Obstructive Sleep Apnea Syndrome – OSAS

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Group 3

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1. ABSTRACT

The gold standard to diagnose obstructive sleep apnea syndrome (OSAS) is polysomnography, which is an examination that requires the recording of many signals over an entire night. Over the years, a lot of effort has been put into simplifying the procedure. However, OSAS diagnosis is still nowadays a very expensive and time-consuming task. The aim of this paper is to propose a novel method for OSAS diagnosis that requires no clinicians to manually identify the respiratory events. In this way, it reduces the overall cost and time of the diagnosis. Unfortunately, our approach was not the best choice for this type of signal variations as the events were not correctly identified, thus most of our findings on the events (apneas and hypopneas) did not correspond to the events determined by the clinicians upon analyzing the signals.

Keywords: *OSAS, respiratory events, polysomnography, apneas and hypopneas.*

2. PROBLEM AND MOTIVATION

The problem investigated is obstructive sleep apnea syndrome (OSAS), we chose this topic in order to improve its diagnosis by testing new methods, using polysomnography raw data. It is known that sleep studies are expensive and require evaluation in specific sleep laboratories, where the patients need to spend the night with dedicated systems and attending personnel [1]. Furthermore, it is labor intensive because the clinicians need to collect and analyze a large amount of data (e.g., EEG, ECG, oximetry, EMG, airflow, etc.) [2]. For these reasons, efforts are being directed to the identification of alternative methods, possibly implementable in portable devices, to permit an automatic and objective detection of apneas, more specifically the OSAS by saving cost, time and work. The aim of this project is a characterization of apneas and hypopneas using the airflow signal.

3. BACKGROUND AND RELATED WORK

The sleep apnea is a sleep disorder characterized by the occurrence of more than five apneas per hour during sleep or the complete cessation of respiratory airflow for more than 10 seconds, which requires a significant respiratory effort to restart normal respiration, with common symptoms such as snoring and repeated breathing pause. This condition can be divided into 3 types, such as the obstructive sleep apnea syndrome (OSAS), the central sleep apnea (CSA), and the mixed apnea (MSA). For our work we have a higher interest in evaluating the OSAS that is expressed by frequent episodes of both apnea and hypopnea [3], [4].

A study, conducted in Portugal [5], linked this health condition to individuals between the ages of 65 and 74, with a prevalence in men. Moreover, suffering from obesity and/or hypertension was a risk indicator of having severe OSAS [5].

OSAS is quite common and easy to control with the use of continuous positive airway pressure (CPAP) therapy machines (Figure 1) to alleviate the symptoms regarding this condition. The problem is that most people suffering from mild symptoms do not associate them with this health condition and this can really worsen their lives. With the CPAP the individual that suffers from OSAS can control the symptoms and can, for example, feel awake during the day, as he can sleep well at night. Most importantly, the use of CPAP decreased the probability of leading to various fatal diseases, such as heart failure, arrhythmias, increased blood pressure, strokes among others [6].

Figure 1 –Continuous Positive Airway Pressure (CPAP) therapy. [7]

Depending on how the sleep apnea occurs we can have different types, if the obstruction to the passage of air is total, it is called apnea, while if it is partial, hypopnea. The diagnosis is made with a polysomnography (PSG) test, which consists of the simultaneous recording of neurophysiological and respiratory variables that make it possible to evaluate the quantity and quality of sleep, as well as to identify the different respiratory events and their cardiorespiratory and neurophysiological repercussions. This test generally uses a minimum of twelve channels for continuous recording of: electroencephalogram (EEG), electrooculogram (EOG) and electromyogram (EMG) to determine sleep stages, oronasal airflow, chest and abdominal wall movements for respiratory effort, and oxygen saturation in order to monitor the effect of respiration, and also the electrocardiogram (ECG) for monitorization of the heart rate and possible arrhythmia screening. The recommended duration of the studies should be at least 6 hours, with a minimum of 180 minutes of sleep.

Recently, the American Academy of Sleep Medicine (AASM) has published a revision of the standards that should guide the recording of Neurophysiology parameters, with the currently recommended leads being: F4-M1, C4-M1 and O2-M1 (Figure 2), while for EOG recording, eye movements are recorded by placing two electrodes, one cm above the external angle of the right eye and one cm below the external angle of the left eye. To record muscle tone by electromyogram (EMG) it is recommended to place three submental electrodes: one in the midline, 1 cm above the lower edge of the mandible, the second 2 cm below the lower edge of the mandible and 2 cm to the right of the midline, and the third 2 cm below the lower edge of the mandible and 2 cm to the left of the midline.

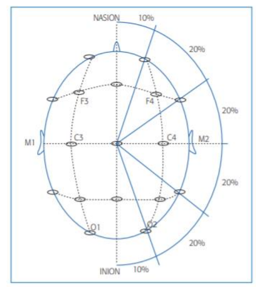

Figure 2 - Recommended leads for the recording of Neurophysiology parameters (American Academy of Sleep Medicine): F4-M1, C4-M1 and O2-M1. [8]

Once these surface electrodes have been placed to record the neurophysiological variables, the respiratory movement curves are obtained. Although the reference procedure for quantifying respiratory effort would be the measurement of esophageal pressure using a catheter, the invasiveness of this technique means that it is not usually used, so other alternative quantitative methods have been developed, such as bands, which can use piezoelectric crystals or be based on inductance plethysmography, which means that the lengthening of the band with respiratory movements generates a change in its electrical behavior, which in turn conditions the shape of the curve recorded. The recording of thoracoabdominal movements is important as it helps to differentiate whether a respiratory event is of obstructive or central origin and, in addition, with the sum of these bands correctly calibrated, the volume of air mobilized can be estimated.

With the patient already lying down, sensors are placed to measure oronasal flow, with the aim of detecting apneas and hypopneas. There are several devices to detect flow, such as thermistors, which have the advantage of being cheap and easy to use, but they only estimate flow qualitatively, by recording the changes in temperature between the air inhaled (cold) and exhaled (warm) through the nostrils and mouth. As they are not able to quantify flow, they cannot reliably identify partial decreases in flow. Other devices measure airflow quantitatively, such as pneumotachographs and nasal pressure probes, which estimate airflow by means of a cannula connected to a pressure transducer. They are now widely used in clinical practice because flow assessment is superior to thermistor measurement, although the results are not good if nasal obstruction is present. On the other hand, arterial oxygen saturation will be measured by percutaneous oximetry, which is based on the color variations experienced by the blood according to the oxyhemoglobin saturation. The oximeter's photoelectric cell, usually placed on the index finger, continuously measures the light absorbance of vascular tissue at two wavelengths.

The most effective medical treatment is the application of positive airway pressure (CPAP), which has few and mild side effects and is generally well tolerated. Once the patient has adapted, the pressure should be adjusted by polysomnography or with autoCPAPs, which are able to vary the pressure until the respiratory events are corrected [8].

Although many different portable PSG devices have been implemented to allow the home monitoring of patients, PSG remains an invasive technique which produces a lot of data, inefficient to analyze through manual processing.

One of the first alternative methods, reported in literature in 2009, attempted to develop a portable system for the automatic detection of OSAS based on snore signals acquisition and spectral analysis [9]. To detect apnea events, the proposed system collects only snoring signals, analyzing and classifying them to discriminate between simple snorers and OSAS patients. In this way, the clinician does not have to examine a full-night acquisition but only the portions of signal characterized by apnea events. The development of a snore based OSAS detector requires a good design of the acquisition stage because the snoring signal can be contaminated by different types of noise, such as background acoustical noise or electromagnetic interference. Although the use of unidirectional microphone can improve signal acquisition, a robust pre-processing stage is required before signal analysis to improve the SNR and allow a more accurate extraction of features [9]. After processing the signal, in the reference paper, the identification of apnea events was performed through frequency analysis of post-apneic snore events. The initial stage of the analysis consisted in a manual separation of the snoring events from the respiratory ones with the help of doctors. Then, a FFT analysis and power spectra evaluation of the selected portions of the original signal was performed. The results show significant differences between the spectra of a generic snore and a post-apneic snore. The differences between the two power spectra suggests a possible method to differentiate snores from post-apnea snores by comparing the number of frequency components above a certain power threshold [9].

In 2012, another approach based on the use of an electronic nose was proposed [10]. Several studies have revealed that OSAS is associated with increased oxidative stress, as well as systemic and local inflammation, as indicated by increased concentrations of pro-inflammatory cytokines and other markers in exhaled breath condensate (EBC). Considering this, the idea of a pattern-recognizing electronic nose capable of distinguishing between OSAS patients and healthy controls followed [10].

A further upgrade involves the development of devices able to detect OSAS in real-time. In 2015, an effective real-time OSAS detection method based on frequency analysis of ECG-derived respiratory (EDR) and heart rate variability (HRV) was proposed [11]. Compared to traditional PSG which requires the measurement of several physiological signals, this method only needs ECG signals to determine the occurrence of an OSA event. In order to be implementable in hardware to achieve the real-time detection and portable application, in the reference study, the simplified Lomb Periodogram was utilized to perform the frequency analysis of EDR and HRV. Before spectra analysis, a removal of noise and artifacts present in the ECG signals is needed. As the Lomb method weights the data on a "per point" basis rather than a "per time interval" basis, it is suitable for the analysis of non-uniform data. The frequency analysis of EDR shows that in normal breathing episodes the dominated respiration frequency is located between 0.15Hz and 0.27Hz, while in sleep apnea episodes the peak in frequency is between 0.01Hz and 0.05Hz [11].

In 2016, a similar detection algorithm was proposed in [12], where particular attention was paid to develop a low-power wearable system. The resulting device showed an extremely low power consumption, with a total lifetime of 252 hours, equivalent to more than 10 days. Furthermore, in [1] the same detection parameters – EDR and HRV – were used into a feed-forward back-propagation artificial neural network (ANN) for a more accurate, automatic detection of OSA events.

In 2017, a further improvement was achieved through a novel approach using the instantaneous heart rate (IHR) as the sole feature [13]. The IHR is a form of HRV, calculated as the reciprocal of each inter-beat interval per minute. IHR measurements of length of around 60 beats were used for training a long short-term memory recurrent neural network (LSTM-RNN) deep learning algorithm. The trained model has been then used for testing IHR data of patients with OSAS and control groups. A step further was taken by testing the robustness of both LSTM-RNN models on a control group with different arrhythmias, which are highly probable in mimicking sleep apnea heart rate variability. IHR values of length of around 60 beats were found to be an extremely robust feature while using LSTM-RNN models.

In 2021, a similar approach was experimented in [14]. In this study, a LSTM convolutional neural network (LSTM-CNN) was used to detect OSA events based on single-lead ECG data. The main advancement of this work concerns the time step used for the analysis of the data. In fact, while most of the methods score OSA events by minute-by-minute analysis, this study aims to reach a 10 seconds-based analysis. The importance of this aspect becomes clear considering that, according to the American Academy of Sleep Medicine (AASM), OSA episodes occur in 10s or more, and therefore, minute-by-minute analysis will lose some OSA events [14]. The results showed that the proposed approach was robust and completely automated, with a total accuracy of 96.1%. The main limitation concerns the classification of transition epochs between a normal and an abnormal event, which can lead to a misclassification of the event due to the lack of contextual information.

Besides the use of features extracted by ECG, another efficient way to detect OSA events is the use of nasal airflow signals recorded by a nasal cannula. In [15], the ability of CNNs to detect obstructive apnea and normal events was tested. Two different types of signals were used: PSG raw nasal airflow signal and nasal wavelet spectrogram. In particular, continuous wavelet transformation (CWT) spectrograms are very useful in showing changes of events that occur at different frequencies. In this case, the input was the spectrograms calculated by using CWT with the analytical Morlet wavelet. Morlet wavelet has good time localization properties which makes it well suited for detecting the transient properties of a signal, overcoming the limitation related to [14].

Even though the above mentioned OSA detection methods are much simpler than traditional PSG technique, they still need to use invasive instruments (electrodes for ECG, cannula for nasal airflow signal) for signal collection. An innovative approach, based on a non-contact intelligent sleep monitoring system, which uses pressure sensors to capture the pressure signals of breathing and heartbeat during sleep was proposed in 2019 [16]. Piezoelectric ceramics sensors are used to capture pressure changes in the chest and abdomen of the human body. Then, heart rate and respiratory rate are extracted from impulse waveforms and respiratory waveforms that are converted by filtering and processing of the pressure signals. Finally, the HRV is obtained by processing the obtained heartbeat signals. At this point, the classification procedure is similar to the ones above explained.

4. APPROACH AND UNIQUENESS

4.1 Material

For this study, we will be using a whole night recording, around 8 hours, of raw polysomnography data saved in EDF format in which it is observed the EEG, Thorax and Abdominal effort belt, airflow, ECG, EOG and Oxygen Saturation (SAO2). The airflow that uses the oronasal thermal airflow sensor in order to be able to score apneas, the nasal pressure transducer to score hypopneas during diagnostic study and the PAP device flow signal to score both apneas and hypopneas in PAP titration study.

Furthermore, it was provided files in txt (plain text) and xml (extensible markup language) format in order to help us identify and visualize the events and the time they occurred since the txt and xml files contained manual or automatic apnea and hypopnea events time tags.

4.2 Methods

4.2.1 Preparation of the signal for the posterior analyses

To initiate our project, we started by reading the files given by the faculty using the *edfread* function in order to be able to read the signals inside the 3 files with the edf format (cvj.edf, ffsg01.edf and vsc01.edf). This function returns the annotations present in the data records in which we only chosen some of the signals inside the header to evaluate, such as the "AIR_FLOWBaAirF", "THORAXBbFaixaT", "ABDOMBcFaixaAB", "SAO2" and the "ECGAaECG1".

To be able to open the files in xml (.spj) format, we use the function xml2struct that converts xml files into a MATLAB struct.

After having all files opened, we extracted the time interval, for each, in which we characterized the starting time as being the time after the light went OFF and therefore, the finishing time, the time when the lights went ON, and also the apnea and hypopnea events.

4.2.1.1 Pre-Processing

Still within this part of the preparation of the signal for posterior analyses, it was created a processing function, that receive the signal to analyze and used a *butter* filter, in which this returns the transfer function coefficients of an 6th-order lowpass digital Butterworth filter with normalized cutoff frequency equal to 2 divided by half the sampling frequency and then it is applied the filter function that filter the input data, that in this case, is the crop of the signal in order to have only the time periods that matter, which means that it is taken from the analyses the beginning and ending of the signal acquisition, using a rational transfer function defined by the numerator and denominator coefficients given with the butter filter.

4.2.2 Identify apneas/hypopneas

The main goal of this project fell on the detection of apneas and hypopneas in which we could have chosen several ways to perform this task, however, we focused on the rules given initially, where the main way to detect these events (apneas and hypopneas) is to use the initial detection of the signal peaks and perform a baseline in order to evaluate the peaks that are below that baseline, in which to be considered apnea, the peak must be 90% below that baseline and to be classified as hypopnea it would have to be located only at 30% below. In the case of classifying a peak interval as an apnea, it would also be classified as a hypopnea due to the rules, however, the classification as hypopnea is excluded, remaining only classified as apnea.

4.2.2.1 Rules for scoring Apneas and Hypopneas

To be able to classify as apnea or hypopnea and to be able to specify these as being central, obstructive, or mixed, we use certain rules such as:

- Classify as apnea when there is a fall in peak airflow excursion by $\geq$ 90% of baseline and when the duration of the event lasts at least 10 seconds;
- Classify as hypopnea when there is a fall in peak airflow excursion by $\geq$ 30% of baseline, when the duration of the event lasts at least 10 seconds and when there is a desaturation of $\geq$ 4%.

It should be noted that the baseline value given for the drop from baseline for both apnea ($\geq$ 90%) and hypopnea ($\geq$ 30%) is a completely arbitrary value, since for apnea we only want to give a value that corresponds to the absent or almost absent airflow and for hypopnea a value that corresponds to a reduction rather than the absent of the airflow. However, due to the interpolation used and with the windowing of the peak excursion, we reduced it to a minimum of 8 seconds as a compensation for these methods.

Furthermore, the classification of apnea as obstructive, mixed, or central is predicated upon respiratory effort, obtained from the "THORAXBbFaixaT", "ABDOMBcFaixaAB" signals.

4.2.3 Relationship with SAO2 and Heart rate from ECG signals

There are multiple studies that correlate these types of events (apnea and hypopnea) with an increase in heart rate and a decrease in the SAO2. These will limit the irrigation and threaten the health of the body cells [17].

5. RESULTS

It was performed an analysis with this 3 files:

- vcs01.edf – 557 events (txt, xml and spj);
- cvj.edf – 97 events (txt, xml and spj) ;
- ffsg01.edf – 100 events (txt, xml and spj)

Firstly, as addressed before, it was calculated the peaks from the airflow from the files taking into account the baseline created. With this it was classified some events as being apneas and hypopneas, as can be seen from Figure 3 and 4, respectively.

After the respiratory event duration was detected and classified as apneas or hypopnea, a frequency analyses to detect respiration movement on both the "ABDOMBcFaixaAB" and "THORAXBbFaixaT" signals was performed obtaining the sub-classifications ("Obstructive", "Mixed" and "Central").

Related to the results obtained in Table 1, the results are so low, thus we can conclude that our analyses were poor. This can be explained by three distinct reasons:

- Most of the apneas were identified as hypopneas resulting in a big number of false positives.
- Since our data on the real respiratory events was performed by busy clinicians, it is to be expected some inaccuracy on these.
- Fast dynamic change of the amplitude of the sensor data was not correlated with its measure and our analyses did not perform well with these variations.

For the calculation of both precision and sensibility, observed in Table 1, the following equations were performed:

Precision = TP / (TP + FP),

Sensibility = TP / (TP+FN),

in which the TP, FP, FN correspond respectively to true positive, false positive and false negative.

Table 1 - Overview of results.

	True Positive	False. Positive	False Negative	Precision	Sensibility
cvj Hypopneas	27	57	115	0.3214	0.1901
cvj Apneas	0	0	12	NaN	0
ffsg01Hypopneas	44	104	158	0.2973	0.2178
ffsg01 Apneas	0	2	30	0	0
vcs01 Hypopneas	101	344	435	0.2270	0.1884
vcs01 Apneas	1	2	364	0.3333	0.0027

6. DISCUSSIONS AND CONCLUSIONS

In this project it was found a lot of limitations, mostly due to the fast dynamic changes in amplitude related to position variations, instrumentation issues or other causes.

We also can add that the rules given to classify both apneas and hypopneas are ambiguous and could be better defined.

It is noted that this acquisition method with the sensors jeopardizes the signal obtained for analyses, so for future work it is recommended an improvement on the data acquisition and/or sensor quality/performance, so many steps forward are still needed.

With this, we can conclude that our work did not achieve satisfactory results but made it possible to visualize and correctly classify some events.

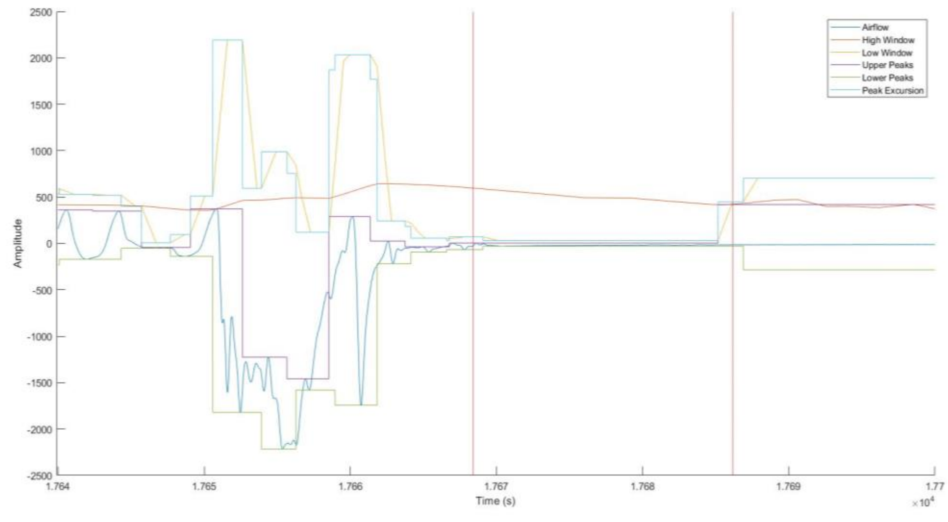

Figure 3 - Visualization of an Apnea.

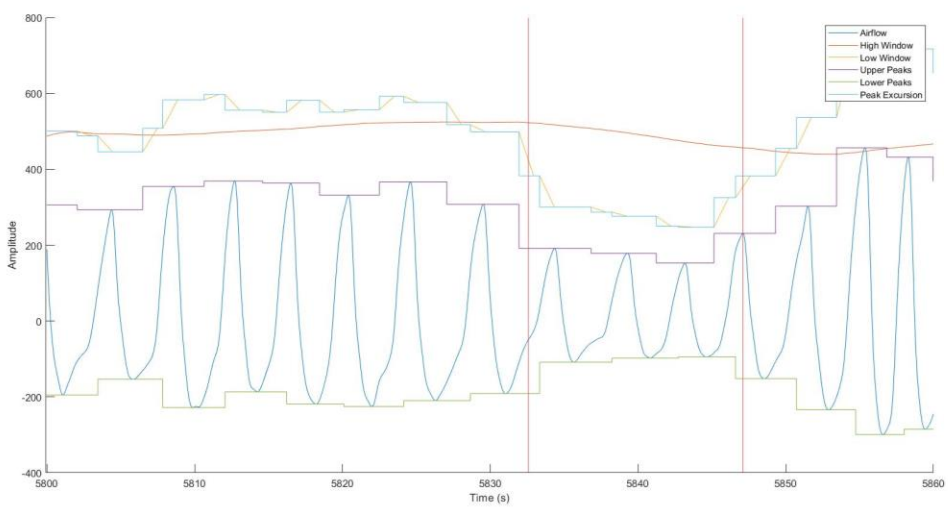

Figure 4 - Visualization of a Hypopnea.

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CV: I am a very dedicated, proactive, fast learner and ambitious person. The interest in Neuropsychiatric has been growing since I started my final project " Pesquisa de Biomarcadores em Esquizofrenia com dados de Ressonância Magnética Funcional", which made me like and invest more in a future related to the area of research.

As a footnote, it should be noted that I really enjoy participating in voluntary work in food distribution and collection for homeless people.

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Computer skills: MS Office (Word, PowerPoint, Excel, Outlook), MATLAB, SPM12, Simulink, CATIA V5C, Python, HTML, Arduino, MySQL.

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CV

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2019 - Bachelor in Biomedical Engineering in Politecnico di Milano, vote: 98/110

Currently, I am at the end of my Erasmus+ experience at Instituto Superior Técnico for my last semester of Master Degree.

In September 2021, I will start my thesis for the Master Degree in Biomedical Engineering, with specialization in Biomaterials & Biomechanics.

In 2020, I have been working for a few months in a fluidodynamic laboratory to test the performance of an aortic valve prosthesis.

Language skills: Italian as native, B2 English level

Digital skills: Office Package, SolidWorks, MATLAB

Besides my educational background, I carry on all the challenges that I undertake with motivation and passion, in work as well as in life in general. I learn fastly and I enjoy working in a team as I think it is more efficient to collaborate with other people having diverse skills and mindsets.

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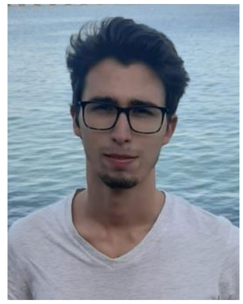

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CV: French scientific baccalaureate in IES Juan de Mairena, Madrid and long-term linguistic inmersion (ERASMUS +) in Sainte Thérèse high school, in Quimper, France.

I am currently in my last year of biomedical engineering degree in the Technical University of Madrid (UPM).

Itinerary in Bioinstrumentation, Biomaterials and Biomechanics: Medical Devices, Biomaterials and Biomechanics

Electrical Engineering Students' European association (EESTEC) organization member: team coordinator in workshops of different topics such as Big data and virtual reality.

Participant in technological workshops and Congresses in different countries like Turkey, Poland or Portugal.

International association for the exchange of students for technical experience (IAESTE) member.

Digital skills: Intermediate Java programming knowledge, MATLAB, Arduino, C/C++, Labview and user knowledge of Microsoft Office Software.

Next year I will do my internship at the Ramon y Cajal hospital in Madrid, working on different surgical applications of 3D printing in traumatology.

I also plan to pursue a master's degree in neuroscience. which is the area I am most interested in at the moment.