the rest of the body.

The driving force by the left ventricle (Figure 5.10) is built with  $P_v(t)$  using the same *sine* wave block as in SIMULINK. The difference here is that it requires a Controlled Voltage Source (CVS) to supply the pulping mechanism. In general, Figure 5.10 gives a reference to the systolic and diastolic movement of the left ventricle.

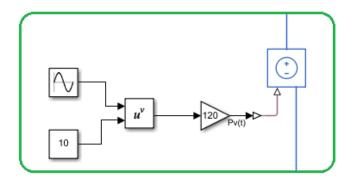


Figure 5.10: Block - Driving force of the left ventricle

Starting from Equation 5.7, the left ventricle pressure is created (Figure 5.11a) but it needs a Voltage Sensor (VS) (Figure 5.11b) to measure the pressure drop from the left ventricle driving force to the aortic valve.

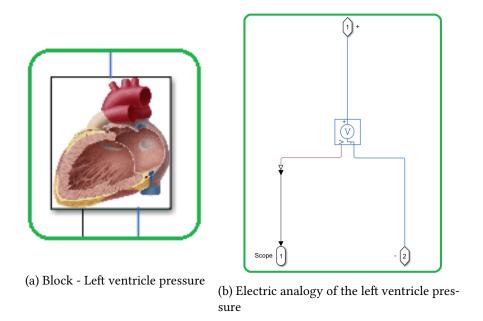


Figure 5.11: Left ventricle pressure

The advantage of SIMSCAPE with respect to SIMULINK is that there is no need to define a different pressure equation because applying the same Sensor in different sections of the circuit will quickly provide the measured values. Meanwhile, in SIMULINK, it would be necessary to implement in this case the Equation 5.8.

Aortic valve (Figure 5.12a) uses the diode block in SIMSCAPE (Figure 5.12b) taking away the need to create the diode block from Equation 5.9. The diode controls the blood passage to the aorta after the aortic pressure is big enough to open, letting the aperture of the aortic valve and the passage of the blood flow.

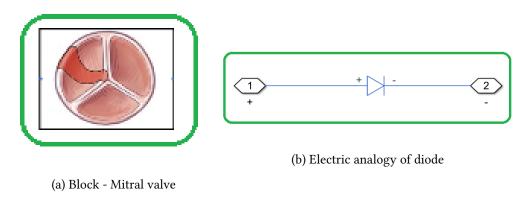


Figure 5.12: Aortic valve

As in the case of measuring the pressure values, a SIMSCAPE Current Sensor (CS) block (Figure 5.13b) will be needed to obtain the blood flow rate block (Figure 5.13a). Therefore, once again, in the block diagram, there is no need to implement the differential equations, in this case, expressed in the Equation 5.6.

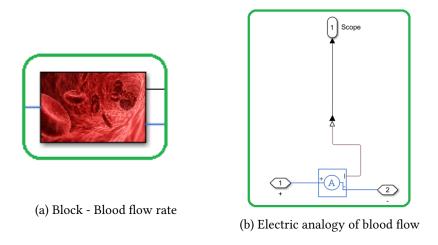


Figure 5.13: Blood flow rate

Figure 5.14 is an analogous 4-element-windkessel model discussed in section 3 where the

electric necessary components parts are built up in parallel.

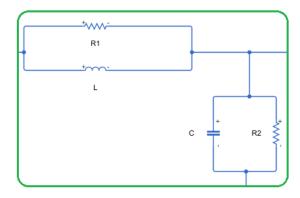


Figure 5.14: Electric analogy of the Windkessel model

Last but not least, Figure 5.15 is made up of two elements: aortic pressure and peripheral pressure. The two are composed of a Voltage sensor connected to the circuit whose function is to measure the aortic and peripheral pressures. Both are based on differential equations 5.7 and 5.8.

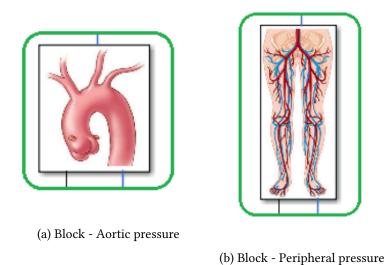


Figure 5.15: Aortic pressure and Peripheral pressure

# 5.5.2 Pulmonary System

A similar approach as with the cardiovascular system has been employed to implement the pulmonary compartment model in SIMSCAPE (Figure 5.16).

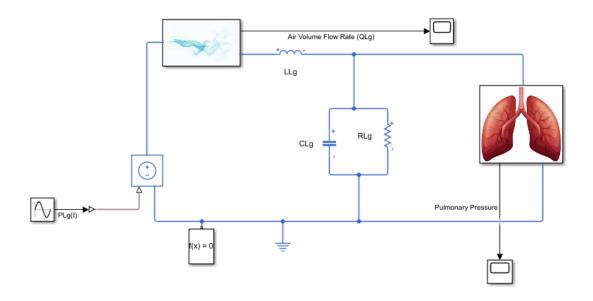


Figure 5.16: Block diagram of the pulmonary system

An air pressure generator has been used to create the respiratory cycle (Figure 5.17).

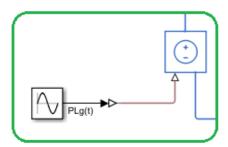


Figure 5.17: SIMSCAPE - Driving force of the respiratory cycle

For the measurement of air volume that is entering the lungs a sensor block has been used (Figure 5.18).

The third block comprehend an electric analogy where it can mimic the airway  $RL_g$  and the lung inertance  $LL_g$  (Figure 5.19) [Ghafarian et al., 2016].

The last brick of this pulmonary scheme is the the one that modulates the pulmonary

pressure (Figure 5.20) as describen in the Equation 5.11.

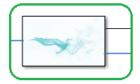


Figure 5.18: SIMSCAPE - Air volume flow rate

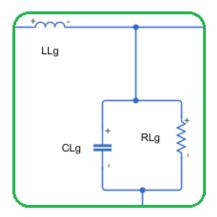


Figure 5.19: Electric analogy connected of the pulmonary system

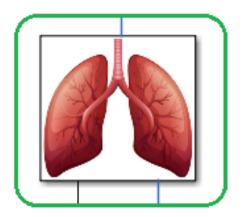


Figure 5.20: SIMSCAPE - Pulmonary pressure

# 5.6 Oriented Object Model of Cardiopulmonary Interactions in SIM-SCAPE

The main use of this section is the implementation of the interactions between the cardiovascular and pulmonary systems using SIMSCAPE.

#### 5.6.1 Exercise model

For the creation of the different physical activities such as rest, walking or running, the model in Figure 5.21 and Figure 5.24 has been implemented at cardiopulmonary level.

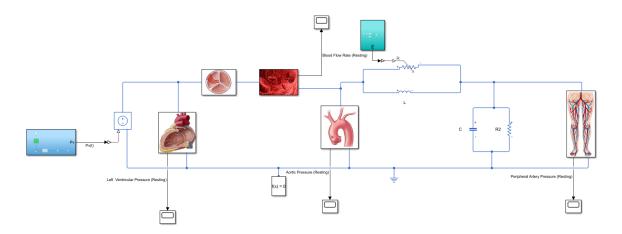


Figure 5.21: Cardiovascular model in exercise conditions

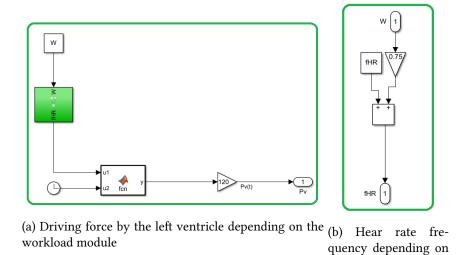
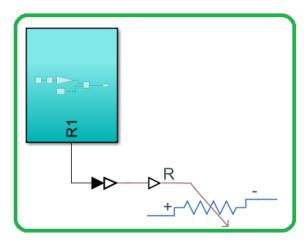


Figure 5.22: Exercise interconnecting elements

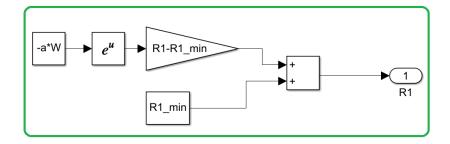
the workload module

Because of the changes in Figure 5.22 in the system model are external to the electric circuit, Equation 5.12 is represented in Figure 5.22b, creating the new frequency that changes with the percentage of work needed. Moreover, this same frequency is taken to generate the same kind of input to the cardiovascular system, as is shown in Figure 5.22a.

Another factor that has been implemented is the variable resistor (Figure 5.23a), where the input it is receiving is Equation 5.13 which is depicted in Figure 5.23b getting R1 as output.



(a) Variable electric resistance



(b) Variable resistance module

Figure 5.23: Variable impedance in the cardiovascular system

The pulmonary system would is represented as shown in Figure 5.24, taking as input the frequency of cardiovascular system conveniently modulated (Figure 5.25). However, the difference is that the interrelation of Equation 5.14 is also being implemented giving PLg as output.

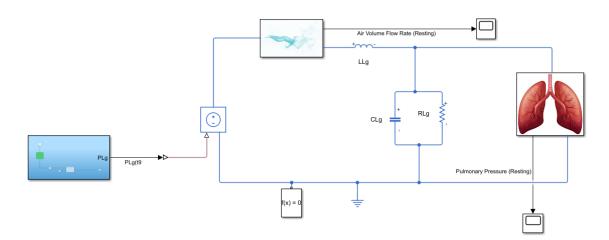


Figure 5.24: Pulmonary model in exercise conditions

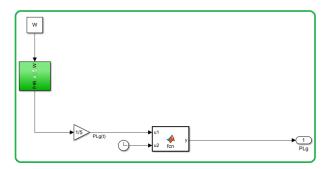


Figure 5.25: Driving force of the alveoli depending on workload module

# 5.6.2 Pulmonary obstruction

Lung obstruction at the level of modelling the pulmonary system increase the value of  $RL_g$  (Figure 5.26). However, the cardiovascular system is related to the pulmonary system through these changes in resistance.

Also the ventricular pressure is affected as said in Equation 5.15 (Figure 5.27a) together with changes in heart rate through the  $K_{obs}$  constant proposed in Equation 5.17 (Figure 5.27b).

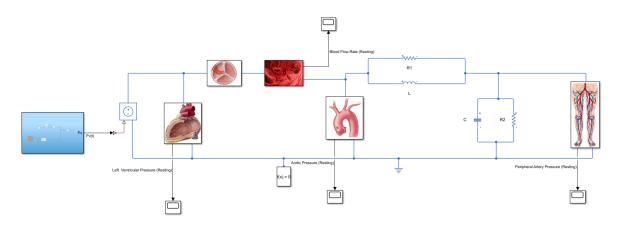
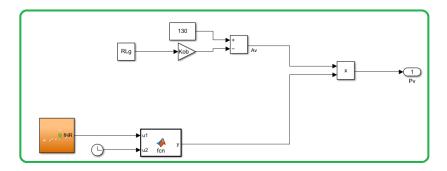
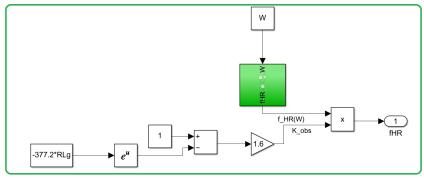


Figure 5.26: Pulmonary obstruction cardiovascular system



(a) Ventricular pressure drop with a variable amplitude module



(b) Heart beat rate change module

Figure 5.27: Left ventricle driving force in pulmonary obstruction

# 5.6.3 Aortic regurgitation

As mentioned before, a ortic regurgitation will involve a change in  $R_{off}$ , so for the pulmonary system Figure 5.28 represent the decrease in blood flow to the muscles and the increase in muscle stiffness (Figure 5.29 and 5.30). For the last case, it is necessary to implement a variable resistor Equation 5.20 and 5.21.

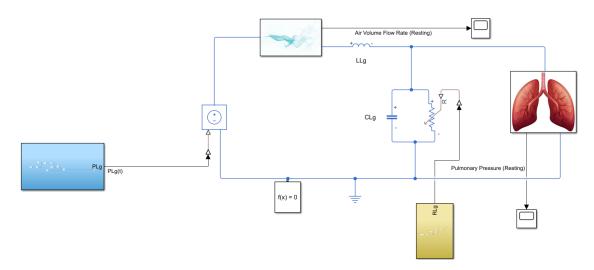


Figure 5.28: Aortic regurgitation in pulmonary system

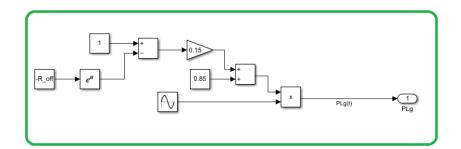


Figure 5.29: Decrease in the muscle blood flow module

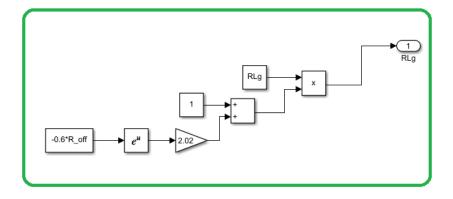


Figure 5.30: Increase of the muscle stiffness module

# 6

# Experiences and results

# 6.1 Results in physiological conditions

The purpose of this section is to test the system's performance under normal exercise conditions and validate the obtained results. For the sake of comparison, the results of [Tsai and Lee, 2011] are going to be used thought out.

#### 6.1.1 Normal conditions

The first analysis to start with is that of the response obtained from the cardiovascular system. As an overview of the whole system at the pressure level is shown in Figure 6.1, showing: left ventricular pressure, aortic pressure and peripheral pressure.

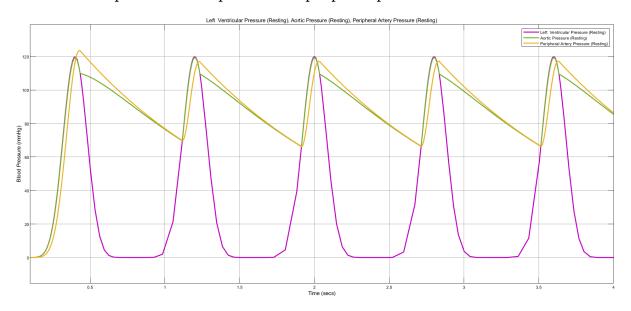


Figure 6.1: Pressures evolution in normal conditions

First of all, is exhibited an increment of left ventricle pressure since it is filled with blood

coming from the left atrium. When the pressure reaches the point of 70 mmHg approximately the aortic valve opens and the left ventricle contracts, known as left ventricle systole, starts reaching a maximum level of pressure of 120 mmHg and conniving the following ejection of the blood to the aorta. This implies that the left ventricle pressure, when it reaches the top, starts to decrease as well as the aortic pressure because the blood flow rate (Figure 6.2) decreases. It is important to mention that in the blood movement does not start until the aortic valve opens and drops when it closes.

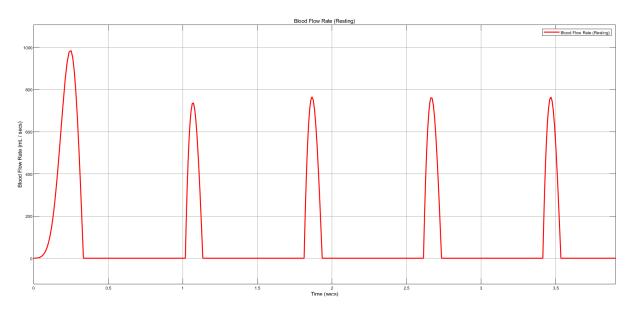


Figure 6.2: Blood flow rate in normal conditions

After a certain point around 110 mmHg, takes place the aortic valve closure, creating the diastole of the left ventricle. The diastole generates a pressure drop above 0 mmHg, some blood remains the left ventricle.

When diastole occurs, the blood flow rate in the aorta drops completely until the cycle of systole and diastole repeats (Figure 6.2). As a note, the maximum peak of blood that goes through the aorta is around 750 mmHg/sec.

Meanwhile, the vessels in peripheral circulation experience the same pressure drops and rises as the aorta. In particular, aortic valve closures are not visible in the peripheral pressure, as the pressure drops until the heart again ejects the blood out of the heart. Figure 6.3 and 6.5 show the left ventricle pressure and aortic and peripheral pressure evolution respectively,

revealing their cyclic behaviour.

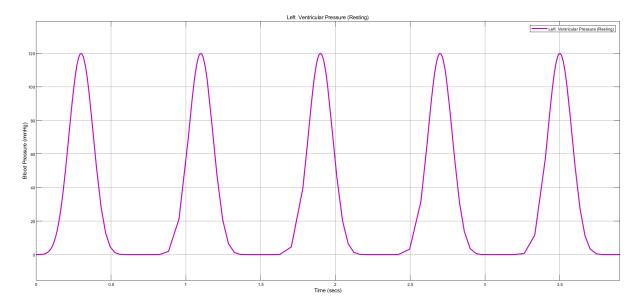


Figure 6.3: Left ventricle pressure in normal conditions

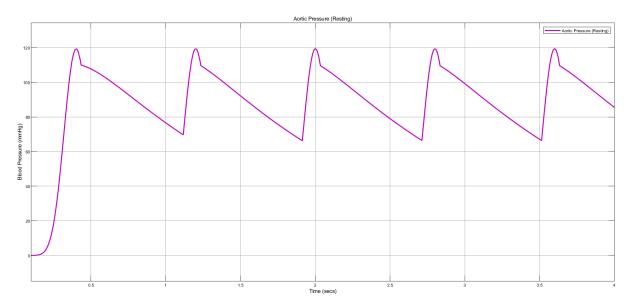


Figure 6.4: Aortic pressure in normal conditions

Regarding the pulmonary system, once the air starts entering the lungs, due to the difference between the atmospheric pressure and the lungs, besides other factors, the pulmonary pressure is starting to increase until the volume flow rate reaches the maximum amount, around 400 mmHg, creating the inspiration.

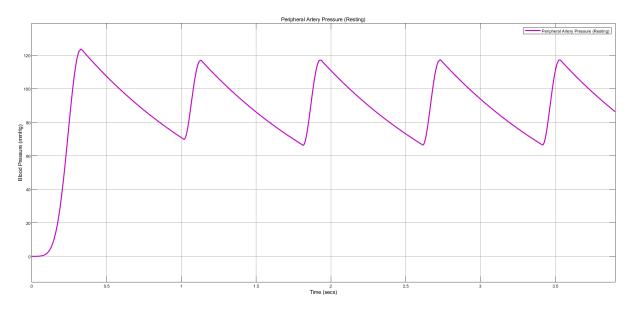


Figure 6.5: Normal condition peripheral pressure

Meanwhile, the expiration produces the release of air, decreasing the pressure and air volume in the lungs. The tidal volume, which is the volume stored during inspiration is 500 mL in normal conditions [Figure 6.6 and 6.7].

Results obtained in normal conditions are in agreement with those of [Tsai and Lee, 2011] and with physiological values that can be find in literature and textbooks.

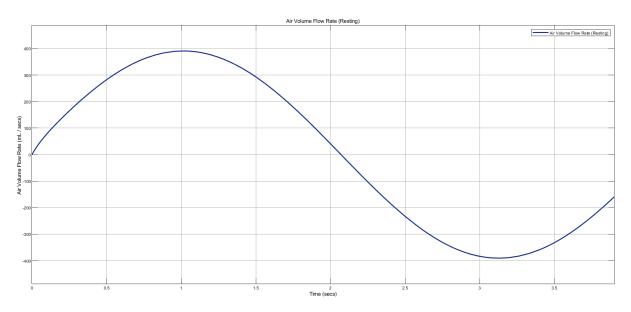


Figure 6.6: Air volume flow rate in normal conditions

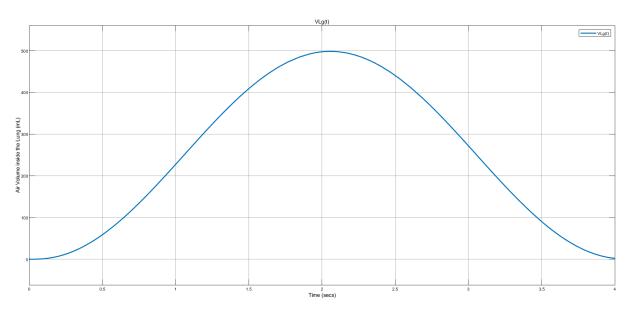


Figure 6.7: Air volume inside the lung in normal conditions

#### 6.1.2 Exercise conditions

As previously was defined, during physical exercise, there is an increase in heart rate and, in turn, a decrease in aortic resistance. Therefore, coupled effect for the respiratory and pulmonary systems will be analysed. For the simulation of physical activity corresponding to walking and running, W values of 33% and 100% respectively have been taken (see Table 5.4).

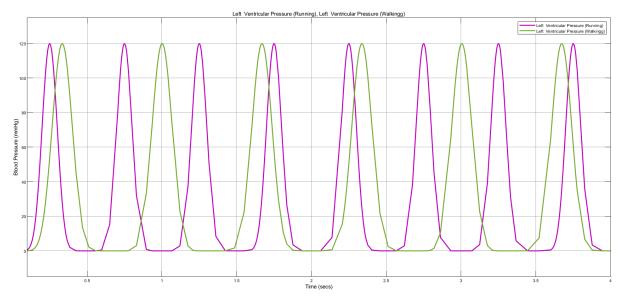


Figure 6.8: Exercise conditions for the left ventricle pressure

In Figure 6.8 are shown left ventricular pressure in both walking and running conditions,

while Figure 6.9 represents the aortic pressure in both activities, the increase in heart rate is mainly highlighted in these figures. The leading cause of the increased frequency is the need to increase the amount of oxygen in the blood during the exercise. It is also visible the decrease of the aortic resistance in Figure 6.10 which shows the blood flow through the aorta. In fact the blood flow frequency increases and also does the aortic blood flow.

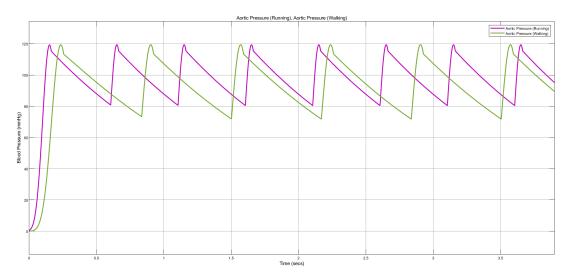


Figure 6.9: Exercise conditions for the aortic pressure

The increased flow rate causes more blood to carry oxygen to the rest of the body, thus increasing ATP production, and creating a greater energy source since the more work a person does during exercise, the more energy will be consumed in terms of oxygen and nutrients carried out by the circulation system.

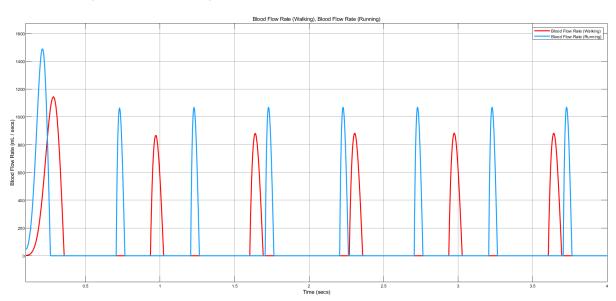


Figure 6.10: Exercise conditions for the blood flow rate

Concerning the pulmonary system, the pulmonar frequency also increases as in cardiac level, as seen in Figure 6.11, where the air volume flow rate continues to reach 400 mmHg, but with increased frequency. However, the maximum air volume reached decreases to 410 mmHg and almost 305 mmHg (Figure 6.12). In that case, this does not imply that the volume is less than before, but it is proportionally the same.

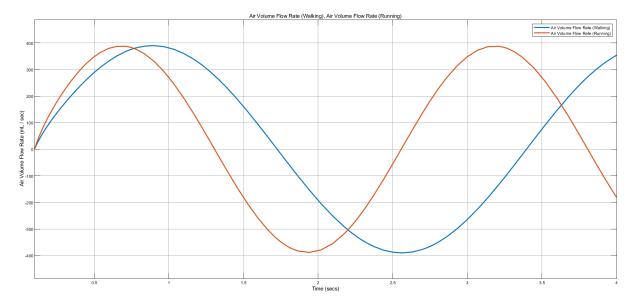


Figure 6.11: Exercise conditions for the air volume flow rate

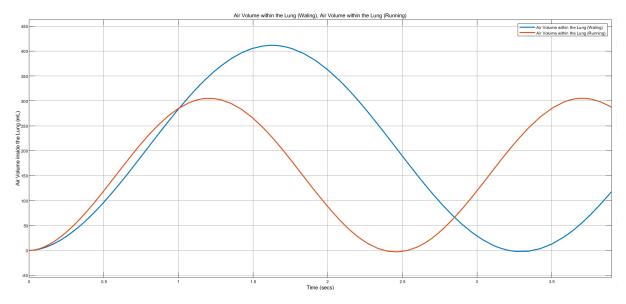


Figure 6.12: Exercise conditions for the air volume within the lung

# 6.2 Results in pathological conditions

After checking that the system interacts appropriately, the most interesting part is to check how the pathologies of one system affect the other and vice versa. Therefore two tests will be performed: aortic valve regurgitation and chronic obstructive pulmonary disease.

#### 6.2.1 Aortic valve regurgitation

For the study of aortic regurgitation, the values obtained for different cases of  $R_{off}$  will be compared, as mentioned in Table 5.7. The ratio between the maximum and minimum blood flow rate can be expressed as a percentage of  $\frac{BFR_{max}}{BFR_{min}}$ , giving the severity of regurgitation. In case of mild aortic regurgitation the percentage obtained of regurgitation volume is set to 9.45% and for the severe case of regurgitation has been set to 27%.

Tests will be performed in case of mild and severe regurgitation as the results obtained are much clearer. Moreover, the model will function properly when the blood flow reduction and increased respiratory resistance collateral effects are appreciated.

When comparing the two cases of aortic regurgitation, it is concluded that, in the case of the cardiovascular system, the more severe is the valve incompetence, the more blood flows back into the left ventricle during ventricular diastole (Figure 6.13). In turn, there is an increased blood flow rate and even earlier ejection of blood into the aorta. This is because the left ventricle is occupied by the remaining blood (not a hundred per cent of the oxygenated blood is ejected by the ventricle), plus the blood that has returned to the ventricle. Therefore, as the left ventricle is receiving blood from the left atrium, a blood push and pressure increase in the ventricle causes the systole of the ventricle before it should occur under normal conditions and at a lower pressure (Figure 6.14).

Meanwhile, as the pulmonary system is not receiving enough blood from the heart, there is a stiffening of the muscles that form part of respiration. This stiffening results in the individual's ability to breathe air much lower than in normal conditions, leading to fatigue and even severe cases of asphyxia.

As shown in Figure 6.15, the air volume flow rate in severe cases has decreased almost four times compared to normal conditions, which implies that the air volume inside the lungs decreases as well (Figure 6.16) due to the increase of pulmonary resistance  $RL_g$ .

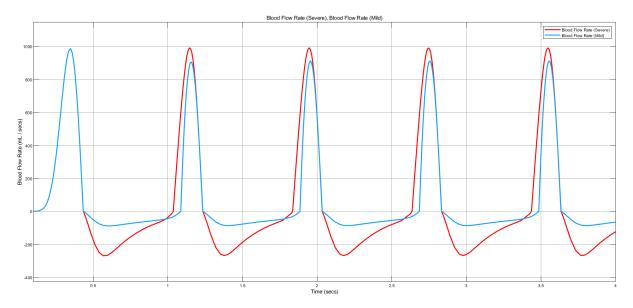


Figure 6.13: Blood flow rate in the aortic valve regurgitation

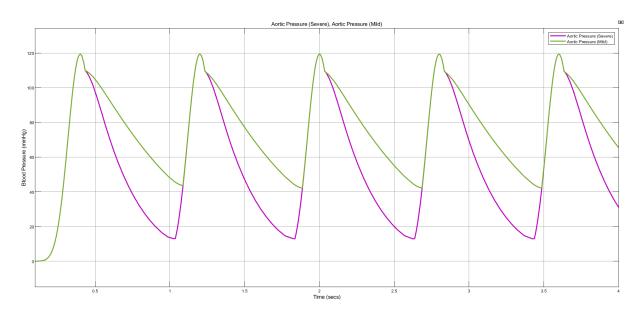


Figure 6.14: Aortic pressure in the aortic valve regurgitation

Much more severe cases of regurgitation than those proposed here could be envisaged. However, these would be unfeasible as the person would probably either be dying of asphyxia or no longer alive.

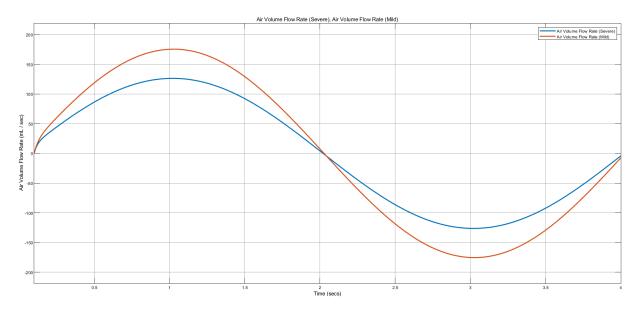


Figure 6.15: Air volume flow rate in the aortic valve regurgitation

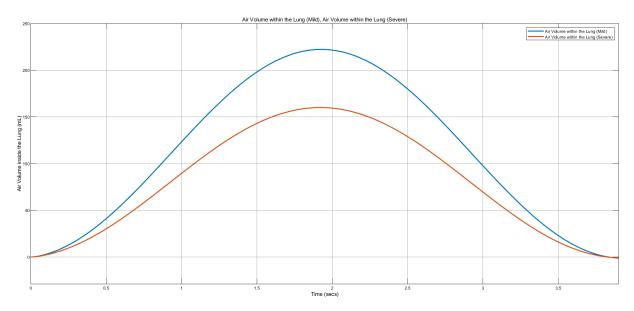


Figure 6.16: Air volume in the aortic valve regurgitation

# 6.2.2 Chronic Obstructive Pulmonary Disease

Lung obstruction, as mentioned in the previous chapter, consists of the variation of the pulmonary resistance  $RL_g$ . Therefore, to simulate the cases of mild and moderate obstruction, the values in Table 5.6 will be used.

At the pulmonary level, the higher is the respiratory resistance, the lower the amount of air that can be taken in during inspiration and stretching (Figure 6.17), which is entirely normal

since obstruction of the airways decreases the air volume (Figure 6.18) or, in other words, the capacity of air that the lungs can hold.

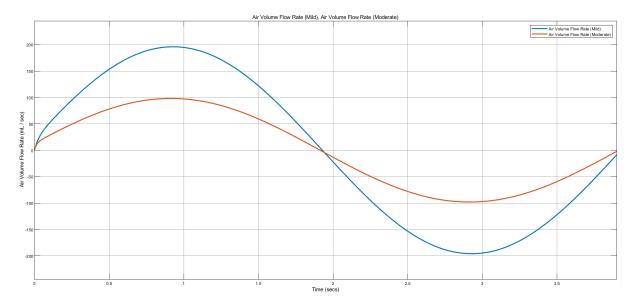


Figure 6.17: Air volume flow rate in the chronic obstructive pulmonary disease

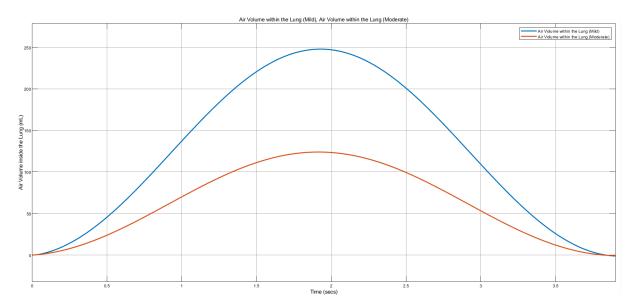


Figure 6.18: Air volume in the chronic obstructive pulmonary disease

Meanwhile, at the cardiovascular level, there is an increase in heart rate as the heart tries to supply the rest of the body with nutrients as quickly as possible (Figure 6.20). However, this increase in heart rate cannot be progressive as it will reach a point where the heart cannot beat any faster, leading to its failure.

Another relevant aspect is the heart failure caused by COPD, which causes the pressure in the heart to drop progressively depending on the degree of COPD. That is because the left ventricle begins to fail as the progression of the disease gets permanent. After all, the heart is a muscle that needs to be nourished with oxygen and eliminate waste substances, but the lung is not performing its function well, and neither is the rest of the system.

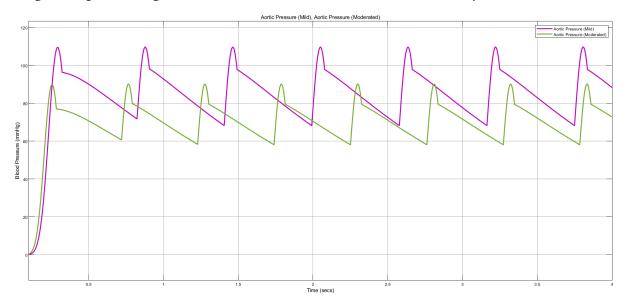


Figure 6.19: Aortic pressure in the aortic chronic obstructive pulmonary disease

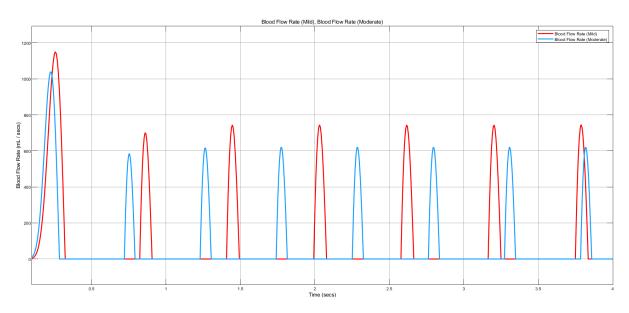


Figure 6.20: Blood flow rate in the chronic obstructive pulmonary disease

An additional effect can be notices referring blood flow rate which exhibits a decreasing due to the oxygen rumination (Figure 6.17).

The results obtained during aortic regurgitation and pulmonary obstruction can be assumed as valid from the qualitative point of view, according to [Kappel, 2012] and [Batzel et al., 2005].

7

# Conclusions and future lines of study

## 7.1 Conclusions

The main objectives of this Final Degree Project was to model a cardiovascular system, which consisted of implementing the cardiovascular and pulmonary systems separately and then interconnecting the two systems to observe how they affect each other. All of this has been accomplished building a block diagram using SIMULINK, and within this, implementing the same system through electrical analogies using SIMSCAPE.

The main advantage of building a model of the cardiopulmonary system dynamics is the possibility for the physician to visualise how a malfunction in the heart affects the lung or vice versa, without the need for the patient to undergo any test. The second advantage of this model is that the system is implemented through Object-Oriented Programming. This implies that the physician, or appropriate personnel, does not require prior knowledge of hydraulics or analogies to interpret the system's results.

# 7.2 Future lines of study

It is important to clarify that this Final Degree Project constructs a straightforward cardiopulmonary system, as the most significant complexity is found in the interconnections in the cardiorespiratory system. Therefore, a possible study would consist of increasing the system's complexity, considering a more complex model including gas exchange at the pulmonary and vascular level. Another implementation would be the introduction of controllers such as PID to be able to control either the performance of an left ventricle assisted devices or an air flow ventilator by by using the cardiopulmonary model here developed as a benchmark.

8

# Conclusiones y líneas futuras

### 8.1 Conclusiones

El objetivo principal de este Trabajo de Fin de Grado ha sido modelar un sistema cardiovascular, lo que ha consistido en implementar los sistemas cardiovascular y pulmonar por separado y posteriormente interconectar ambos sistemas para observar cómo se afectan mutuamente. Todo ello se ha llevado a cabo construyendo un diagrama de bloques utilizando SIMULINK, y dentro de éste, implementando el mismo sistema mediante analogías eléctricas utilizando SIMSCAPE.

.

La principal ventaja de construir un modelo de la dinámica del sistema cardiopulmonar es la posibilidad de que el médico visualice cómo un mal funcionamiento del corazón afecta al pulmón o viceversa, sin necesidad de que el paciente se someta a ninguna prueba. La segunda ventaja de este modelo es que el sistema se implementa mediante programación orientada a objetos. Esto implica que el médico, o el personal adecuado, no necesita tener conocimientos previos de hidráulica o analogía para interpretar los resultados del sistema.

### 8.2 Lineas futuras

Es importante aclarar que este Trabajo de Fin de Grado construye un sistema cardiopulmonar sencillo, ya que la complejidad más significativa se encuentra en las interconexiones del sistema cardiorrespiratorio. Por lo tanto, un posible estudio consistiría en aumentar la complejidad del sistema, considerando un modelo más complejo que incluya el intercambio de gases a nivel pulmonar y vascular. Otra implementación sería la introducción de controladores como el PID para poder controlar el funcionamiento de un dispositivo asistido por el ventrículo izquierdo o un ventilador de flujo de aire utilizando el modelo cardiopulmonar aquí desarrollado como referencia.

# **Bibliography**

- Akers, A., Gassman, M., & Smith, R. (2006). *Hydraulic Power System Analysis (Fluid Power and Control)* (Vol. 16). http://www.amazon.com/Hydraulic-Power-System-Analysis-Control/dp/0824799569
- 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.
- Álvarez, F. V., De Miguel Díez, J., & Álvarez-Sala, J. L. (2008). EPOC y acontecimientos cardiovasculares. *Archivos de Bronconeumologia*, 44(3), 152–159. https://doi.org/10.1016/S1579-2129(08)60030-0
- American Health Association. (2022). Ejection Fraction Heart Failure Measurement. https://www.heart.org/en/health-topics/heart-failure/diagnosing-heart-failure/ejection-fraction-heart-failure-measurement
- Badr, M. F. (2017). Modeling and simulation of the analogous mechanical and electrical systems.
- Barile, M. (2020). Pulmonary Edema: A Pictorial Review of Imaging Manifestations and Current Understanding of Mechanisms of Disease. *European Journal of Radiology Open*, 7, 100274. https://doi.org/10.1016/j.ejro. 2020.100274
- Barzel, B., Lim, K., Burke, S. L., Armitage, J. A., & Head, G. A. (2015). Specific role of dietary fat in modifying cardiovascular and locomotor activity 24-h rhythms. *Chronobiology International*, 32(5), 668–676. https://doi.org/10.3109/07420528.2015.1032414
- Batzel, J. J., Timischl-Teschl, S., & Kappel, F. (2005). A cardiovascular-respiratory control system model including state delay with application to congestive heart failure in humans (Vol. 50). https://doi.org/10.1007/s00285-004-0293-3
- Burattini, R., & Bini, S. (2011). Physiological interpretation of inductance and low-resistance terms in fourelement windkessel models: Assessment by generalized sensitivity function analysis. *Medical Engineering and Physics*, 33(6), 739–754. https://doi.org/10.1016/j.medengphy.2011.01.012
- Carter, P., Lagan, J., Fortune, C., Bhatt, D. L., Vestbo, J., Niven, R., Chaudhuri, N., Schelbert, E. B., Potluri, R., & Miller, C. A. (2019). Association of cardiovascular disease with respiratory disease. *Journal of the American College of Cardiology*, 73(17), 2166–2177. https://doi.org/https://doi.org/10.1016/j.jacc.2018.11.
- Catanho, M., Sinha, M., & Vijayan, V. (2012). Model of Aortic Blood Flow Using the Windkessel Effect. *Mathematical Methods in Bioengineering*, 15. http://www.isn.ucsd.edu/courses/beng221/problems/2012/BENG221\_Project%20-%20Catanho%20Sinha%20Vijayan.pdf
- $Computing, P. \ (n.d.). \ Ohm's \ Law. \ https://makeabilitylab.github.io/physcomp/electronics/ohms-law.html$
- Cuesta Merino, D. (2016). *Modelado Orientado a Objetos Global del Sistema Cardiorrespiratorio* (Master's thesis).

  Universidad de Málaga. https://riuma.uma.es/xmlui/bitstream/handle/10630/12657/DavidCuestaMerinoMEMORIA.

  pdf?sequence=1&isAllowed=y

- Diamantis, G., Aggelos, E., Demetrios, P., & Anogeianakis, G. (2017). Heart rate variability in chronic obstructive pulmonary. *Res Rev Insights*.
- $Forum.~(2017).~El~impacto~global~de~la~enfermedad~respiratoria.~https://gard-breathefreely.org/wp-content/uploads/2017/11/Firs2017\_esp\_web.pdf$
- Ghafarian, P., Jamaati, H., & Hashemian, S. M. (2016). A review on human respiratory modeling. *Tanaffos*, 15(2), 61–69.
- Han, M. K., McLaughlin, V. V., Criner, G. J., & Martinez, F. J. (2007). Pulmonary diseases and the heart. *Circulation*, 116(25), 2992–3005. https://doi.org/10.1161/CIRCULATIONAHA.106.685206
- Hauser, J., Parak, J., Lozek, M., & Havlik, J. (2012). System Analyze of the Windkessel Models. Space, 100, 5.
- Hellsten, Y., & Nyberg, M. (2016). Cardiovascular adaptations to exercise training. *Comprehensive Physiology*, *6*(1), 1–32. https://doi.org/10.1002/cphy.c140080
- Hlaváč, M. (2004). Windkessel model analysis in matlab. *Proceedings of 10th conference STUDENT EEICT*, (3), 5. http://www.feec.vutbr.cz/EEICT/2004/sbornik/03-Doktorske\_projekty/01-Elektronika/09-lahvo.pdf
- Kappel, F. (2012). Modeling the dynamics of the Cardiovascular-respiratory System (CVRS) in humans, a survey. *Mathematical Modelling of Natural Phenomena*, 7(5), 65–77. https://doi.org/10.1051/mmnp/20127506
- Kappel, F., Lafer, S., & Peer, R. O. (1997). A model for the cardiovascular system under an ergometric workload. Surv. Math. Ind. 7, 239–250.
- Koeppen, B., & Stanton, B. (2017). Berne and Levy Physiology. Elsevier Gezondheidszorg.
- Lee, R. M., & Tsai, N. C. (2013). Dynamic model of integrated cardiovascular and respiratory systems. *Mathematical Methods in the Applied Sciences*, *36*(16), 2224–2236. https://doi.org/10.1002/mma.2748
- Low, A. T., Medford, A. R., Millar, A. B., & Tulloh, R. M. (2015). Lung function in pulmonary hypertension. Respiratory Medicine, 109(10), 1244–1249. https://doi.org/10.1016/j.rmed.2015.05.022
- Luisada, A. A., & MacCanon, D. M. (1972). The phases of the cardiac cycle. *American Heart Journal*, 83(5), 705–711. https://doi.org/https://doi.org/10.1016/0002-8703(72)90412-7
- Mathworks, C., & Drive, A. H. (2020). Getting Started Guide R 2020 a.
- $MathWorks, T. \ (n.d.). \ What \ Is \ MATLAB? \ https://es.mathworks.com/discovery/what-is-matlab.html$
- Molnar, C. (2015). 11.3 Circulatory and Respiratory Systems Concepts of Biology 1st Canadian Edition. https://opentextbc.ca/biology/chapter/11-3-circulatory-and-respiratory-systems/
- National Cancer Institute. (n.d.). NCI Dictionary of Cancer Terms. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/pulmonary-edema
- Oh, K. W., Lee, K., Ahn, B., & Furlani, E. P. (2012). Design of pressure-driven microfluidic networks using electric circuit analogy. *Lab on a Chip*, 12(3), 515–545. https://doi.org/10.1039/c2lc20799k
- Olson, H. F. (1958). Dynamical analogies (Vol. 2729). Van Nostrand Princeton.
- Peate, I. (2015). Anatomy and physiology for nurses at a glance. Wiley Blackwell.
- Pérez de la Plaza, E., & Fernández Espinosa, A. M. (2018). Aparato respiratorio. Procedimientos relacionados. Tecnicas basicas de enfermería, 134–156.

- Pérez-Ríos, M., Schiaffino, A., Montes, A., Fernández, E., López, M. J., Martínez-Sánchez, J. M., Sureda, X., Martínez, C., Fu, M., Continente, X. G., Carretero, J. L., & Galán, I. (2020). Smoking-Attributable mortality in Spain in 2016. *Archivos de Bronconeumología (English Edition)*, 56(9), 559–563. https://doi.org/10.1016/j.arbr. 2020.07.005
- Rutten, F. H., Cramer, M. J. M., Lammers, J. W. J., Grobbee, D. E., & Hoes, A. W. (2006). Heart failure and chronic obstructive pulmonary disease: An ignored combination? *European Journal of Heart Failure*, 8(7), 706–711. https://doi.org/10.1016/j.ejheart.2006.01.010
- Scanlon, V., & Sanders, T. (2006). Essentials of Anatomy And Physiology (5th ed.). F a Davis Co.
- Simscape. (n.d.). https://es.mathworks.com/products/simscape.html
- Soltesz, E. G., & Carabello, B. (2017). Aortic regurgitation. *Cardiology Secrets*, 277–283. https://doi.org/10.1016/B978-0-323-47870-0.00030-1
- Swamy, G., Kuiper, J., Gudur, M. S., Olivier, N. B., & Mukkamala, R. (2009). Continuous left ventricular ejection fraction monitoring by aortic pressure waveform analysis. *Annals of Biomedical Engineering*, *37*(6), 1055–1068. https://doi.org/10.1007/s10439-009-9675-4
- The MathWorks, I. (2013). Getting Started Guide R 2013 b, 95. http://www.mathworks.se/help/pdf\_doc/simulink/sl\_gs.pdf
- Tortora, G., & Derrickson, B. (2013). Principios de anatomía y fisiología (13th ed.). Editorial Médica Panamericana.
- Tsai, N. C., & Lee, R. M. (2011). Interaction between cardiovascular system and respiration. *Applied Mathematical Modelling*, *35*(11), 5460–5469. https://doi.org/10.1016/j.apm.2011.04.033
- Verhoeff, K., & Mitchell, J. R. (2017). Cardiopulmonary physiology: Why the heart and lungs are inextricably linked. *Advances in Physiology Education*, 41(3), 348–353. https://doi.org/10.1152/advan.00190.2016
- WHO. (2017). Enfermedades cardiovasculares. https://www.who.int/es/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)
- Wikipedia. (2022a). Hydraulic analogy. https://en.wikipedia.org/wiki/Hydraulic analogy
- Wikipedia. (2022b). Lung volumes. https://en.wikipedia.org/wiki/Lung\_volumes
- Wikipedia. (2022c). Mechanical–electrical analogies. https://en.wikipedia.org/wiki/Mechanical%E2%80%93electrical\_analogies#:%7E:text = Mechanical%E2%80%93electrical%20analogies%20are%20used,between%20mechanical%20and%20electrical%20parameters.
- Wikipedia. (2022d). Respiratory system. https://en.wikipedia.org/wiki/Respiratory\_system
- Young, A. L., Langston, C. S., Schiffman, R. L., & Shortsleeve, M. J. (2001). Mitral valve regurgitation causing right upper lobe pulmonary edema. *Texas Heart Institute Journal*, 28(1), 53–56.
- Zagrai, A. (2007). Electro-mechanical analogies for modeling the structural impedance response. *Health Monitoring of Structural and Biological Systems 2007*, *6532*(65320), 65320F. https://doi.org/10.1117/12.715948



E.T.S de Ingeniería Informática Bulevar Louis Pasteur, 35 Campus de Teatinos 29071 Málaga