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Learning Respiratory System Function in BME Studies by Means of a Virtual Laboratory: RespiLab

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***Abstract*—One of the career areas included in the field of Biomedical Engineering (BME) is the application of engineering system analysis: physiologic modeling, simulation, and control. This paper describes a virtual laboratory and related practical sessions designed for the analysis and the study of the human respiratory system. The laboratory is based on the compilation of several models described in the literature. Presented application has been built using MATLAB/Simulink and Easy Java Simulations (EJS), combining good computation capabilities that are completely interactive. The virtual laboratory is designed in order to understand the operation of the respiratory system under normal conditions and pathological situations, and to predict respiratory variables at different levels of ventilator stimuli and conditions. The presented virtual laboratory has been used and evaluated by students of the Master of Science degree on BME. Experience has shown that this virtual laboratory is a very useful tool for learning the complex response of the human respiratory system.**

***Index Terms*—Biomedical engineering (BME), easy Java simulations (EJS), interactivity, respiratory system.**

I. Introduction

BIOMEDICAL ENGINEERING (BME) applies electrical, mechanical, chemical, optical, and other engineering principles to understand, modify, or control biologic systems, as well as to design and manufacture products that can monitor physiologic functions and assist in the diagnosis and treatment of patients [1]. In a few words, BME is the application of engineering sciences and technology to medicine and biology. Because of the interdisciplinary nature of this activity, considerable interplay and overlapping of interest and effort are present between engineering and biologic points of view.

A tool that has been proved to be efficient to shortcut and simplify the access to new concepts and technologies is interactivity [2], [3]. Interactivity allows one to understand qualitatively the influence of parameters in the system behavior without the need of an in-depth knowledge of a certain subject. This situation is usually the case in BME, where engineers do not need a deep knowledge of certain medical topics (and vice versa). In this work an application developed to apply this concept is presented.

BME is different from other engineering areas in the sense of obtaining results from experimental procedures and reproducing real physiological situations. Interacting with the human body (collaboration of volunteers or patients to be analyzed, instrumentation with specials safety conditions, ethic and legal requirements for the protocols, etc.) is very difficult and expensive and even dangerous in certain situations. The use of virtual labs is proposed to overcome this drawback and allow students and researchers to interact with the human body. These labs can be built in a complete interactive way, so that the students can easily understand the qualitative behavior behind the complex models used to represent the human body.

The respiratory control system is a nonlinear, multioutput, delayed-feedback dynamic system which is constantly being perturbed by physiologic and pathologic disturbances [4]. Deep mathematical models, such as the one used in this work, are quite complex [5], [6]. Thus, to study their behavior analytically is difficult. Instead, they must be studied by means of numerical simulations. Additionally, these models have a high number of parameters which may modify qualitatively the system response, so that performing many simulations under different conditions is necessary to understand the complete system function. Presented, virtual laboratory and proposed practical sessions improve the learning process by guiding the experiments and focusing on the most relevant parameters.

The goal of practical sessions is not that students know the mathematical model nor its blocks in detail but that they understand its behavior qualitatively. Proposed sessions help students to build their own mental model of the respiratory system which is the main objective of these sessions.

Both the virtual laboratory and the sessions are appropriate for a course about biomedical systems or physiology included in a Master of Science degree on BME where students come from technical bachelors: electrical, mechanical, or computer science, among others. Such is the case of a course about biomedical system modeling that belongs to the Master of Science degree on BME at the Technical University of Catalonia. This degree is composed by 120 European Credit Transfer System (ECTS) credits split into four semesters. Only little or even no background on respiratory physiology is necessary to carry out the practical sessions. The course contents are explained in more detail in Section IV, and the design of the lab and associated lectures are according to the spirit of Bologna Process and the ECTS [7].

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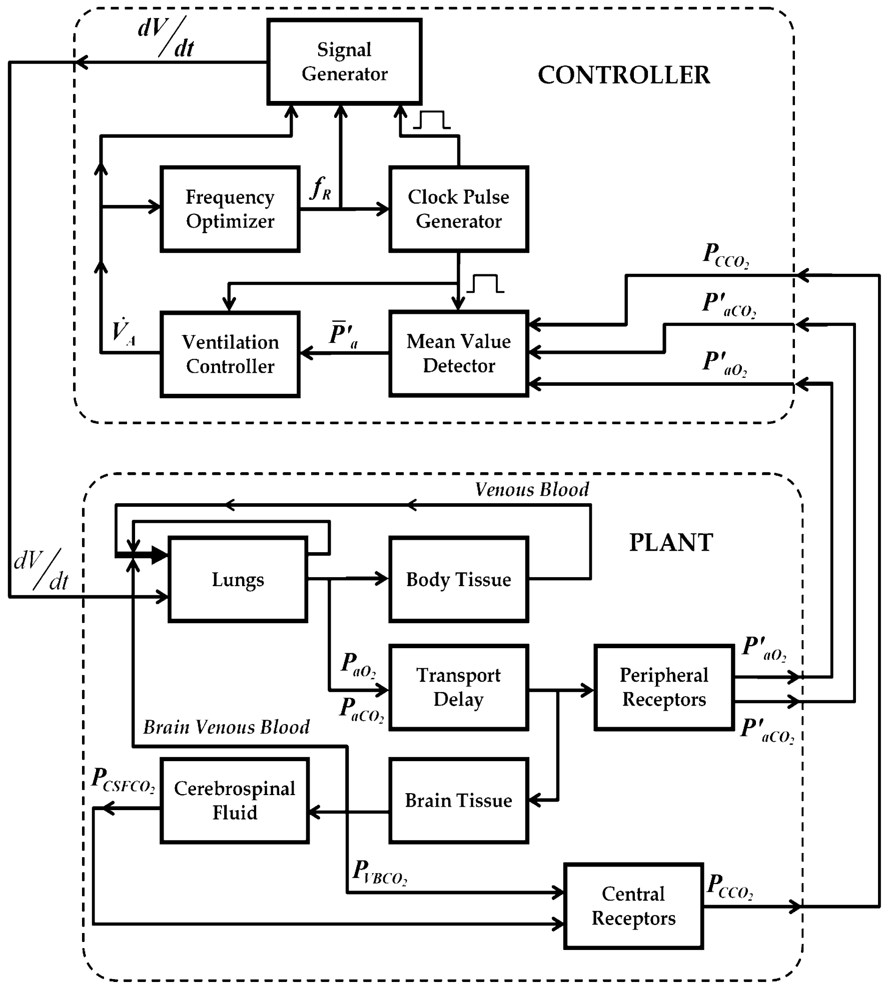

Fig. 1. Block diagram of the respiratory control system from [5], [6].

The paper is organized as follows. Section II describes the core of RespiLab, that is, the model of respiratory control system and the main physiological and external disturbances that can be studied with the virtual laboratory. Section III explains the tool, its interactive elements, plot options, and examples. The use of the virtual laboratory is shown in Section IV by means of three laboratory sessions. The course where the tool has been included is also described. Section V presents survey results from the students and describes the experience using RespiLab. Finally, conclusions are drawn in Section VI.

II. The Respiratory Control System

A. Model Description

Many empirical and functional models have been proposed in the literature to describe various aspects of the respiratory system. Some of these models correspond to a complete description of the closed-loop system and assume one structure that includes different intermediate processes (Fig. 1).

This biological system is dedicated to a specific physiologic function: the exchange of O_2 and CO_2. Control of ventilation is automatic and normally involuntary in the presence of different stimuli from a change in metabolic activity to a modification of external environment. The respiratory system adjusts alveolar ventilation, $\dot{V}_A$, to the demands of the body so that the arterial CO_2 pressure, $Pa\mathrm{CO}_2$, and arterial O_2 pressure, $Pa\mathrm{O}_2$, remain practically constant or under acceptable ranges. This condition is called homeostasis [8].

In the plant, there are blocks and variables indicating physiological processes: gas concentrations in veins and arteries ($C_v\mathrm{CO}_2/\mathrm{C}_v\mathrm{O}_2$ and $\mathrm{C}a\mathrm{CO}_2/\mathrm{C}a\mathrm{O2}$, respectively), gas exchange in body tissue and brain, circulatory mixing, and circulation time delay from tissues to chemoreceptors. Central and peripheral chemoreceptors get the $Pa\mathrm{CO}_2$ and $Pa\mathrm{O}_2$ and send this information to the controller located in the medulla. The model includes important variables in the respiratory pattern generation as tidal volume, V_T, and respiratory frequency, f.

The model described in [5] and [6], which is used in the virtual laboratory, considers a controller whose parameters of respiratory pattern are calculated every cycle as it happens physiologically. Additionally, to simulate more properly inspiration and expiration intervals, lung volume (v) follows:

$$\frac{dv}{dt} = \pi \dot{V}_A \sin(2\pi f t). \quad (1)$$

According to this equation, the respiratory flow (dv/dt) describes a sinus whose parameters, $\dot{V}_A$ and f, are computed every breath to minimize the respiratory work output [5], [6].

The model also considers the interaction between cardiac output, Q, and respiratory function ($Pa\mathrm{CO}_2, Pa\mathrm{O}_2$ and metabolic rate).

B. Ventilatory Stimuli

Exercise is one of the most common and important stimulus of the respiratory system; its ventilatory response is the most used stimulus for the model validation and for understanding changes in respiratory variables. During exercise, O_2 consumption and CO_2 production ($\dot{V}\mathrm{CO}_2$) increase considerably to counterbalance the metabolic increased demand. A value of $\dot{V}\mathrm{CO}_2 = 0.2$ l/min is considered at rest. It increases with exercise.

Hypoxia can result from disturbances of respiration or a reduction in pressure of inspired air as occurs at high altitudes. For the simulation, an input variable, $P_I\mathrm{O}_2$, is considered with values lower than 159 Torr (21% of atmospheric pressure), that correspond to normal conditions at sea level. It is related to a decrease in $Pa\mathrm{O}_2$. The level of hypoxia corresponding to a specific altitude is obtained by means of the ideal gas law described in [9].

Hypercapnia corresponds to a presence of CO_2 in the inhaled gas or CO_2 retention. Hypercapnia is the most frequent and main stimulus in the hypoventilation imbalance during acute respiratory failure; O_2 decreases and CO_2 levels increase, particularly in patients with Chronic Obstructive Pulmonary Disease (COPD) [10]. An input variable, $P_I\mathrm{CO}_2$, is considered whose value is 0 Torr (0% of atmospheric pressure) in normal conditions and increases with the hypercapnic stimulus.

C. Optimization of Respiratory Frequency

Respiratory frequency (f) is one of the most important variables for physiologists and physicians. It is calculated in the model [6] on a minimum respiratory work basis as found in [11]. Lungs elastance, E_{rs}, airway resistance, R_{rs}, and sinusoidal flow waveform as given by (1) are considered in the Otis, *et al.*, frequency equation [11]

$$f_{\mathrm{Otis}\ et\ al.} = \frac{-E_{\mathrm{rs}}V_D + \sqrt{(E_{\mathrm{rs}}V_D)^2 + 4E_{\mathrm{rs}}R_{\mathrm{rs}}\pi^2 V_D \dot{V}_A}}{2\pi^2 R_{\mathrm{rs}} V_D} \quad (2)$$

where V_D is the dead space volume given by [5]

$$V_D = 0.1698\dot{V}_A + 0.1587. \quad (3)$$

However, some researchers have considered that (2) is only useful at rest or with low exercise. Mead [12] showed that respiratory frequency with moderate exercise may be determined more closely on the basis of optimal inspiratory pressure-time integral as a measure of the energy cost of breathing developed by the respiratory muscles. Mead [12] obtained the following equation:

$$f_{\mathrm{Mead}} = \sqrt[3]{\frac{E_{\mathrm{rs}}^2 \dot{V}_A}{4\pi^2 R_{\mathrm{rs}}^2 V_D}}. \quad (4)$$

Similarly, the optimization principle has also been applied to the prediction of ventilatory variables like airway caliber and dead space volume [13]. Widdicombe and Nadel [13] found the following equation for the optimal respiratory frequency in moderate and severe exercise:

$$f_{\mathrm{Widdicombe\ Nadel}} = \sqrt{\frac{E_{\mathrm{rs}}\dot{V}_A}{4R_{\mathrm{rs}}V_D}}. \quad (5)$$

These three, (2), (4), and (5), are well known by the researchers, and they can be considered more appropriate depending on ventilatory conditions. The existence of different equations shows that problems of respiratory control, such as neural control of the respiratory cycle remain unsolved in spite of the voluminous literature generated over the years. All three equations can be used in the model selected for the virtual laboratory to evaluate differences in the respiratory variables at different levels of stimulus.

D. Restrictive and Obstructive Diseases

Two main types of lung disease, obstructive and restrictive, are related to changes in the following respiratory parameters: resistance (R_{rs}) and elastance (E_{rs}) [14]. Remember that both mechanical parameters are included in (2), (4), and (5).

Restrictive lung diseases are caused either by an alteration in lung tissue, by disease of the chest wall, or by neuromuscular apparatus. A decrease is noted in the lungs ability to expand, or a decrease in the lungs' ability to transfer O_2 to the blood (or CO_2 out of the blood). In these conditions, the total lung volume and the transfer of oxygen from air to blood may be reduced. Restrictive disorders include sarcoidosis, interstitial pneumonitis, pulmonary fibrosis, and pneumonia.

In obstructive lung conditions, airways are narrowed, usually causing an increase in the time that the lungs spend to be emptied. Obstructive lung disease can be caused by conditions such as emphysema, bronchitis, infection (which produces inflammation), and asthma; it also includes the common COPD.

Typical values of resistance and elastance for normal adult subjects, are 2.6 $\mathrm{cmH_2O/l/s}$ and 10 $\mathrm{cmH_2O/l}$, respectively [15]. On the other hand, the values of mechanical parameters depend on the grade of illness in obstructive and restrictive patients. One subject could be considered as an obstructive or restrictive patient, if his respiratory resistance or elastance is higher than twice their normal values [16], [17].

III. Virtual Laboratory Description

A. Tool Development

Presented software application is based on Easy Java Simulations (EJS) [18]–[20], an open source Java-based tool that

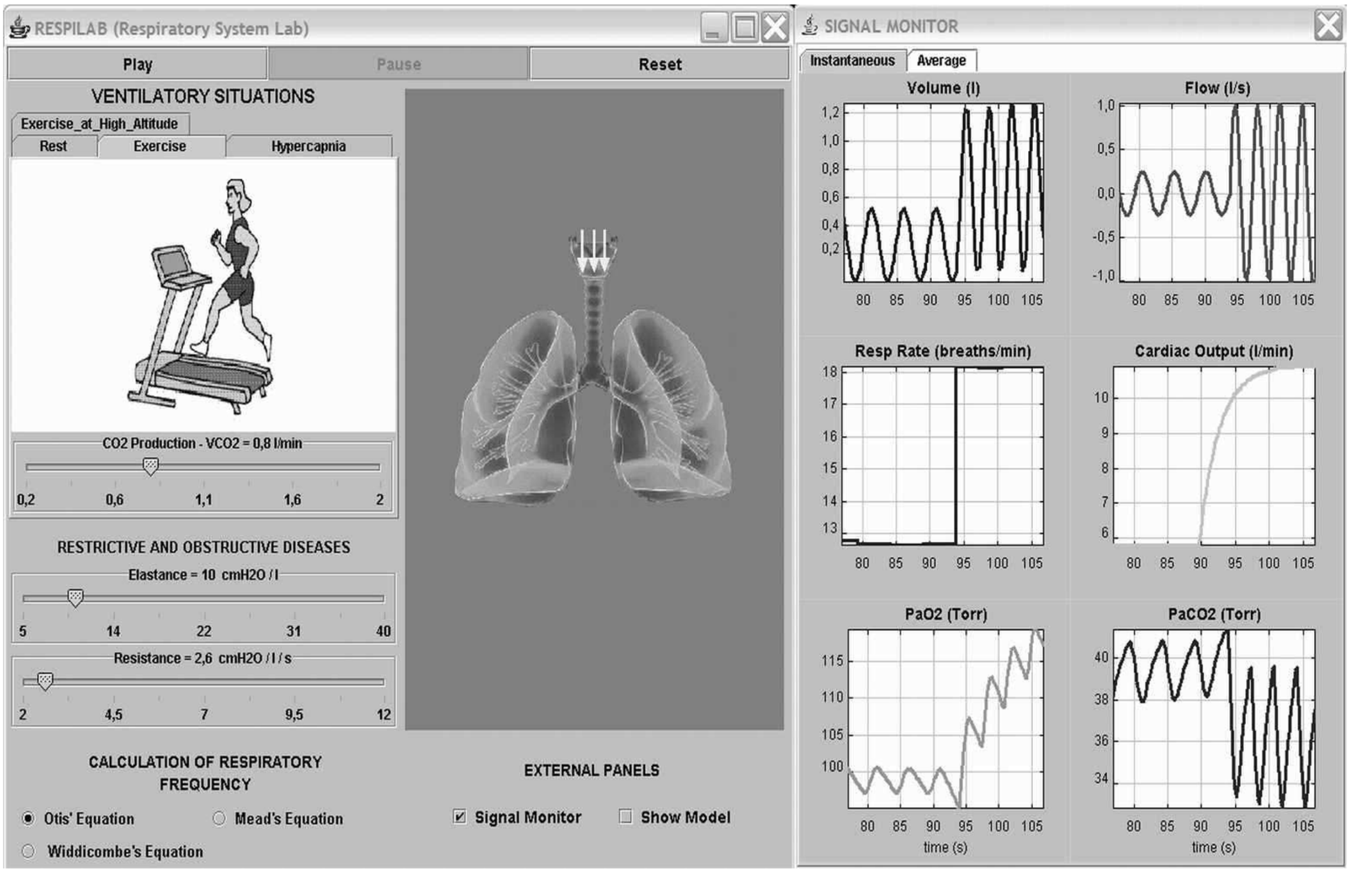

Fig. 2. Interface of the Virtual Laboratory. Interactive Module and Signals Monitor are shown on the left and right side, respectively.

allows creating interactive dynamic simulations. An EJS application is composed by three main elements, the model, the view, and the interactivity. The model is developed by the designer (transparent for the user), and it can be developed by introducing in EJS a set of differential equations or by using a previous developed simulation model based on another computation tool such as MATLAB/Simulink. Since the respiratory model is quite complex [5], the simulation model has been implemented in MATLAB/Simulink to profit from computation capabilities of this tool. The MATLAB/Simulink can be easily linked to the other elements to make interactive the complete system [21].

The other elements, the view and the interactivity, have been completely designed and implemented in EJS. These elements, are the interface to the user, and offer a friendly and interactive way to interact with the laboratory.

B. Interactive Elements

Interface of the virtual laboratory called RespiLab is shown in Fig. 2. The interactive module is on the left side where interesting parameters can be changed by means of sliders and tabs to simulate different ventilatory conditions. A multisignal scope can be seen in the right side of the interface when the user selects the corresponding option.

The interactive module is composed of three important types of simulations.

- Ventilatory situations such as rest, exercise, hypercapnia, and a combination of exercise and hypoxia.
- Restrictive and obstructive diseases.
- Calculation of respiratory frequency.

In the first one, a user can select the kind of stimulus by clicking one of the four tabs available. A representative animated picture is shown in each tab: a person seated on a bench when a resting condition is simulated, a climber at the top of a mountain for exercise at high altitude, a person breathing deeply inside a closed tent for hypercapnia, and a runner on a treadmill to show exercise as it can be seen in Fig. 2. In the last two pictures, their animation is faster with higher levels of exercise or hypercapnia. These animations contribute to the clear identification of the stimulus under simulation, helping the user in the creation of his mental model.

A user can change the level of stimulus modifying the value of a respiratory parameter by means of a slider.

- Exercise: Variable $\dot{V}CO_2$ can be changed from 0.2l/min. at rest to a maximum value of 2l/min.
- Altitude: User can simulate exercise at an altitude from sea level to 6 Km (which correspond to different levels of hypoxia).
- Hypercapnia: Variable $P_I CO_2$ is modified from 0 Torr in normal conditions up to 50 Torr.

Regarding pulmonary pathologies, both mechanical parameters can be modified simultaneously: E_{rs} from 5 to 40 cmH_2O/l and R_{rs} from 2 to 12 cmH_2O/l/s. Besides, one of the three optimization bases presented in Section II-C for the calculation of respiratory frequency can be selected by the user (Fig. 2).

A big picture of two lungs is shown in the middle of the virtual laboratory, and their sizes change according to the air volume inhaled or exhaled during the simulation. Their increase and reduction during inspiration and expiration, respectively, is proportional to the respiratory volume. Furthermore, three arrows over the upper airway are moved upwards and downwards indicating the entry and exit of the air. The size of the arrows is proportional to the respiratory flow.

Finally, standard options in virtual laboratories are provided, such as to "play," to "pause," to "reset," and to save the simulation results ("save-sim"). The last option is available when the simulation is paused, and it allows saving of the average values of all the variables shown in the signal monitor in one MATLAB file (Fig. 3). Saved simulation data permit further analysis and comparison with experimental data. Furthermore, external windows appear when the user clicks the options "Show Model" (the MATLAB/Simulink model is shown) and/or "Signal Monitor."

C. Plots and Examples

One of the two kinds of plots are shown when the corresponding tab of a signal scope is selected by the user: Instantaneous and Average. In the former, the following variables are shown during the respiratory cycles, corresponding to the last 30 s: respiratory volume, flow and frequency, cardiac output, PaO_2, and $PaCO_2$ (Fig. 2). Inspiration and expiration intervals during each respiratory cycle are clearly observed by means of the sinus waveform. In the Average option, changes of variables inside the respiratory cycle are not shown, but their average values calculated each cycle since the beginning of simulation: tidal volume, total ventilation, respiratory rate, cardiac output, PaO_2, and $PaCO_2$ (Fig. 3). A couple of illustrative examples are presented below to show the capabilities of the tool. The main characteristic, interactivity, cannot be easily presented in a written text. Nevertheless, several of the useful tools from the virtual laboratory are presented.

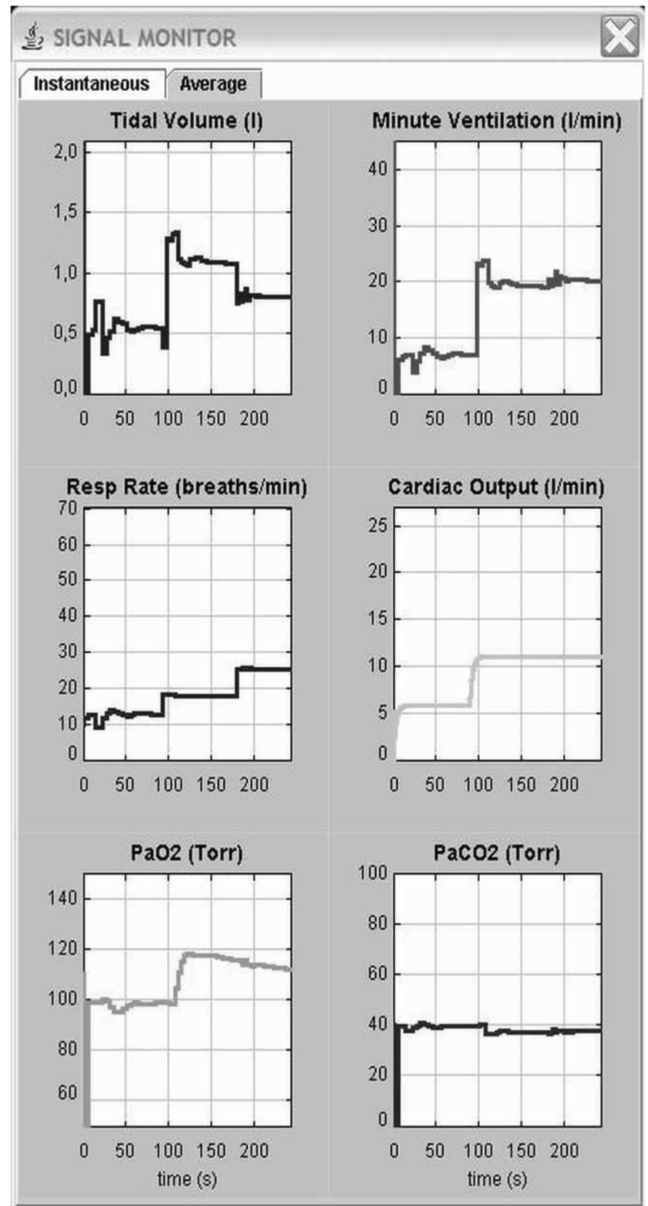

Fig. 3. Multisignal scope for the average values.

First, a change from resting conditions ($\dot{V}CO_2 = 0.2$ l/min) to a specific level of exercise ($\dot{V}CO_2 = 0.8$ l/min) is produced at 90 s. Instantaneous signals are shown in Fig. 2 where changes in all the variables can be observed at that moment. Amplitude of the respiratory volume is much higher because the subject breathes more deeply and also faster (respiratory frequency goes up from 12 until 18 breaths/min). That is why amplitude of respiratory flow also increases. This increase does not permit $PaCO_2$ to rise (it may be a little lower) although the production of CO_2 in tissues increases because of exercise (homeostasis). Logically, an increment in $PaCO_2$ goes with a decrease of PaO_2. These effects can be also seen in Fig. 3 where average values are shown. Tidal volume and total ventilation increase according to the changes mentioned. Besides, a transient response can be observed between 90–120 s, approximately. It corresponds to the real human respiratory behavior when a person starts exercising until his respiration settles in a specific ventilatory pattern. Finally, cardiac output doubles his value because of the exercise.

A second situation is simulated at 3 min while the exercise is performed: from typical values of mechanical parameters related to a normal subject ($E_{\rm rs} = 10$ cmH$_2$O/l and $R_{\rm rs} = 2.6$ cmH$_2$O/l·s) to values corresponding to a restrictive patient ($E_{\rm rs}$ goes up until 37 cmH$_2$O/l [22]). The objective is to evaluate differences in the breathing pattern between a healthy person and a restrictive patient. Instantaneous signals are shown in Fig. 4. Very small changes are observed in cardiac output and gas pressures in the same way as amplitude of respiratory flow. Nevertheless, the patient breathes smoother and faster to keep the same flow amplitude. All of these changes are also observed in the breath-by-breath average values (Fig. 3).

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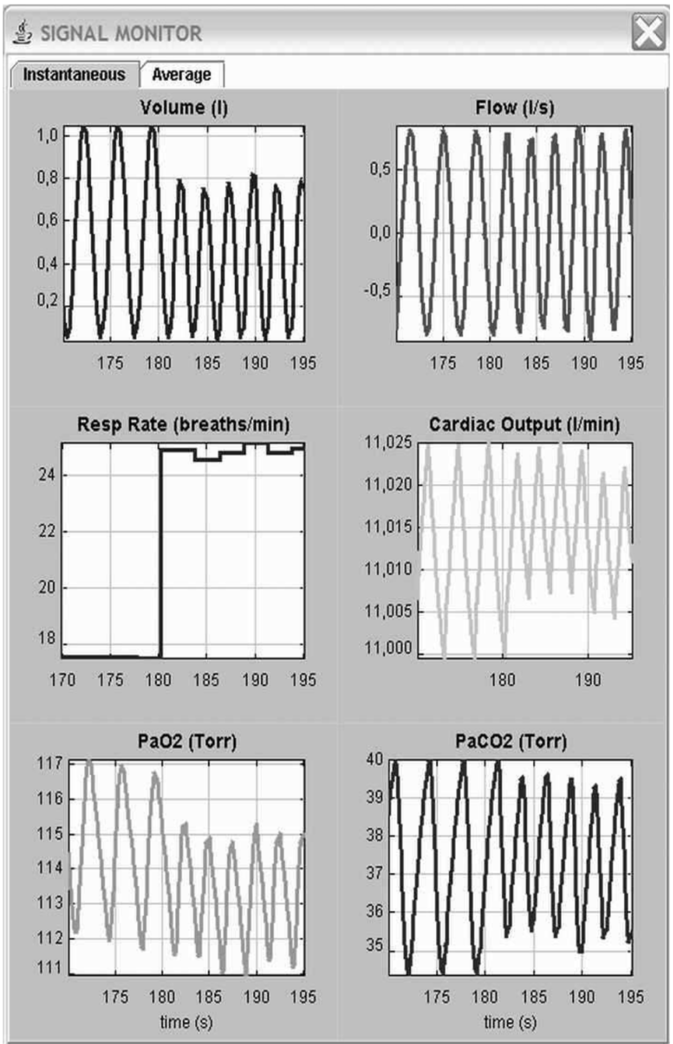

Fig. 4. Multisignal scope for instantaneous values.

IV. Using the Virtual Laboratory

A. Curriculum Framework

RespiLab has been incorporated in the laboratory sessions of a course about *Biomedical System Modeling*. The modeling course consists of 5 credits and is located in the second semester. Table I shows the course contents.

Students have received a course on physiological background in the previous semester where general topics on life science are explained. A very short description of ventilation mechanics and gas exchange is mentioned among other biological systems. Besides, all the students come from technical bachelors. Thus, they also have at least a minimum background in control engineering in order to be applied and extended in the course on *Biomedical System Modeling*.

Experiments are not considered as isolated problems to be solved, but as a general project which is addressed to allow the students to build their own "Mental Model" of the Respiratory System. "Mental Model" is a concept defined in physiology education as the mental organization of factual information that allows these facts to be used to accomplish tasks in the real world (such as solving problems or predicting the physiological behavior) [23]. The interactive options of the virtual laboratory and the practical sessions have been designed so that students identify the most important cause-effect relationships and phenomena from the respiratory function. During this discovery process, which takes place during the session, students construct the "mental model" according to the obtained experience.

Practical sessions have been also designed according to the criteria of ECTS mentioned in Section I. Allocation of credits is based on the bottom-up approach where the sessions are examined in view of their learning outcomes: one must know what the learner is expected to be able to do after successful completion.

TABLE I
THE COURSE CONTENTS

1) Introduction
   a) Historical background
   b) System analysis
   c) Differences between engineering and physiological control systems
2) Mathematical Modeling
   a) Generalized system properties
   b) Distributed-parameter versus lumped-parameter models
   c) Transfer function. Linearization
   d) Application of control theory to biological systems
3) Static Analysis of Physiological Systems
   a) Introduction
   b) Regulation of glucose
   c) Optimization in physiological control
   d) Regulation of cardiac output and respiratory control system
4) Time-Domain Analysis
   a) Dynamic system identification and temporal series analysis
   b) Open-loop versus closed-loop dynamics in biological systems
   c) Dynamics of neuromuscular reflex motion
5) Frequency-Domain Analysis
   a) Introduction
   b) Frequency response of a model of circulatory control
   c) Frequency response of glucose-insulin regulation
6) Stability Analysis: Linear Approaches
   a) Classical control tools to analyze stability
   b) Relative stability
   c) Stability analysis of the pupillary light reflex
   d) Model of Cheyne-Stokes breathing

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Sessions with RespiLab are designed to build up a coherent and quality driven study content using all of these ideas.

There are three sessions based on students' work equivalent to four hours each (0.4 ECTS credits in total). Sessions are carried out by pairs of students with one part in the laboratory assisted by an instructor and another one as a private work. Before these sessions with RespiLab, another laboratory introduces MATLAB to the students. In that session, students learn how to define and manage matrices, plot variables in figures, and program short functions and scripts among others. This knowledge is sometimes applied in the sessions with RespiLab, especially in the following ones during the course.

The first session is an introduction to the main concepts of the respiratory physiology to strengthen the theoretical background. Bibliography and documents are provided through Internet to permit the students to work by themselves. RespiLab User Manual and the complete Laboratory Guide are also available to be read before attending the next Session.

The second and third session follow a written "observe and record" (cookbook) format after a brief introduction on the specific topic to be explained [24]. Students are asked to reproduce several experiments based on the study of the respiratory system response under different stimuli and pathologies to accomplish the purpose of evaluating and strengthening the students' "mental model." In the second session, students analyze simulation results with respect to experimental data of one healthy subject under hypercapnia stimulation to consolidate their previous theoretical knowledge on the matter. In the same way, in the third session the goal is to analyze simulation results with respect to experimental data, but in this case experimental data belongs to one restrictive patient under exercise stimulus, one step forward in the analysis. Therefore, the goal in the two sections is the same to be in agreement with the main objective of consolidation of the students' mental model.

The first two hours and a half of each session is performed by using the RespiLab software in the laboratory. The remaining 90 min are performed during regular hours and students are asked to compare the simulation results with experimental data using MATLAB software and obtaining final conclusions. Values of respiratory variables in each exercise must be written in one report with additional comments and conclusions obtained by the students to evaluate their rationale analysis. The report composed by tables, answers, data, comments, etc. has to be delivered to the instructor through Intranet in each session before attending the next one.

Documents, Virtual Laboratory and Laboratory Guides are provided in a Web-based format [25].

These documents are the following.

- *RespiLab Laboratory Guide* with the description of all the sessions.
- *Laboratory Report* to be filled in by the students with the results, answers and comments after each Session.
- *RespiLab User Manual.*
- *RespiLab Survey Questionnaire.*

In addition, complementary teaching material is provided to the students through an Intranet such as the documents to be read for the first session and MATLAB files with experimental data to be used in the last two.

The assessment of laboratory sessions consists of two parts that provide the same contribution to the mark. The first one corresponds to the laboratory reports delivered after each session. The reports must be completely filled in and accompanied by rational comments, including associations between the experience with the virtual laboratory and physiology and control concepts. Besides the behavior of the students during the sessions, such as their receptivity to the lecturer's explanations, their logical answers and questions and their ability to perform the experiments are also considered. For the second part, the student is evaluated in order to know if his Mental Model of the respiratory system and his rationality and ability are high enough to answer the practical questions proposed in the exam at the end of the course. This part is very important because a purpose of the virtual lab is that students will be able to recognize respiratory situations and pathologies from experimental data, and to predict the behavior of the system when one specific stimulus occurs.

B. Sessions Description

1) Session 1: Introduction of Respiratory System: The objectives are that after this session the students should be able to understand the following.

- The basic phenomena of breathing mechanisms (why they are produced and how they are regulated).
- The main parts of the body or components involved in the respiration and their role.
- The most important respiratory variables and stimuli to be evaluated in the following sessions.

This is a virtual session where the students must read two documents and visit a Web link by themselves. They must answer a short questionnaire with seven questions related to the teaching material provided. The answers have to be delivered through Intranet before attending the second session.

2) Session 2: Respiratory System Response Under Ventilatory Stimuli: As main goals, after this Session students should be able to do the following.

- To use RespiLab in different conditions and different respiratory stimuli: rest, hypercapnia, hypoxia, exercise.
- To analyze and obtain conclusions from the results of simulations by means of experimental data and by means of the knowledge acquired from reading the documents suggested in the previous session.
- To understand the complexity of the respiratory system and its interaction with the cardiovascular system.
- To identify the sensitivity of the respiratory system to environment characteristics.

At the end, students have to check the three different equations to calculate the f during an increased hypercapnic stimulus (Section II-C). Experimental data corresponding to a healthy volunteer is provided to compare his changes of V_T and f as a function of ventilation, V_E, with respect to the three simulations using (2), (4), and (5). First, the comparison is

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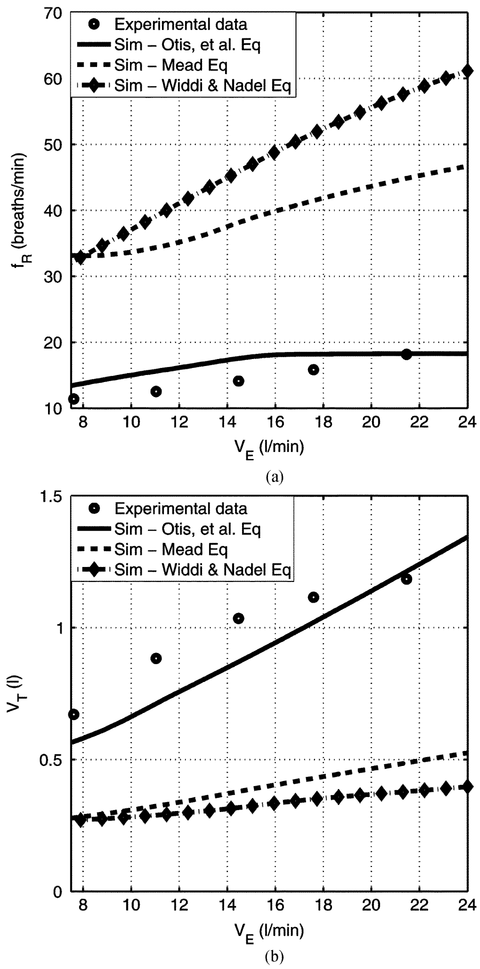

Fig. 5. (a) Respiratory frequency and (b) tidal volume as a function of total ventilation during hypercapnia. Different traces are used with the following equations: Otis, *et al.* (continuous), Mead (dashed), Widdicombe and Nadel (diamonds) to compare with experimental data (dots).

TABLE II
PREDICTION ERROR DURING HYPERCAPNIA WITH DIFFERENT EQUATIONS TO CALCULATE RESPIRATORY FREQUENCY

Equation	Prediction Error(%)	
	V_T	f
Otis, et al.	11.9	15.9
Mead	61.1	163.2
Widdicombe and Nadel	67.5	216.5

performed by inspection (Fig. 5), and later comparison is quantified by means of the prediction error (6)

$$P_{\mathrm{Error}}(\%) = \frac{1}{n}\sum_{i=1}^{n}\left|\frac{Xi_{\mathrm{real}} - Xi_{\mathrm{sim}}}{Xi_{\mathrm{real}}}\right| * 100 \quad (6)$$

where Xi_{real} and Xi_{sim} the value of V_T and f for a certain value of V_E in study (experimental or simulated, respectively), and n is the number of stimulus levels. These errors obtained by the students are shown in Table II. Thus, students conclude that the best option for hypercapnia stimulus is the Otis, *et al.*, equation based on the minimization of the respiratory work.

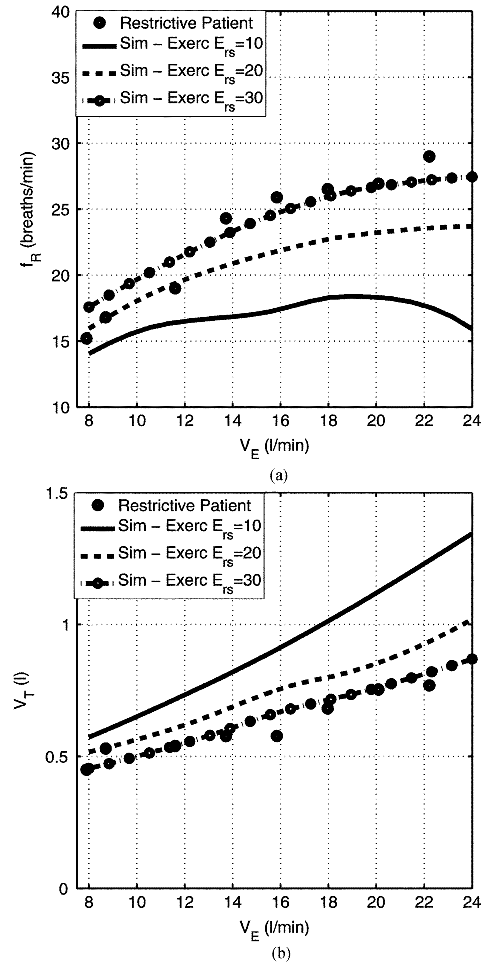

Fig. 6. (a) Respiratory frequency and (b) tidal volume as a function of total ventilation during exercise. Different traces are used with the following elastance values: 10 cmH_2O/l (continuous), 20 cmH_2O/l (dashed), 30 cmH_2O/l (dotted) to compare with data from a restrictive patient (dots).

TABLE III
PREDICTION ERROR DURING EXERCISE WITH DIFFERENT VALUES OF ELASTANCE

Elastance (cmH2O/l)	Prediction Error(%)	
	V_T	f
10	43.4	27.5
20	16.2	11.1
30	5.3	5.4

3) Session 3: Respiratory Diseases Based on Mechanical Loads: At the end of this session students should be able to do the following.

- To simulate respiratory pathologies by means of RespiLab.
- To analyze and obtain conclusions from the results of simulations by means of comparing these results with experimental data and by means of the knowledge acquired from reading the suggested documents in the first session.
- To understand the effect of an increase in respiratory resistance or elastance, that they correspond to physiopathological states in the ventilatory pattern.

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TABLE IV
RESPILAB SURVEY QUESTIONNAIRE

S1	RespiLab offers a comprehensive review of the human respiratory system.
S2	RespiLab has helped me to improve my understanding of the respiratory system.
S3	I have enjoyed learning the human respiratory system using RespiLab.
S4	RespiLab is interactive enough.
S5	RespiLab has helped my ability to work in group.
S6	RespiLab reponse time was fine.
S7	RespiLab is easy to use.
S8	The GUI offered by RespiLab is clear.
S9	I prefer using RespiLab instead of other simulation oriented environments (i.e. Simulink Files, MATLAB Files).
S10	RespiLab Manual is complete enough.

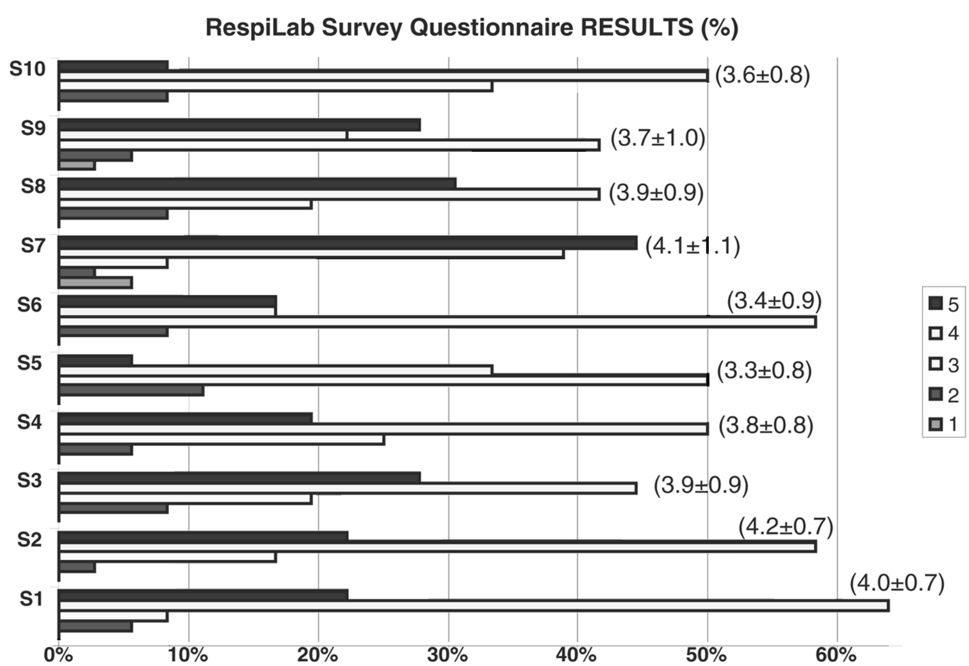

Fig. 7. Survey Questionnaire Results. Marks correspond to 5 = Strongly Agree; 4 = Agree; 3 = Neither Agree, Nor Disagree; 2 = Disagree; 1 = Strongly Disagree. Results are in percentage of total students ($n = 36$). Marks in mean and standard deviation are also shown between brackets for each question.

Effect of changes in mechanical parameters of the respiratory system is analyzed by simulating different values during rest at sea level and at 2500 m of altitude. Then, simulation results related with a sudden increase of exercise level are saved to calculate the settling time of the respiratory system (defined with respect to 5% of the final value of respiratory variables). Finally, a subject with a double and three times the normal elastance value is simulated for different levels of exercise. Results are compared with experimental data from a restrictive patient by inspection (Fig. 6) and by calculating the prediction error using (6) (Table III) with the same methodology used in the previous session. As the prediction error decreases when the elastance value is higher, students conclude that a restrictive disease is related to an increase of the respiratory elastance.

V. SURVEY QUESTIONNAIRE

The survey questionnaire shown in Table IV has been proposed to evaluate the level of the following objectives achievement.

- To analyze its usefulness as a tool for a better understanding of the global respiratory control system (S1 and S2).
- To evaluate the successful use of interactivity to make easier the learning process and its impact in the work in group (S3–S5).
- To identify advantages and disadvantages of graphical user interface (GUI) and tool performance to improve them (S6–S8).
- To evaluate the students satisfaction using RespiLab with respect to other software (S9).

- To inquire if the documentation included with RespiLab is clear and complete (S10).

RespiLab has been used by 36 students of Master of Science on BME (Section IV-A). All the students have been requested to answer (with marks 1–5) an anonymous questionnaire and to submit it to the instructor.

Results of survey questions are shown in detail in Fig. 7. Lowest marks correspond to questions S5 and S6 that are related with the second and third objectives mentioned above. The former is associated with the work in a group. This aspect is not especially strengthened by the tool but in the exercises performed during the laboratory sessions. They are performed in groups of two, and the collaboration between them should be expected in the work distribution and the interpretation of results and conclusions. However, response time of the RespiLab is, in general, appropriate considering the huge complexity of the complete model, but for the students, not simulating certain respiratory conditions do not seem fast enough depending on the computer computation power. Although students are sometimes impatient for obtaining the final results in the simulations, they have to learn that the human respiratory system also takes its time to respond under certain stimulus as it happens in real life. Regarding the last question S10, RespiLab User Manual has been extended after receiving the answers of the questionnaire.

The highest marks are obtained in the first two questions related with the understanding and comprehension of the respiratory system by means of the virtual laboratory. Thus, the main objective is reached completely. The other questions with high marks are related to the interactivity and the facility to be used. Students also prefer to use RespiLab instead of other software with less friendly interfaces. Confirmation is made on the important and high utility of virtual laboratories for learning. Finally, average marks in all questions are between 3.3 and 4.2. Thus, in general, the conclusion is that RespiLab is considered by the students to be a useful and interesting tool.

VI. Conclusion

In this paper a virtual laboratory designed to analyze the human respiratory control system and three related practical sessions have been introduced. The tool has been used and evaluated by students in a course of Master of Science degree. This laboratory is completely graphic and interactive so that it can be used to illustrate the behavior of the human respiratory control system under certain circumstances or pathologies and the influence of relevant parameters in the system. This virtual laboratory allows the students to obtain sensations and experience that would be very difficult otherwise because of the difficulties in performing experimental human studies. The use of virtual laboratories and interactivity in BME has proved to be an efficient way to shortcut the learning process and improve the students capabilities.

The tool has been built combining MATLAB/Simulink and EJS. While MATLAB/Simulink allows the implementation of complex models in a straightforward manner, EJS allows one to design attractive views and to introduce interactivity easily. This combination is quite suitable for virtual laboratory development.

Three practical sessions have been designed according to the criteria of ECTS, based on the student work load required to achieve the objectives specified in terms of learning outcomes. Students must identify several cause-effect relationships and phenomena from the respiratory system function. One part of the sessions is carried out in the Laboratory assisted by an instructor and another one as a private work.

Experience and students' evaluations show that presented virtual laboratory with related sessions are very useful to help the student build their "mental model" of the respiratory system. This "mental model" is based on the observation of the respiratory system response under different ventilatory situations and pathological conditions.

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