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University of Applied Sciences

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BACHELOR THESIS

Analysis of the three-dimensional segmented Poincaré plot for complex coupling analyses of the autonomic regulation

Aran Garcia Vidal

Matrikel nº 643342

Biomedical Engineering Degree

Supervisor: Prof. Dr. Andreas Voß

Mentor: Prof. Claudia Fischer

Tutor: Prof. Dr. Beatriz F. Giraldo

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Abstract

Pregnancy is still one of the most delicate stages in a woman's life, especially in the third world countries. In this project, we propose to characterize and analyse the respiratory and cardiovascular systems using the Poincaré plot. 112 pregnant women that suffered different pregnancy illnesses and 10 Non-pregnant women were analysed.

In this project we implement a new algorithm to an already established method of analysis, the 3 dimension Segmented Poincaré Plot Analysis (3DSPPA).

RR, SYS, DIA and T_{RESP} time series were extracted from the ECG, blood pressure and respiratory flow signals, respectively.

Parameters that describe the importance of the concentrations of the scatterplot of the Poincaré method along their relative positions, related to a series of levels described by the user, were extracted. An analysis of those extracted parameters lead to our results.

These results show a difference between the studied parameters from every health condition analysed leading us to be able to discern between them with our algorithm.

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1. INTRODUCTION

1.1. Motivation

I was personally motivated to do this project since it was my Bachelor thesis and my intention was to take the maximum profit from it. Learn how to work in a research cluster, understand the methodology of the actual method, meet senior researchers and with the opportunity to do it abroad.

I have to say that the part of the project that has been writing down this document has been by far the most difficult of them but with the help provided, mostly by Prof. Dr. Giraldo, we have achieved a document which has no similarity with the first version that I presented.

With this project we intend to the prediction of pathologies in pregnant women while using a post processing signal method which adds something unique to the already established analysis method.

We have achieved the main objective of this project but unfortunately not all the secondary objectives.

1.2. Problem Statement

Given a dataset consisting in 112 pregnant women who suffered different pregnancy associated illnesses and using a 10 healthy Non-pregnant women as a group control where we have acquired for 30 minutes the electrocardiogram, blood pressure and respiration signals, it is possible to be able to discern between health conditions using the method known as 3DSPPA?

In order to do so, we propose a new algorithm that analyses the concentration of the samples alongside the distribution of themselves once they have been analysed with the 3DSPPA.

1.3. Objectives

Main objective

To analyse a dataset with the method of the three-dimensional segmented Poincaré plot for complex coupling analyses of the autonomic regulation

Specific objectives

1. To investigate the possibility of differentiating between health conditions using a method
2. To implement an algorithm into the already existing program which performs the 3DSPPA
3. To develop a graphical user's interface (GUI) able to represent the method

1.4.   Significance of the study

The findings of this study will redound to the benefit of society since every day new tools are designed to work with data and more people is studying ways to analyse high amounts of data, the so called *big data* field area. Thus, we are coding an algorithm that we found no prove someone had used before. Therefore, the results of this project can be discussed and the programs used in the future, if somebody finds them appropriate for his/her own interest.

2. PHYSIOLOGICAL BACKGROUND

2.1.   Electrocardiogram

The electrocardiogram is a method of graphic tracing (ECG or EKG) of the electric current generated by the heart muscle during a heartbeat. The tracing is recorded with an electrocardiograph, and it provides information on the condition and performance of the heart. The first electrocardiograph was developed in 1903 and during the late 1960s, computerized electrocardiography came into use in many of the larger hospitals .

Electrocardiograms are made by applying electrodes to various parts of the body. Electrodes that record the electrical activity of the heart are placed at 10 different locations. After the electrodes are in place, a millivolt from a source outside the body is introduced so that the instrument can be calibrated. Standardizing electrocardiograms makes it possible to compare them as taken from person to person and from time to time from the same person.

The normal electrocardiogram, shown in Figure 2.1, shows typical upward and downward deflections that reflect the alternate contraction of the atria (the two upper chambers) and of the ventricles (the two lower chambers) of the heart. The first upward deflection, P, is due to atrial contraction and is known as the atrial complex. The other deflections—Q, R, S, and T—are all due to the action of the ventricles and are known as the ventricular complexes. Any deviation from the norm in a particular electrocardiogram is indicative of a possible heart disorder (Britannica, Encyclopaedia Britannica, 2018).
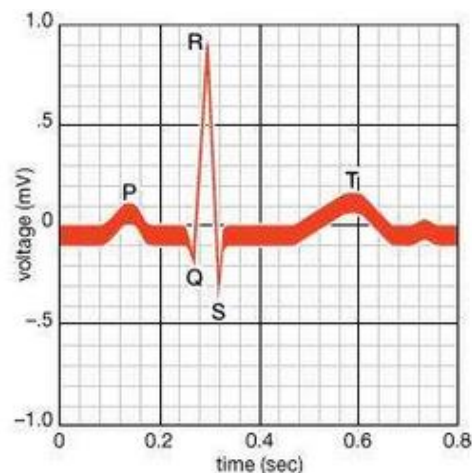

Figure 2.1: Electrocardiogram showing the deflections that reflect the alternate contractions of the atria and the ventricles of the heart during one heartbeat

2.2.   Blood pressure

The blood pressure is defined by the pressure exerted by the blood upon the walls of the blood vessels and especially arteries, usually measured on the radial artery by means of a sphygmomanometer, and expressed in millimetres of mercury. It depends on the strength with which the heart contracts, the elasticity of the arterial walls, the capillary resistance, the return venous tension and the blood volume and viscosity. The blood flow rate is directly proportional to blood pressure, so the higher the pressure, the higher the flow rate (Bermejo, 2018).

In humans, blood pressure is usually measured indirectly with a special cuff over the brachial artery (in the arm) or the femoral artery (in the leg). There are two pressures measured, as shown in Figure 2.2: the systolic pressure (the higher pressure), which is the force that blood exerts on the artery walls as the heart contracts to pump the blood to the peripheral organs and tissues, and the diastolic pressure (the lower pressure), which is residual pressure exerted on the arteries as the heart relaxes between beats.

In healthy individuals, systolic pressure is normally between 100 and 140 millimetres of mercury (mmHG). Diastolic pressure is normally between 60 and 100 mmHg (Britannica, Encyclopaedia Britannica, 2018).
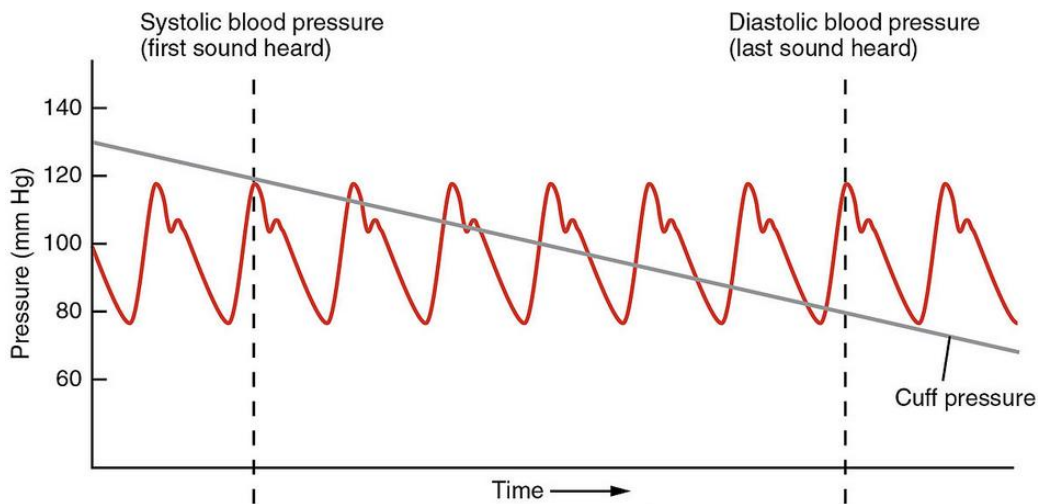

Figure 2.2: Graphic of a blood pressure signal where we can see the systolic and diastolic blood pressures

2.3.   Respiration signal

Phenomenon of gaseous exchange between a living organism and its environment, through which it takes oxygen (O_2) and releases carbon dioxide (CO_2) and water. Humans do this process by doing the pulmonary ventilation, which is the process of moving air into and out of the lungs to facilitate gas exchange. The respiratory system uses both a negative pressure system and the contraction of muscles to achieve pulmonary ventilation. The negative pressure system of the respiratory system involves the establishment of a negative pressure gradient between the alveoli and the external atmosphere. As the lungs fill with air, the pressure within the lungs rises until it matches the atmospheric pressure. At this point, more air can be inhaled by the contraction of the diaphragm and the external intercostal muscles, increasing the volume of the thorax and reducing the pressure of the lungs below that of the atmosphere again.

To exhale air, the diaphragm and external intercostal muscles relax while the internal intercostal muscles contract to reduce the volume of the thorax and increase the pressure within the thoracic cavity. The pressure gradient is now reversed, resulting in the exhalation of air until the pressures inside the lungs and outside of the body are equal. At this point, the elastic nature of the lungs causes them to recoil back to their resting volume, restoring the negative pressure gradient present during inhalation. In medicine, this pressure is acquired giving the information of the respiratory signal and all the parameters associated can be extracted to give the physician personnel information about the health of the respiratory system of the subject.

An adult in quiet breathing mobilizes 6-7 liters of air every minute, and his respiratory rate is 12 to 18 per minute, with the average or expired amount of air in each cycle of about 500 ml.

2.4.   Pregnancy

The state of carrying a developing embryo or fetus within the female body. This condition can be indicated by positive results on an over-the-counter urine test, and confirmed through a blood test, ultrasound, detection of fetal heartbeat, or an X-ray. Pregnancy lasts for about nine months, measured from the date of the woman's last menstrual period (LMP). It is conventionally divided into three trimesters, each roughly three months long (MedicineNet, 2018).

2.5.   Pre-eclampsia

Preeclampsia is a pathology characterized by edema, proteinuria and arterial hypertension that always occurs after the twenty-fourth week of pregnancy. The edemas are usually located on the face, hands, ankles and feet, and usually lead to an increase in weight of about two kilos a week. Proteinuria is the presence of proteins in urine obtained by probing. The cause of preeclampsia is not very clear. It seems that it could be due to ischemia (lack of blood supply) of the uterus and the placenta, which would lead to the release of some substances with hypertensive and diuretic effect (Fontaneda, 2018), (Redman & Sargen, 2005), (Robeera, et al., 1989).

2.6.   Pregnancy-Induced Hypertension

Gestational hypertension or pregnancy-induced hypertension (PIH) is the development of new hypertension in a pregnant woman after 20 weeks gestation without the presence of protein in the urine or other signs of pre-eclampsia. Hypertension is defined as having a blood pressure greater than 140/90 mm Hg. Gestational hypertension is one of the most common disorders seen in human pregnancies. Though relatively benign on its own, in roughly half of the cases of gestational hypertension the disorder progresses into pre-eclampsia, a dangerous condition that can prove fatal to expectant mothers.

The underlying cause of gestational hypertension in humans is commonly believed to be an improperly implanted placenta. Humans have evolved to have a very invasive placenta to facilitate better oxygen transfer from the mother to the fetus, to support the growth of its large brain.

2.7.   Chronic hypertension

Chronic hypertension is high blood pressure that was present before the woman become pregnant or that occurs in the first half, before 20 weeks, of her pregnancy.

High blood pressure (HBP) is a long-term medical condition in which the blood pressure in the arteries is persistently elevated. High blood pressure usually does not cause symptoms. Long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease, vision loss, chronic kidney disease, and dementia (Mabie, Pernoll, & Biswas, 1986), (Seely & Ecker, 2011).

3. POINCARÉ PLOT ANALYISIS

3.1.   Henri Poincaré

Jules Henri Poincaré, 1854 – 1912, was a French mathematician, theoretical physicist, engineer, and philosopher of science, Figure 3.1.

As a mathematician and physicist, he made many original fundamental contributions to pure and applied mathematics, mathematical physics, and celestial mechanics. He was responsible for formulating the Poincaré conjecture, which was one of the most famous unsolved problems in mathematics until it was solved in 2002–2003 by Grigori Perelman.

In his research on the three-body problem, Poincaré became the first person to discover a chaotic deterministic system which laid the foundations of modern chaos theory.

He is also considered to be one of the founders of the field of topology.

Figure 3.1: Henri Poincaré

3.2.   Poincaré Plot Analysis

Traditional Poincaré plot analysis (PPA) represents a two-dimensional graphical and quantitative representation of a time series dynamics (Golińska, 2013).

Two-dimensional pseudo-phase space plots represent univariate system behaviour investigating signal values as a function of their previous ones whereas phase space plots represent multivariate system behaviour investigating interactions of at least two different signals. The method known as Poincaré plot is a species of recurrence plot used to quantify self-similarity in processes, usually periodic functions. It also receives the name of 'return map'. This method plots a time series as a function of the current and the previous values (Che-Hao, et al., 2012).

Given a time series of the form

$$x_t + x_{t+1} + x_{t+2} +, \dots,$$

A Poincaré map in its simples form follows the following equations:

$$f(x_t) = x_{t-1} \; for \; t = 2 \dots t$$

Once the data has been plotted, an ellipse can be drawn into the plot along the line of identity whereas the centre represents the mean value of the time series and the axes are the respective standard deviations, SD_1 and SD_2.

In Figure 3.2, we can see an example of a 2DPPA where *RR* axis are defined by the beat-to-beat interval, the time elapsed between a heartbeat and the following one.
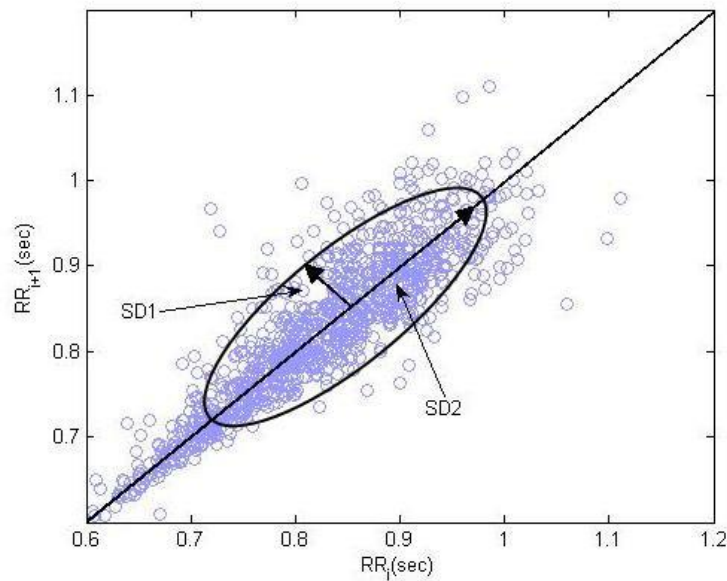

Figure 3.2: Example of a 2DPPA where we can see the standard deviations of the data and the ellipse that they define.

It has been proved that variations of SD1 and SD2 values are related to variations in the heart rate frequency.

3.3.   Segmented Poincaré Plot Analysis

The SPPA retains nonlinear features from a system based on PPA, representing an enhanced pseudo-phase space quantification method. The Poincaré plots are two-dimensional graphical representations (as a cloud of points) of a time series plotted against its subsequent one. The calculation of PPA standard indices provides the basis for SPPA.

The SPPA method functions as follows:

1. The linear indices of SD1 and SD2 are calculated according to traditional PPA
2. The cloud of points presented by PPA is then rotated α = 45° around the main focus of the plot
3. Starting from the centre of the cloud of points, a grid of 12 ×12 rectangles is drawn into the plot. The size of each rectangle is adapted to SD1 (height) and SD2 (width).
4. The number of points within each rectangle related to the total number of points is counted to obtain the single probabilities.

Once this has been done we can proceed to analyse the results (Karmakar, Brennan, Voss, & Palaniswami, 2018).

3.4.   3-dimension Segmented Poincaré Plot Analysis

Once the 2DSPPA was established as an analysis method, the researchers thought that could be interesting to add a new dimension to the plot, add a new variable. With this idea in mind, they created a program which applies this method to a dataset introduced by the user.

As we have 3 dimensions, the equations that describe the 3DSPPAdiffer a little bit from the equations that describe the 2DSPPA. For the 2DSPPA we had $f(x_t) = x_{t-1}\ for\ t = 2 \ldots t$. Now, for the 3DSPPA the formula is

$$f(x_t) = (x_{t-1}, x_{t-2})\ for\ t = 3 \ldots t$$

If instead of a single variable, our goal is to plot different variables in our axis, then the formula changes to

$$f(x_t) = (y_t, z_t)\ for\ t = 1 \ldots t$$

Once the dataset has been scattered in a 3D matrix, the same idea to divide it within 12x12x12 cubes described previously based on SD_1, SD_2 and SD_3 is applied to the matrix and afterwards, the concentration of points per cube is calculated.

4. MATERIALS AND METHODS

4.1. Dataset

In this project, we collected data from 112 women from the University Hospital Leipzig which had different conditions in their pregnancy period. The classification was made based on the clinical diagnosis provided by the medic personal that was taking care of them in this period. Sixty-six of them had a normal pregnancy (PREG), 13 suffered from chronical hypertension (CH), 19 developed a pre-eclampsia (PE), and 14 suffered from pregnancy-induced hypertension (PIH).

As a control group, 10 non-pregnant (NoPREG) women from the Department of Medical Engineering and Biotechnology, University of Applied Sciences Jena were investigated.

In Table 4.1 we can see a summary of the patients

Health condition	Number of subjects
Non-pregnant – NoPREG	10
Pregnant – PREG	66
Pre-eclampsia – PE	19
Pregnancy-induced hypertension – PIH	14
Chronical hypertension – CH	13

Table 4.1: Summary of the patients

From all 122 subjects of the study, 30 minutes of ECG, respiration (T_{RESP}), non-invasive systolic (SYS), and diastolic (DIA) blood pressure were continuously recorded and analysed.

For more information on how the data was taken see (Fischer & Voss, 2014)

After the acquisition, this dataset was processed using the 3DSPPA method described previously. This analysis generates a 3D matrix which represents the interactions between the coupling of the 3 elected signals. Afterwards, this construction is represented with 1728 cubes that form a 12x12x12 matrix. Finally, the concentration of points inside every cubes is calculated, which produces as a result a row of cells, each one corresponding to a different cube in the matrix (Fischer & Voss, 2014).

This row of 1728 cells is the input information of our algorithm.

4.2.   Implemented method

We are not the first ones approaching medical data using the 3DSPPA, but in this section we propose a method developed with the objective to see if our algorithm could reach conclusions faster and using less data or extract more information of the same amount of data.

We have worked with the dataset described previously processed by a program which gives us the 3DSPPA of the dataset.

Our intention was to find a classification method that was able to discern between the different health conditions. In order to do so we analysed if the concentration of the points could give us more information and we coded the following algorithm with this objective.

This algorithm is divided in two different programs which are later described.

1. Being given a row of 1728, one per each cube, containing the concentration of points inside each cube, the program calculates the mean distribution of points per cube

$$Mn_{ppc} = {100}/{N_c}$$

where N_c is the number of cubes whose concentration is greater than zero.

2. In the interest of establishing different levels based on the concentration of points per cube, the program asks the user to introduce a number of thresholds that will define those levels as

$$Level\ 1 >\ th_1 \cdot Mn_{ppc}$$
$$th_1 \cdot Mn_{ppc} \geq Level\ 2 >\ th_2 \cdot Mn_{ppc}$$
$$th_2 \cdot Mn_{ppc} \geq Level\ 3 >\ th_3 \cdot Mn_{ppc}$$
$$th_3 \cdot Mn_{ppc} \geq Level\ 4 >\ th_4 \cdot Mn_{ppc}$$
$$th_4 \cdot Mn_{ppc} \geq Level\ 5 >\ th_5 \cdot Mn_{ppc}$$
$$th_5 \cdot Mn_{ppc} \geq Level\ 6 >\ th_6 \cdot Mn_{ppc}$$

The program is coded to work with a minimum of three thresholds and a maximum of six.

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In favour of distinguishing better between levels, the graphic representation includes colouring each level with a different colour.

In this project, the results are presented with the following thresholds

$$th_1 = 20$$
$$th_2 = 15$$
$$th_3 = 10$$
$$th_4 = 5$$
$$th_5 = 3$$
$$th_6 = 2$$

From this first step of the total algorithm, we obtain a file formed by the cubes that belong to the defined levels. From this cubes, we know the patient they belong to, their position/coordinate, their concentration of points and the threshold that defines their level.

At this point we calculated, for each health condition, the mean distribution per cube for all its patients obtaining five files, one per condition, in other words, we calculated the mean concentration of points for every cell thus obtaining a global file from all the patients with the same health condition. Once this was done, we applied to this files the program coded so far and obtained a file containing the list of cubes separated by levels – Annex 8.3 – of the mean distribution from all the patients sharing the same health condition.

In Table 4.2 we can observe an example with 5 patients having the same health condition.

Being

$$S_{g,c} = \frac{1}{t} \sum_{r=1}^{t} x_{r,c}$$

per g = *Global*, c = 1… 1728 and t equal to the number of subjects in the group where N represents only the cubes that had a greater concentration of points than zero.

For the second part is necessary to define In the second program, it asks the user which level he/she would be interested in asking as a needed input the threshold that defines that level. Once the level of interest is defined, the user has to introduce also the file obtained previously of the health condition he is interested in.

	Cube 1	Cube 2	…	Cube 1727	Cube 1728	Mean
Patient1	$x_{1,1}$	$x_{1,2}$	…	$x_{1,1727}$	$x_{1,1728}$	$\sum_{i=1}^{1728} x_{1,i} \big/ N_1$
Patient2	$x_{2,1}$	$x_{2,2}$	…	$x_{2,1727}$	$x_{2,1728}$	$\sum_{i=1}^{1728} x_{2,i} \big/ N_2$
Patient3	$x_{3,1}$	$x_{3,2}$	…	$x_{3,1727}$	$x_{3,1728}$	$\sum_{i=1}^{1728} x_{3,i} \big/ N_3$
Patient4	$x_{4,1}$	$x_{4,2}$	…	$x_{4,1727}$	$x_{4,1728}$	$\sum_{i=1}^{1728} x_{4,i} \big/ N_4$
Patient5	$x_{5,1}$	$x_{5,2}$	…	$x_{5,1727}$	$x_{5,1728}$	$\sum_{i=1}^{1728} x_{5,i} \big/ N_5$
Global	$S_{g,1}$	$S_{g,2}$	…	$S_{g,1727}$	$S_{g,1728}$	$\sum_{i=1}^{1728} x_{g,i} \big/ N_g$

Table 4.2: Example of obtaining the global interactions between signals

The last piece of information needed for the program to work are the results obtained in the first part of the program from all the patients having the same health condition of interest – the first part of the program is prepared to give such file –.

Once the program has the level of interest (*LOI*) defined by the inputted threshold, the results from the global distribution file (*GD*) and the results from the patients of the health condition of interest (*MCOI*), it will search in *GD's* file the position of the cubes that belong to *LOI*. After that, it will search in *MCOI's* file the values of those cubes, store them and give them as an output.

In Figure 4.1 we can see a basic representation of the algorithm:

In the output's file we can see that it will have three fix columns, *Filename*, *Idgroup* and *Idsignal* which intention is to give the user enough amount of information to discern between every possible combination of parameters. The others columns will vary for each *LOI (level of interest)*.

In Table 4.3 we can see an example of the output file. In this example, *LOI* = 20. This means that the program searched in *GD* the position of the cubes that belonged to level 1, or what is the same, had a greater concentration of points 20 times the mean distribution of *GD*. Once the cubes were located in *GD*, the program searched for the properties of the cubes that were in the same position in *MCOI*, and, as we can see, none of the cubes that belonged to level 1 in *GD* belonged to that same level in *MCOI*.
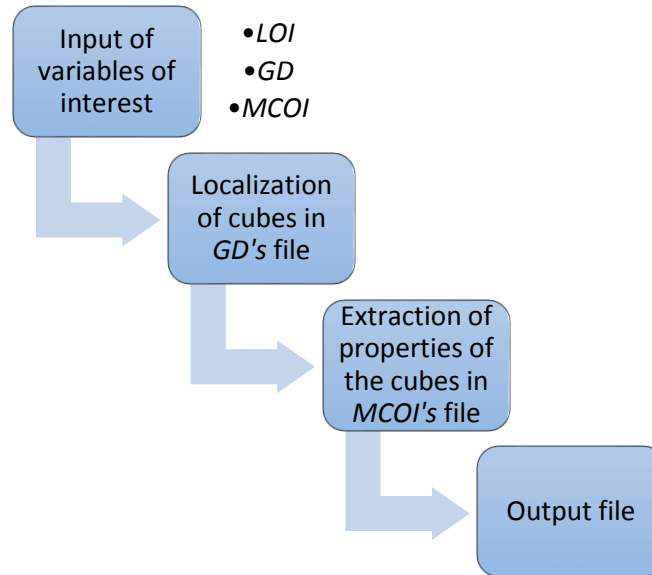
Figure 4.1: Basic representation of the algorithm

In the *GD* file, the cube that was originally in the position 786, belonged to level 1. In the *MCOI's* file the patient *AF6060670* had, in the position 786 a value of 9'56911. This value places it in *AF606070* file's level 2.

Filename	Idgroup	Idsignal	786	TH	787	TH
AF6060670_preg_RR_SYS_DIA	4	RR_SYS_DIA	9,56911	15	10,74426	15
AG2261280_preg_RR_SYS_DIA	4	RR_SYS_DIA	7,02098	10	7,55245	10
AK3100781_preg_RR_SYS_DIA	4	RR_SYS_DIA	2,80034	3	2,80034	3
AK4270474_preg_RR_SYS_DIA	4	RR_SYS_DIA	3,74616	5	3,49455	5

Table 4.3:Filename; Idgroup = 1…5; Idsignal = RR_SYS_DIA, RR_SYS_RESP, RRDIA_RESP, SS_DIA_RESP; Cell number 1 and its threshold associated; Cell number 2 and its threshold associated

It is important to remark that

- It is important to see the difference between *GD* file and *MCOI's* file.
- The same thresholds have been used to define the levels in both files.
- The mean concentration is different in every cube for every patient and at the same time, different from the cubes in *GD.*

4.3. Application developed

The entire app has been coded using MATLAB. © 1994-2018 The MathWorks, Inc

The first program we have coded gives the user two files as a results. One of them is a 3 dimension plot which is a representation of one patient's data. In this 3D plot, the user will

be able to see the cubes marked in different colours depending on the variables introduced by him/her previously in the program. The second file, is the input used in the second program I have coded. The second script gives the user the information of a selected range of concentrations previously defined by himself/herself.

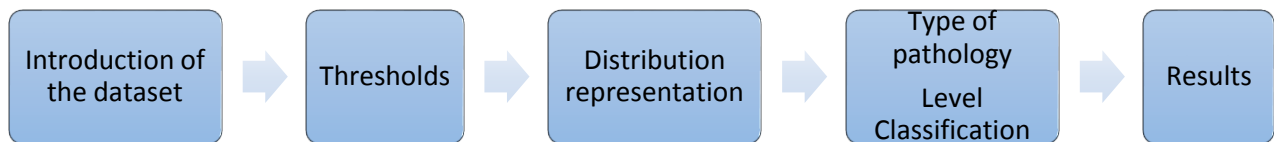In Figure 4.2 you can see how the 2-steps program works essentially.

Figure 4.2: Algorithm of the 2-steps program

Part 1

The first part includes a Graphical User's Interface – GUI – (Fig. 4.3), which is, by definition, the means in which a person controls a software application or hardware device that includes graphical elements, such as windows, icons and buttons (Christensson, 2018).

The GUI is composed by the next sections:

1. Load Data button

The first thing that every user of a science UI has to do is to load his/her data to the program. Once this button has been presses, the program will ask from which file it should load the preferred data. It will also ask the row numbers of the first and last patient that limit the group that wants to be loaded into the program.

2. Single Patient Area

In this area, the user will be asked to introduce the variables, such as the thresholds defining the levels. Once the variables are introduced, he/she will need to press the *Load Patient* button to see the results in the graphic area.

3. Batch mode

In this zone, the user will be able to get and save the results from various subject without the need to input them. Essentially, the program will load the information from the first subject introduced, will compute the results and the graphic associated to this user and will jump to the next subject until the last one.

The advantage of this mode is that the user will have only one file with the results from all the subjects analysed with this method. Otherwise, he/she would have a file for every patient analysed using the *Single patient area.*

Nevertheless, the program will give a graphic for every patient, thus the user will be able to check the information from a subject with the graphic associated to that subject.

The program will also ask the user where he/she would like to save both output files automatically.

4. Graphic area

This is the place where the graphic will appear once the user has pressed the *Load Patient* button with all the information needed provided.

5. Define the labels

In this section, the user will be able to define the label associated to every axis. As stated previously, we have used mostly the combination of *RR-SYS-DIA*. Thereby this combination is the showed by defect.

6. Save Data button

If the user press this button, he/she will be able to save the results from the patient which is currently displayed in the graphic area.

7. View options

This sections serves to change the view of the graphic. MATLAB already gives us the option to manually rotate the graphic but if the user wants to have different graphics alienated the within the same direction he/she will need to fill this section.

By defect, *Azimuth* = 45º and *Elevation* = 45º.

Part 2

The second program that our algorithm needs the global file's output from the first part as an input. It also needs the threshold that will define the *LOI* and a subject file's output as input.

Once the user has given the program all the necessary inputs for it to calculate the analysis it has been designed for, the last part that the user has to do is to tell the program in which directory he/she would like to save the results of the algorithm.
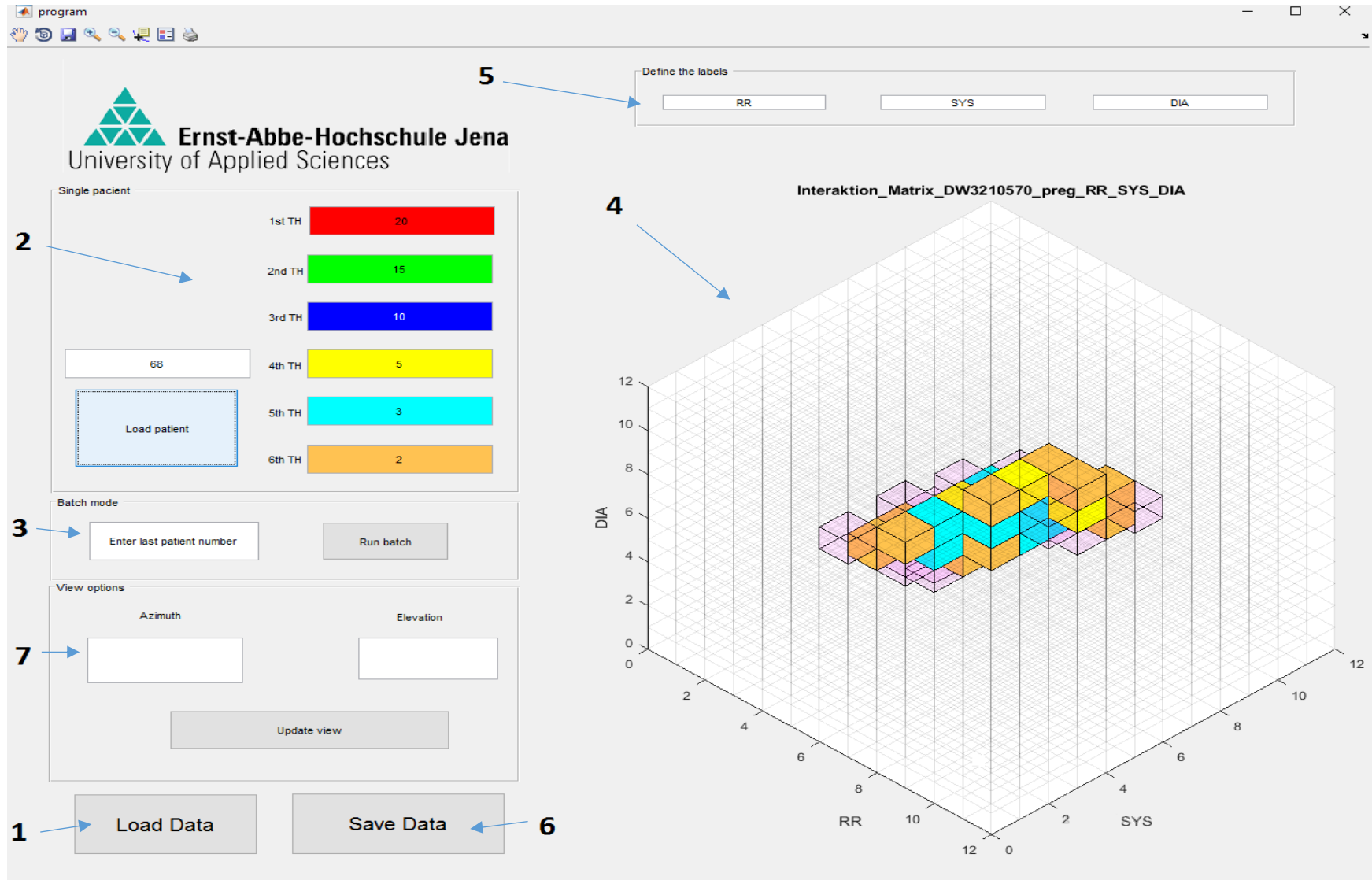
Figure 4.3: Example of the GUI

5. RESULTS

As described previously, we were interested in finding the cubes that had a greater concentration of points so this, the existence of some regions that had greater influence from the analysed variables. Since the same thresholds have been used when defining the levels of all the subjects, we thought it could be interesting to show the variance of the thresholds from the subjects' files against the threshold from the global file.

When comparing the different thresholds with the coordinates where they appear we have obtained the following results.

Non-pregnant group

In Table 5.1 we can see the results obtained from our group of non-pregnant patients.

- TH_1 represent the threshold that defines *LOI*
- **Coordinates** represent the position in the 3D matrix where the cube is located.
- **Box number** represent the position of the cell in the initial row of 1728 cells.
- **Avg. conc.** represents the average concentration of the cube between all the non-pregnant patients.
- **Avg. TH_2** represents the average threshold of the cube between all the non-pregnant patients.

TH_1	Coordinates	Box number	Avg. conc.	Avg. TH_2
15	**6 6 6**	931	4,4951	5,1
10	**6 7 7**	786	4,4435	4,8
10	**6 7 6**	787	3,8495	4,4
10	**7 7 7**	798	3,9371	4,1
10	**6 6 7**	930	3,1957	3,6
10	**6 6 5**	932	2,5260	2,7
10	**7 6 7**	942	1,4872	1,8

Table 5.1: Results of the non-pregnant group

In Table 5.1, the first row means that in the global file, the cube in the coordinates (6, 6, 6) or in other words, the cell located in the position 931 belonged to the level 2 since $TH_1 = 15$. On the other hand, the program calculated the average concentration of points and the average threshold in this cube for all the non-pregnant patients.

If we plot this results comparing the average concentration against the average threshold we obtain the graphic shown in Figure 5.1.
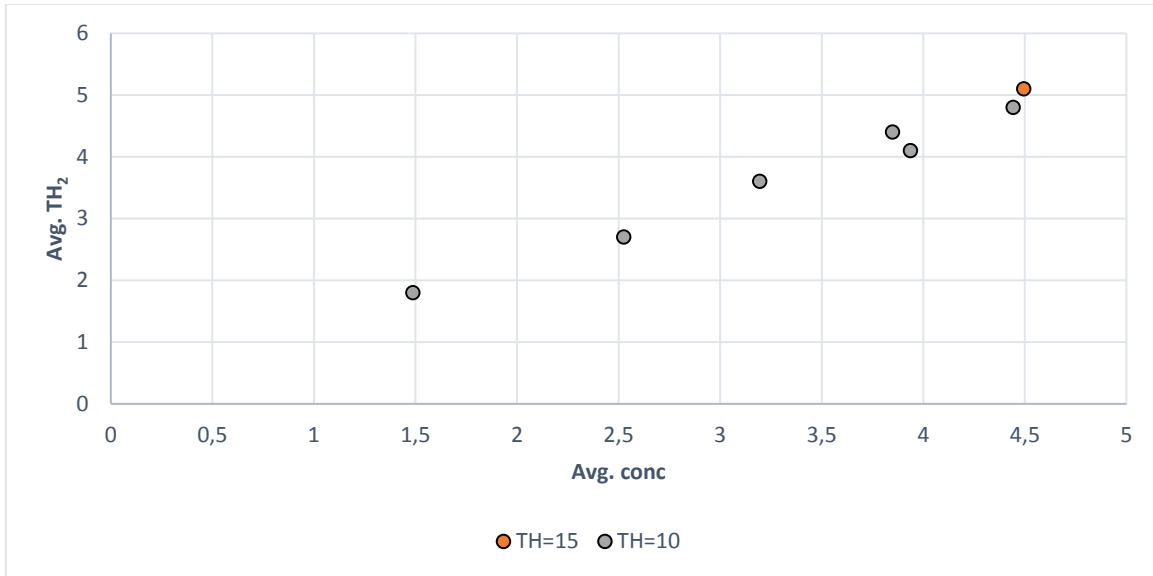
Figure 5.1: Graphic representation of the non-pregnant group results. Avg. conc. Vs Avg. TH$_2$

We would expect the cubes belonging to higher levels to have both greater average concentration of points and average threshold and in this case, this happens as expected.

In this case, we can also notice that in the global non-pregnant file the lack of cubes belonging to the Level 1, or in another way, cubes with threshold = 20.

Pregnant group

In Table 5.2 we can see the results obtained from our group of pregnant group.

TH$_1$	Coordinates	Box number	Avg. conc.	Avg.TH$_2$
20	**6 7 6**	786	6,5388	9,12
20	**6 7 5**	787	5,7730	7,42
20	**7 7 7**	798	4,3001	5,32
20	**7 7 6**	799	4,2660	4,85
20	**6 6 7**	930	3,7351	4,21
20	**6 6 6**	931	3,4515	3,91
20	**7 6 7**	942	2,5454	3,06
20	**7 6 6**	943	1,8204	2,14
15	**7 6 8**	941	3,0482	3,68
15	**7 7 5**	797	2,0233	2,43
10	**7 8 7**	654	2,9899	3,83
10	**7 8 6**	655	2,4846	3,14
10	**6 7 4**	788	1,9718	2,64
10	**7 7 5**	800	1,6387	2,20
10	**6 6 5**	932	1,2501	1,62
10	**7 6 5**	944	0,7461	1,02
10	**6 5 7**	1074	0,4085	0,56
10	**6 5 6**	1075	0,2188	0,30
10	**7 5 7**	1086	0,1258	0,18

Table 5.2: Results of the pregnant group

If we plot this results comparing the average concentration against the average threshold we obtain the graphic shown in Figure 5.2.

In the Figure 5.2, we can notice that all the levels studied have representation in the results of the global pregnant file. On the other hand though, we can observe that the order that we expected, defined as the cubes belonging to higher levels having greater average concentration and average threshold, has been altered since we can find cubes belonging to the Level 2 and Level 3 in higher positions than cubes belonging to Level 1.
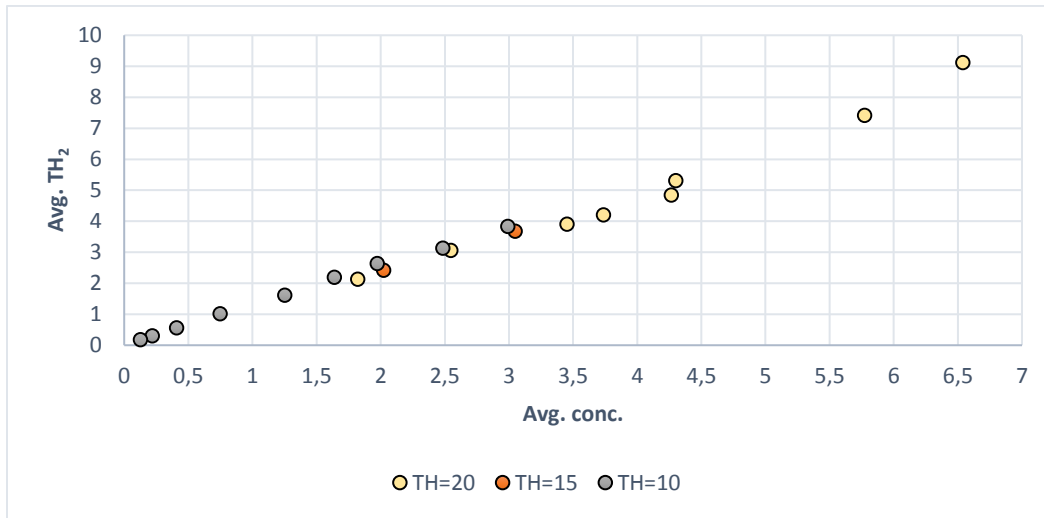
Figure 5.2: Graphic representation of the pregnant group results; Avg. conc. Vs Avg. TH$_2$

Pregnancy Induced Hypertension group

In Table 5.3 we can see the results obtained from our group of PIH patients.

TH$_1$	Coordinates	Box number	Avg. conc.	Avg.TH$_2$
20	**7 7 7**	798	6,2213	7,69
20	**7 6 7**	942	5,1106	5,85
15	**7 7 8**	797	5,3776	6,71
15	**7 7 6**	799	4,0113	4,57
15	**7 6 8**	941	1,6567	2,00
15	**7 6 6**	943	0,8368	1,00
10	**6 7 6**	786	4,1254	5,29
10	**6 7 5**	787	3,0990	3,79
10	**7 7 7**	796	1,9529	2,36
10	**6 6 7**	930	1,1688	1,57
10	**6 6 6**	931	0,2058	0,29

Table 5.3: Results of the PH group

If we plot this results comparing the average concentration against the average threshold we obtain the graphic shown in Figure 5.3.

The results from the global PIH file follow the same line as the previous results since we find representation from the three levels studied and an altered distribution from what we expected.
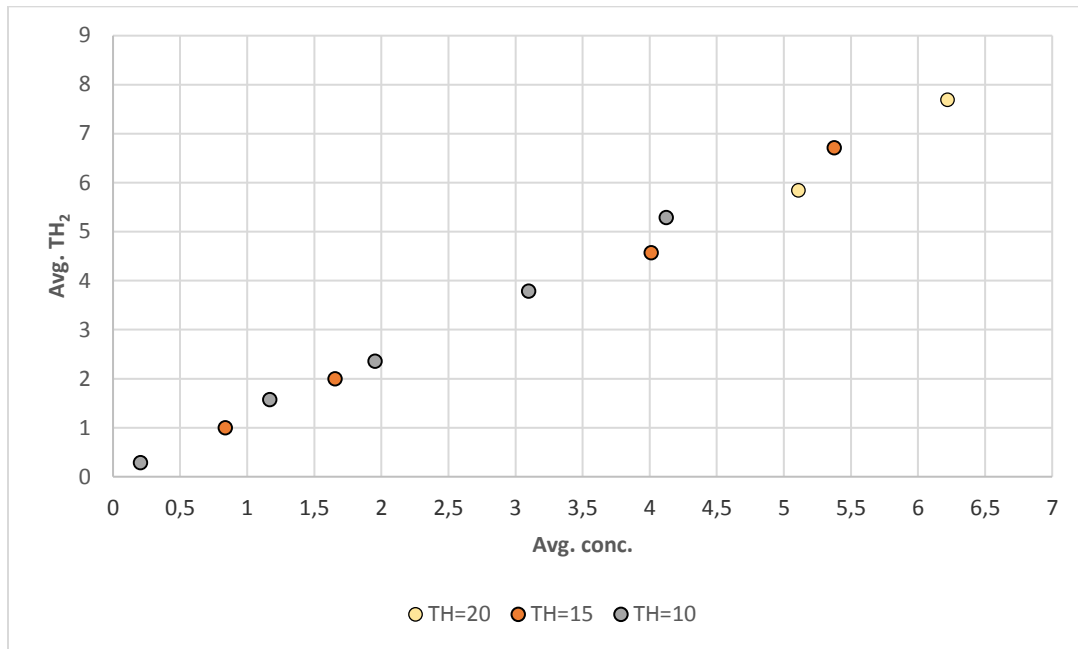
Figure 5.3: Graphic representation of the PIH group results; Avg. conc. Vs Avg. TH$_2$

Chronical Hypertension group

In Table 5.4 we can see the results obtained from our group of CH patients.

TH$_1$	Coordinates	Box number	Avg. conc.	Avg.TH$_2$
20	**7 7 7**	798	5,9838	8,54
20	**7 7 6**	799	5,1443	6,62
20	**7 6 7**	942	3,7369	5,08
20	**7 6 6**	943	3,0200	3,54
15	**6 7 7**	786	4,0423	4,92
15	**6 7 5**	787	3,3966	4,46
15	**6 6 7**	930	2,3302	3,08
15	**6 6 6**	931	2,0529	2,38
10	**7 7 8**	797	3,5384	5,00
10	**7 7 5**	800	2,8588	3,54
10	**7 6 8**	941	0,6674	0,92
10	**7 6 5**	944	0,3726	0,54

Table 5.4: Results of the CH group

If we plot this results comparing the average concentration against the average threshold we obtain the graphic shown in Figure 5.4.
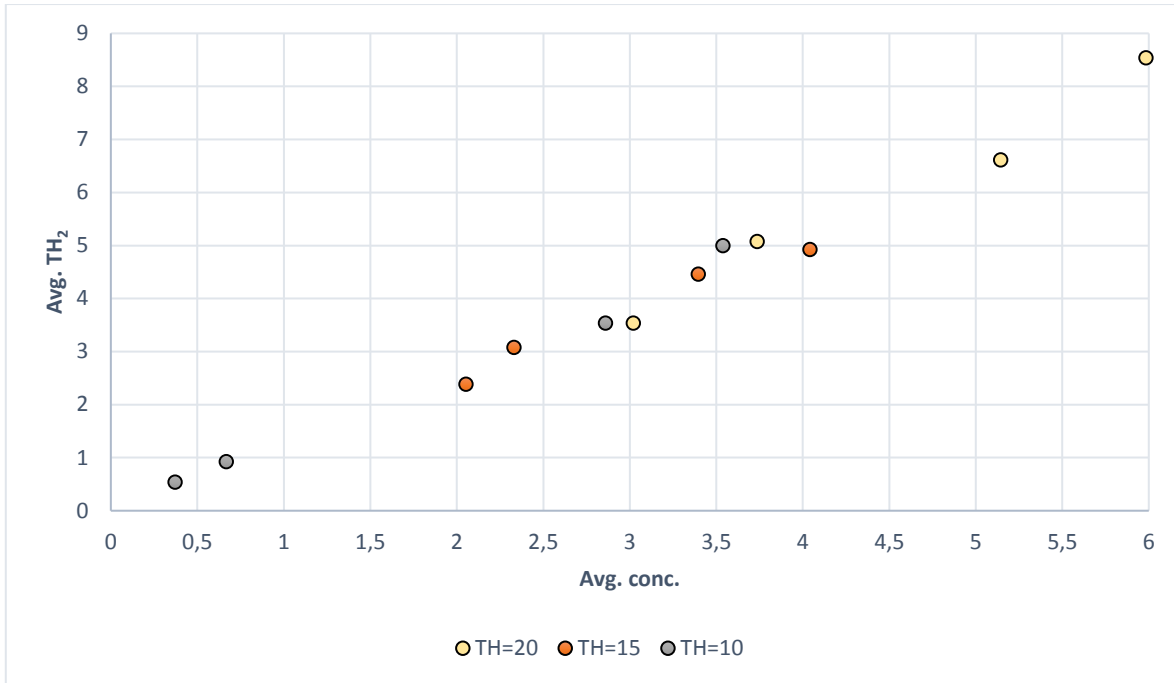

Figure 5.4: Graphic representation of the CH group results; Avg. conc. Vs Avg. TH$_2$

As stated previously, we would expect the cubes belonging to higher levels to have both greater average concentration of points and average threshold. Nevertheless, in this case we observe that cubes from the global CH file have both lower average concentration and average threshold than others belonging to lower levels.

Pre-Eclampsia group

In Table 5.5 we can see the results obtained from our group of PE patients.

TH$_1$	Coordinates	Box number	Avg. conc.	Avg.TH$_2$
20	**677**	786	5,9902	7,79
20	**676**	787	4,4265	5,58
20	**777**	798	3,9403	4,89
20	**776**	799	3,7918	4,26
20	**667**	930	3,1581	3,95
20	**666**	931	2,8495	3,26
20	**767**	942	2,0257	2,37
15	**766**	943	3,1494	4,05
10	**678**	785	3,5929	4,54
10	**668**	929	2,0677	2,62
10	**765**	944	1,5172	1,85

Table 5.5: Results of the PE group

If we plot this results comparing the average concentration against the average threshold we obtain the graphic shown in Figure 5.5.
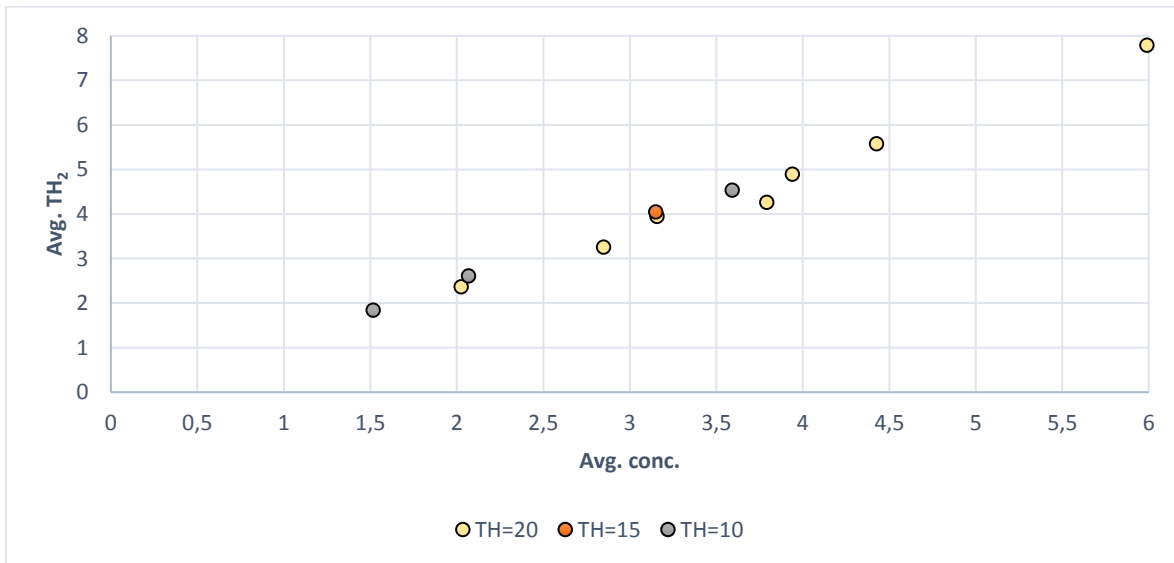

Figure 5.5: Graphic representation of the PE group results; Avg. conc. Vs Avg. TH$_2$

On the final graphic of this style that we present, we observe representation from every studied level and a distribution that does not follow what we expected.

Once we had these results we proceeded to analyse them.

In Figure 5.6 we can see the graphic that shows the average concentration Vs the average TH_2 for all the health conditions.
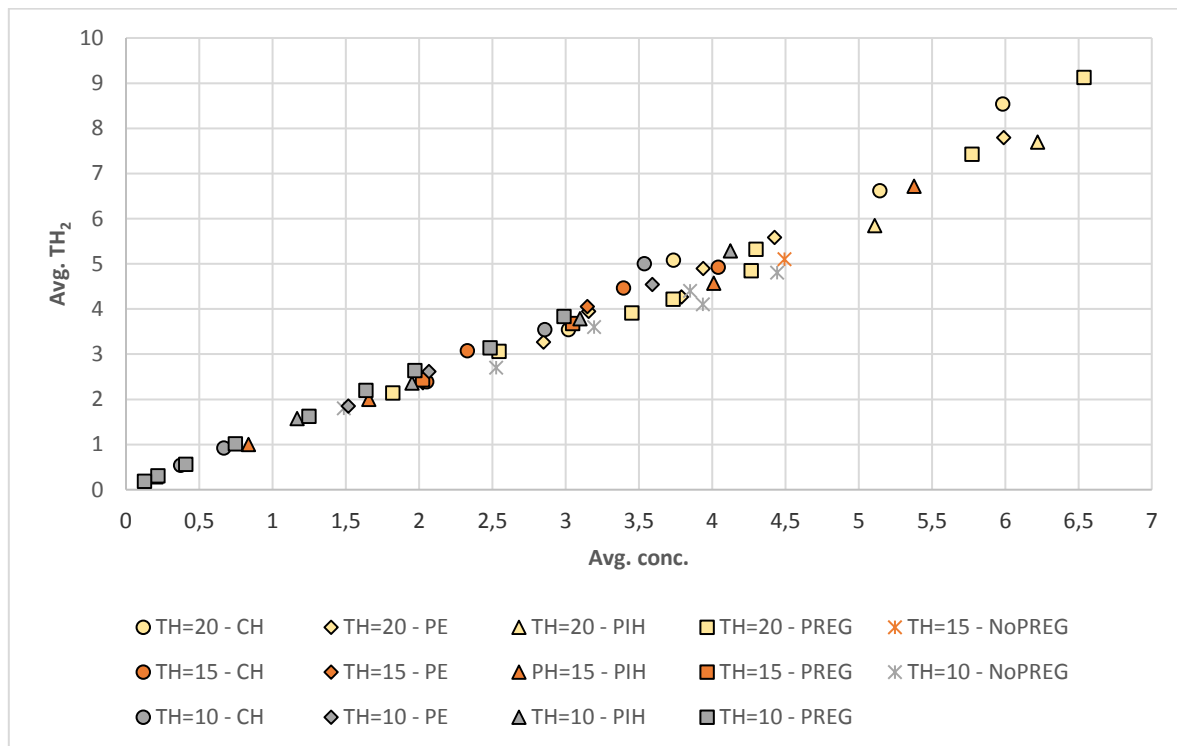

Figure 5.6: Graphic representation of all groups' results

Note that every colour is a different threshold and every form is a different health condition.

In Figure 5.6 we can observe that a cube belonging to the second level, threshold = 15, from the PIH global file is located in a higher position than most of the other cubes but we cannot determine the reason why this cube has both greater average TH_2 and average concentration.

Even though, we can see that an important percentage of blue forms, they belong to Level 1, are found in the upper right part of the graphic, followed by orange forms, belong to Level 2, and grey forms as we move close to 0 in both axis.

In Figure 5.7, we can see a graphic representation of how many occasions a cells appears in any global file and to which level it belongs.

Since we are interested in the cubes that appear in most occasions, we order them in decreasing order from the occasions that they appear in Level 1 to Level 3.
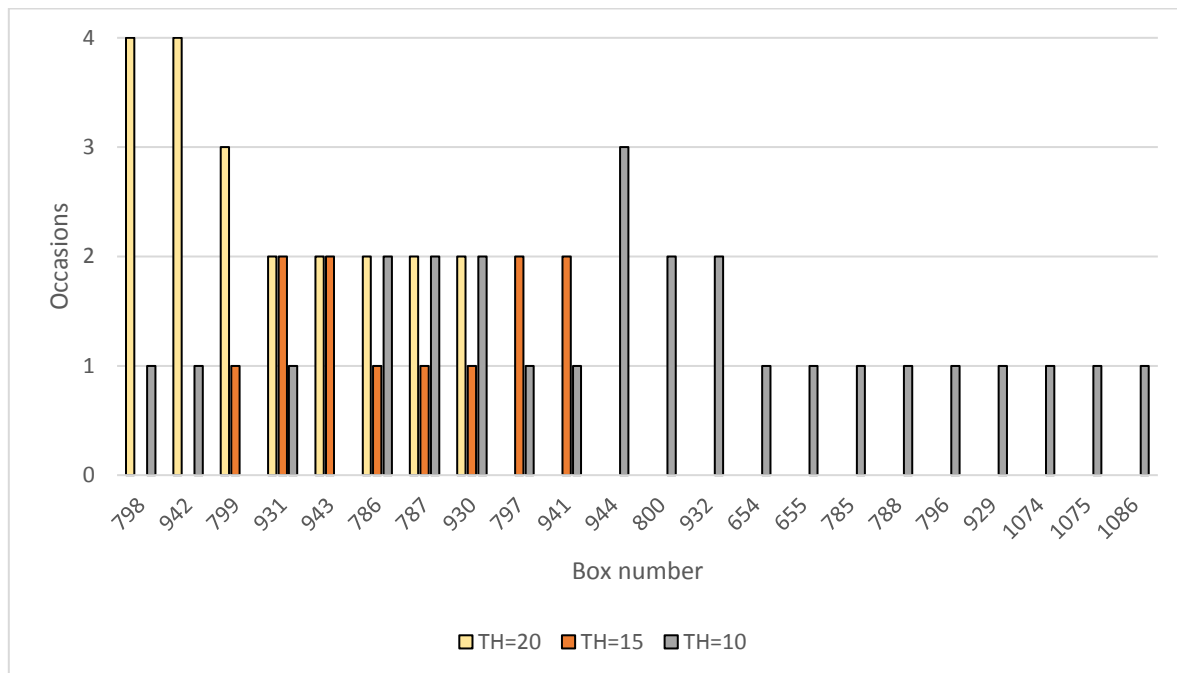

Figure 5.7: Graphic representation of how many occasions a specific cell appears and to which level belongs when such a thing happens

We can observe that the cells 798 and 942 appear in four occasions in Level 1 and one in Level 3. This cells belong to the cubes in the positions (7, 7, 7) and (7, 6, 7) respectively. Hereunder, the cell 799, which is the cube (7, 7, 6) appears in three occasions in Level 1 and one in Level 3. As we move further from the centre of the matrix, the occasions decrease as so does the levels of belonging.

The final graphic that we will show in this section is Figure 5.8, which shows per global health condition's file, how many cubes appear in every level.
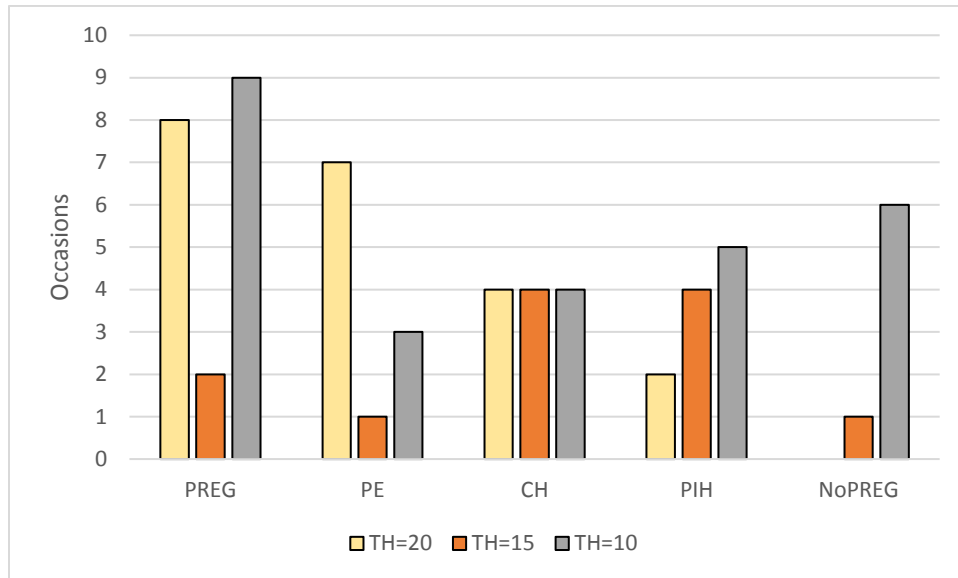
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Figure 5.8: Graphic representation of how many cubes appear per level per health condition

In Figure 5.8 we can see, for example, that the global pregnant file has eight cubes that belong to Level 1 meanwhile the global non-pregnant file has none.

6. DISCUSSION AND CONCLUSIONS

With the analysis of our results we have reached the following conclusions:

- We have been able to create a program that can plot the information from the patients in a GUI that was also coded based on different thresholds which are provided by the user and save this information. Moreover, the program is able to give the results in a batch mode, which means that there is no need to input the patients one per one but many as wanted at the same point.
- We have been able to say that with the information provided, the results were able to differentiate between medical conditions using our results.

Nevertheless, we have not reached all the objectives that we wanted to achieve, since the addition of the algorithm describe in this project has not been added to the 3DSPPA program.

On the other hand, we have been unable to determine a volume of interest that would differentiate instantly between the different conditions, and we also have to say that our conclusions, this conclusions, may not be able to be reproduced in a different set of data with different patients or health conditions.

As engineer, I have learned how to make a study of different technologies and approaches, and from some criteria choose those that best suit the needs of the project. We have managed to work individually and know how to choose the most optimal solution for each problem taking into account the contributions provided by the people asked for help.

The result of this project is the creation of two informatics tools that have been developed entirely from scratch and given specific conditions, may help in the future into achieve a better diagnosis of the health conditions of the subjects.

As a continuation of the project we would recommend this program to be tested in another environments and a different set of data, since we cannot affirm that our conclusions of this project would be able to be applied in all the possible tests.

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8. ANNEXES

8.1. Index of figures

8.2. Index of tables

8.3.   Global files' results

Non-pregnant global file's results

Filename	Idgroup	Idsignal	TH_1	X Coord	Y Coord	Z Coord	Cell number	Value
Non-preg	1	RR_SYS_DIA	15	6	6	6	931	4,4951
Non-preg	1	RR_SYS_DIA	10	6	7	7	786	2,8553
Non-preg	1	RR_SYS_DIA	10	6	7	6	787	3,8743
Non-preg	1	RR_SYS_DIA	10	7	7	7	798	3,8448
Non-preg	1	RR_SYS_DIA	10	6	6	7	930	2,8972
Non-preg	1	RR_SYS_DIA	10	6	6	5	932	3,1285
Non-preg	1	RR_SYS_DIA	10	7	6	7	942	3,2615
Non-preg	1	RR_SYS_DIA	5	6	7	5	788	2,6083
Non-preg	1	RR_SYS_DIA	5	7	7	8	797	2,2001
Non-preg	1	RR_SYS_DIA	5	7	7	6	799	2,1423
Non-preg	1	RR_SYS_DIA	5	8	7	8	809	1,3761
Non-preg	1	RR_SYS_DIA	5	8	7	7	810	1,3288
Non-preg	1	RR_SYS_DIA	5	6	6	4	933	1,5624
Non-preg	1	RR_SYS_DIA	5	7	6	8	941	1,8781
Non-preg	1	RR_SYS_DIA	5	7	6	6	943	2,2903
Non-preg	1	RR_SYS_DIA	5	6	5	6	1075	1,9857
Non-preg	1	RR_SYS_DIA	5	6	5	5	1076	1,4413

Table 8.1: Non-pregnant global file's result; TH₁: threshold associated to the cube; X, Y, Z Coordinates: Position of the cube in the matrix; Cell number: Position of the cube in the initial row; Value: Average value in the cube between all the subjects of this group

Pregnant global file's results

Filename	Idgroup	Idsignal	TH_1	X Coord	Y Coord	Z Coord	Cell number	Value
pregnant	4	RR_SYS_DIA	20	6	7	7	786	3,5273
pregnant	4	RR_SYS_DIA	20	6	7	6	787	3,2968
pregnant	4	RR_SYS_DIA	20	7	7	7	798	5,3234
pregnant	4	RR_SYS_DIA	20	7	7	6	799	4,1857
pregnant	4	RR_SYS_DIA	20	6	6	7	930	3,6232
pregnant	4	RR_SYS_DIA	20	6	6	6	931	3,5681
pregnant	4	RR_SYS_DIA	20	7	6	7	942	5,1763
pregnant	4	RR_SYS_DIA	20	7	6	6	943	4,2675
pregnant	4	RR_SYS_DIA	15	7	7	8	797	2,4192
pregnant	4	RR_SYS_DIA	15	7	6	8	941	2,1853
pregnant	4	RR_SYS_DIA	10	7	8	7	654	1,7236
pregnant	4	RR_SYS_DIA	10	7	8	6	655	1,3095
pregnant	4	RR_SYS_DIA	10	6	7	5	788	1,4741
pregnant	4	RR_SYS_DIA	10	7	7	5	800	1,5565
pregnant	4	RR_SYS_DIA	10	6	6	5	932	1,5405
pregnant	4	RR_SYS_DIA	10	7	6	5	944	1,5213
pregnant	4	RR_SYS_DIA	10	6	5	7	1074	1,3568
pregnant	4	RR_SYS_DIA	10	6	5	6	1075	1,3679
pregnant	4	RR_SYS_DIA	10	7	5	7	1086	1,7065
pregnant	4	RR_SYS_DIA	10	7	5	6	1087	1,4011
pregnant	4	RR_SYS_DIA	5	6	8	7	642	1,1459
pregnant	4	RR_SYS_DIA	5	6	8	6	643	1,1466
pregnant	4	RR_SYS_DIA	5	7	8	8	653	0,8759
pregnant	4	RR_SYS_DIA	5	5	7	7	774	0,9368
pregnant	4	RR_SYS_DIA	5	5	7	6	775	0,8495
pregnant	4	RR_SYS_DIA	5	6	7	8	785	1,1042
pregnant	4	RR_SYS_DIA	5	7	7	9	796	0,7449
pregnant	4	RR_SYS_DIA	5	8	7	8	809	0,8460
pregnant	4	RR_SYS_DIA	5	8	7	7	810	1,1209
pregnant	4	RR_SYS_DIA	5	8	7	6	811	0,9006
pregnant	4	RR_SYS_DIA	5	5	6	7	918	0,8419
pregnant	4	RR_SYS_DIA	5	5	6	6	919	0,8726
pregnant	4	RR_SYS_DIA	5	6	6	8	929	1,0915
pregnant	4	RR_SYS_DIA	5	7	6	9	940	0,6688
pregnant	4	RR_SYS_DIA	5	8	6	7	954	1,0358
pregnant	4	RR_SYS_DIA	5	8	6	6	955	0,9693
pregnant	4	RR_SYS_DIA	5	7	5	8	1085	0,7205

Table 8.2: Pregnant global file's result; TH_1: threshold associated to the cube; X, Y, Z Coordinates: Position of the cube in the matrix; Cell number: Position of the cube in the initial row; Value: Average value in the cube between all the subjects of this group

Pre-Eclampsia global file's results

Filename	Idgroup	Idsignal	TH_1	X Coord	Y Coord	Z Coord	Cell number	Value
PE	3	RR_SYS_DIA	20	6	7	7	786	4,1233
PE	3	RR_SYS_DIA	20	6	7	6	787	4,0734
PE	3	RR_SYS_DIA	20	7	7	7	798	3,8587
PE	3	RR_SYS_DIA	20	7	7	6	799	3,8281
PE	3	RR_SYS_DIA	20	6	6	7	930	4,1911
PE	3	RR_SYS_DIA	20	6	6	6	931	3,6451
PE	3	RR_SYS_DIA	20	7	6	7	942	4,2975
PE	3	RR_SYS_DIA	15	7	6	6	943	3,2142
PE	3	RR_SYS_DIA	10	6	7	8	785	2,0988
PE	3	RR_SYS_DIA	10	6	6	8	929	1,8571
PE	3	RR_SYS_DIA	10	7	6	5	944	1,9144
PE	3	RR_SYS_DIA	5	6	8	7	642	1,1528
PE	3	RR_SYS_DIA	5	6	8	6	643	1,2071
PE	3	RR_SYS_DIA	5	7	8	7	654	1,0681
PE	3	RR_SYS_DIA	5	7	8	6	655	1,2607
PE	3	RR_SYS_DIA	5	5	7	6	775	1,2422
PE	3	RR_SYS_DIA	5	6	7	9	784	1,0065
PE	3	RR_SYS_DIA	5	6	7	5	788	1,2363
PE	3	RR_SYS_DIA	5	7	7	8	797	1,0331
PE	3	RR_SYS_DIA	5	7	7	5	800	1,7500
PE	3	RR_SYS_DIA	5	8	7	7	810	1,2595
PE	3	RR_SYS_DIA	5	5	6	7	918	0,9356
PE	3	RR_SYS_DIA	5	5	6	6	919	1,2930
PE	3	RR_SYS_DIA	5	6	6	5	932	1,3022
PE	3	RR_SYS_DIA	5	7	6	8	941	1,3456
PE	3	RR_SYS_DIA	5	8	6	7	954	1,2505
PE	3	RR_SYS_DIA	5	8	6	6	955	0,9245
PE	3	RR_SYS_DIA	5	6	5	7	1074	1,4230
PE	3	RR_SYS_DIA	5	6	5	6	1075	1,1327
PE	3	RR_SYS_DIA	5	7	5	7	1086	1,2479
PE	3	RR_SYS_DIA	5	7	5	6	1087	0,9565

Table 8.3: Pre-Eclampsia global file's result; TH_1: threshold associated to the cube; X, Y, Z Coordinates: Position of the cube in the matrix; Cell number: Position of the cube in the initial row; Value: Average value in the cube between all the subjects of the group

Pregnancy Induced Hypertension global file's results

Filename	Idgroup	Idsignal	TH_1	X Coord	Y Coord	Z Coord	Cell number	Value
PIH	5	RR_SYS_DIA	20	7	7	7	798	5,3412
PIH	5	RR_SYS_DIA	20	7	6	7	942	5,2493
PIH	5	RR_SYS_DIA	15	7	7	8	797	3,0408
PIH	5	RR_SYS_DIA	15	7	7	6	799	2,8724
PIH	5	RR_SYS_DIA	15	7	6	8	941	2,9658
PIH	5	RR_SYS_DIA	15	7	6	6	943	3,5498
PIH	5	RR_SYS_DIA	10	6	7	7	786	2,2704
PIH	5	RR_SYS_DIA	10	6	7	6	787	2,2299
PIH	5	RR_SYS_DIA	10	7	7	9	796	1,9034
PIH	5	RR_SYS_DIA	10	6	6	7	930	2,4829
PIH	5	RR_SYS_DIA	10	6	6	6	931	2,6758
PIH	5	RR_SYS_DIA	5	6	8	7	642	0,9572
PIH	5	RR_SYS_DIA	5	7	8	8	653	1,0882
PIH	5	RR_SYS_DIA	5	7	8	7	654	1,5739
PIH	5	RR_SYS_DIA	5	7	8	6	655	0,9737
PIH	5	RR_SYS_DIA	5	6	7	5	788	1,2814
PIH	5	RR_SYS_DIA	5	7	7	5	800	1,1535
PIH	5	RR_SYS_DIA	5	6	6	5	932	1,7899
PIH	5	RR_SYS_DIA	5	6	6	4	933	1,0940
PIH	5	RR_SYS_DIA	5	7	6	9	940	1,4501
PIH	5	RR_SYS_DIA	5	7	6	5	944	1,3554
PIH	5	RR_SYS_DIA	5	6	5	7	1074	1,0805
PIH	5	RR_SYS_DIA	5	6	5	6	1075	1,0675
PIH	5	RR_SYS_DIA	5	7	5	7	1086	1,3803
PIH	5	RR_SYS_DIA	5	7	5	6	1087	0,9565

Table 8.4: Pregnancy Induced Hypertension global file's result; TH_1: threshold associated to the cube; X, Y, Z Coordinates: Position of the cube in the matrix; Cell number: Position of the cube in the initial row; Value: Average value in the cube between all the subjects of the group

Chronical Hypertension global file's results

Filename	Idgroup	Idsignal	TH_1	X Coord	Y Coord	Z Coord	Cell number	Value
CH	2	RR_SYS_DIA	20	7	7	7	798	4,7177
CH	2	RR_SYS_DIA	20	7	7	6	799	4,1278
CH	2	RR_SYS_DIA	20	7	6	7	942	4,8172
CH	2	RR_SYS_DIA	20	7	6	6	943	4,2462
CH	2	RR_SYS_DIA	15	6	7	7	786	2,9780
CH	2	RR_SYS_DIA	15	6	7	6	787	2,8114
CH	2	RR_SYS_DIA	15	6	6	7	930	3,3911
CH	2	RR_SYS_DIA	15	6	6	6	931	2,9622
CH	2	RR_SYS_DIA	10	7	7	8	797	2,0000
CH	2	RR_SYS_DIA	10	7	7	5	800	1,9280
CH	2	RR_SYS_DIA	10	7	6	8	941	1,8678
CH	2	RR_SYS_DIA	10	7	6	5	944	2,4198
CH	2	RR_SYS_DIA	5	6	8	7	642	0,9130
CH	2	RR_SYS_DIA	5	7	8	7	654	1,5857
CH	2	RR_SYS_DIA	5	7	8	6	655	1,1630
CH	2	RR_SYS_DIA	5	6	7	8	785	1,4131
CH	2	RR_SYS_DIA	5	6	7	5	788	1,1477
CH	2	RR_SYS_DIA	5	7	7	4	801	1,0738
CH	2	RR_SYS_DIA	5	8	7	7	810	1,1580
CH	2	RR_SYS_DIA	5	8	7	6	811	0,8962
CH	2	RR_SYS_DIA	5	5	6	6	919	0,9488
CH	2	RR_SYS_DIA	5	6	6	8	929	1,5024
CH	2	RR_SYS_DIA	5	6	6	5	932	1,2817
CH	2	RR_SYS_DIA	5	7	6	4	945	1,1812
CH	2	RR_SYS_DIA	5	6	5	7	1074	1,0098
CH	2	RR_SYS_DIA	5	6	5	6	1075	1,1234
CH	2	RR_SYS_DIA	5	7	5	7	1086	1,5384
CH	2	RR_SYS_DIA	5	7	5	6	1087	1,3604

Table 8.5: Chronical Hypertension global file's result; TH_1: threshold associated to the cube; X, Y, Z Coordinates: Position of the cube in the matrix; Cell number: Position of the cube in the initial row; Value: Average value in the cube between all the subjects of the group