Internship Report

Table des matières

[Glossary 4](#_Toc17450321)

[Intro 5](#_Toc17450322)

[1. Context 6](#_Toc17450323)

[1.1. Internship context 6](#_Toc17450324)

[1.1.1. Monash University 6](#_Toc17450325)

[1.1.2. ESCE Department 6](#_Toc17450326)

[1.1.3. The team 6](#_Toc17450327)

[1.2. Medical background 7](#_Toc17450328)

[1.2.1. Preterm Neonates’ Immaturity 7](#_Toc17450329)

[1.2.2. Respiratory Distress Syndrome 7](#_Toc17450330)

[1.2.3. RDS Therapies 7](#_Toc17450331)

[1.3. The Project 8](#_Toc17450332)

[1.3.1. Purpose 8](#_Toc17450333)

[1.3.2. Study design 8](#_Toc17450334)

[1.3.3. Procedure 8](#_Toc17450335)

[1.3.4. Stages of Analysis 9](#_Toc17450336)

[2. Pre-processing 10](#_Toc17450337)

[2.1. Purpose 10](#_Toc17450338)

[2.2. Crying removing 11](#_Toc17450339)

[2.2.1. Labelling 11](#_Toc17450340)

[2.2.2. Anaylisis of differences between CSs and NCSs 11](#_Toc17450341)

[2.2.3. Threshold Establishing 11](#_Toc17450342)

[2.2.4. Results 11](#_Toc17450343)

[2.3. Noise Filtering 11](#_Toc17450344)

[2.3.1. Butterworth Filter 11](#_Toc17450345)

[2.3.2. Implementation 11](#_Toc17450346)

[2.3.3. Results 11](#_Toc17450347)

[2.4. Discussion 12](#_Toc17450348)

[3. Features extraction 13](#_Toc17450349)

[3.1. Methods 13](#_Toc17450350)

[3.1.1. Temporal Features 13](#_Toc17450351)

[3.1.2. Spectral Coefficients 13](#_Toc17450352)

[3.1.2.1. Linear Predictive Coefficients - LPC 13](#_Toc17450353)

[3.1.2.2. LSF 14](#_Toc17450354)

[3.1.3. Spectral Fit 14](#_Toc17450355)

[3.1.3.1. Gaussian Mixture Model 14](#_Toc17450356)

[3.1.3.2. Moving Average F 14](#_Toc17450357)

[3.1.4. Perceptual Spectral Features 15](#_Toc17450358)

[3.1.4.1. Brightness 15](#_Toc17450359)

[3.2. Results 15](#_Toc17450360)

[3.3. Discussion 15](#_Toc17450361)

[4. Conclusion 15](#_Toc17450362)

[6. Vocabulary 16](#_Toc17450363)

[Annex 1 16](#_Toc17450364)

[Annex 2 17](#_Toc17450365)

[Annex 3 18](#_Toc17450366)

[7. References 19](#_Toc17450367)

# Glossary

SRT :

RDS :

CS : Crying Segment

NCS: Non-Crying Segment

Intensive Care Unit (NICU),

# Intro

Every year, an estimated 15 million babies are born preterm, and this number is rising. Complications due to their immaturity are the leading cause of infant mortality[[1]](#endnote-2).

* Une des complications: Deficience respiratoty
* Combien cela touche d’enfants? Quels sont les risques ?
* Plusieurs façons d’aider suivant la gravité, dont injection de surfactant.

But du projet :

* But global : ???
* Identify acoustic differences in the breath sounds of preterm neonates with RDS before and after SRT.
* En particulier en signal processing : trouver des features dont la différence sera la plus importante ?

*That is more than 1 in 10 babies.*

*and many survivors face a lifetime of disability.*

*Preventing deaths and complications from preterm birth starts with*

Slightly fewer than 12 percent of all babies are premature. Overall, the rate of premature births is rising, mainly due to the large numbers of multiple births in recent years.

Durée du stage

# Context

## Internship context

### Monash University

Monash University is the largest university in Australia and one of the major world universities, especially for its research departments. With approximately 55,000 students, it owns campuses in Australia, Malaysia and South Africa.

I did my internship in Clayton Campus, the main campus of [Monash University](https://en.wikipedia.org/wiki/Monash_University) both in terms of size and student population. Clayton is a suburb of [Melbourne](https://en.wikipedia.org/wiki/Melbourne), in the state of [Victoria](https://en.wikipedia.org/wiki/Victoria_(Australia)), Australia.



Figure 1: Monash University, with my building and my desk

### ESCE Department

My internship took place in the Electrical and Computer Systems Engineering (ECSE) department. It covers a diverse field that encompasses biomedical, computer systems, electronics, electrical power, robotics and telecommunications.

Like the university, the department is international, with various professors or PhDs from the Middle East and Asia. In total, twenty-two professors and about thirty PhDs and Post-Docs work in the department.

### The team

My supervisor is Faezeh Marzbanrad. She is a lecturer who joined the University of Monash in 2016. Her research interests include biomedical signal processing, machine learning and statistical data analysis, as well as fetal, maternal and neonatal healthcare technologies. On maternity leave during my internship, I met her every week by videoconference.

I also worked in partnership with a medical team, including Lindsay Zhou and Arabella King. Lindsay Zhou is a doctor of [the Department of Paediatrics, in Monash Children’s Hospital. Specialized in neonatal medicine, he is conducting a large study on preterm neonates with RDS. Arabella, meanwhile, is a 5th-year medical student who decided to take a break from her studies to do a year of research. With Lindsay as supervisor, she works more specifically on the consequences of the SRT. I worked on the engineering side of her thesis.](https://www.researchgate.net/institution/Monash_University_Australia)

Another student, Davood Fattahi, work in collaboration with Faezeh Marzbanrad.

## Medical background

### Preterm Neonates’ Immaturity

Normally, a pregnancy lasts about 40 weeks. A neonate will be considered as preterm if he is born before 37 weeks of pregnancy have been completed.

When a baby is premature, he is not fully developed, which often causes serious disorders. The newborn’s difficulty degree is usually related to his gestational age: it is greater the earlier he is born.[[2]](#endnote-3) It affects a lot of parts, including the central nervous system, the cardiovascular system and the respiratory system.[[3]](#endnote-4)

### Respiratory Distress Syndrome

The Respiratory Distress Syndrome (RDS) is a breathing disorder that affects newborns and particularly premature infants as it results from the respiratory system immaturity.

RDS occurs when there is not enough of a substance in the lungs called surfactant. This liquid is produced by the lungs and plays a key role by reducing the surface tension between liquid and air in each alveolus. The production of surfactant begins by 24 weeks’ gestation, which is very late in pregnancy. Consequently, the vast majority of babies born under 32 weeks’ gestation need respiratory supports. [[4]](#endnote-5)

### RDS Therapies

The RDS can lead to serious consequences, including death. Different treatments exit to overcome respiratory dysfunction, which ensure that the infants' organs get enough oxygen to work well.

**Respiratory supports** - First and foremost, all enfants who have breathing problems need breathing aids. Different supports exist, summarized in the table ... below. According to their clinical signs, neonates will have one support rather than another.

Figure … : The different respiratory supports in Monash Children’s Hospital

**Surfactant replacement therapy (SRT)** - The course of therapy depends on the lung immaturity seriousness, and some newborns will need additional treatment. When newborns need a lot of oxygen, it means that their surfactant production is very insufficient, even non-existent. The SRT is then necessary, which aims to give surfactant to the neonate lungs. This treatment is now a well-established therapy in the Neonatal Intensive Care Unit (NICU), but opinions still differ for its use[[5]](#endnote-6). *When should it be used? What dose to inject?* In addition, the surfactant is not always well absorbed, and never in the same way. Mettre article Today, the Monash Children's Hospital uses it when the baby needs more than 30% oxygen, but research in this area continues to be conducted.



<https://extranet.who.int/rhl/topics/newborn-health/care-newborn-infant/who-recommendation-early-administration-surfactant-intubated-preterm-newborns-respiratory-distress>

Figure 3: Preterm neonate receiving surfactant

## The Project

### Purpose

In Monash, a large study is in progress on newborns, whether regarding their respiratory or cardiac signals. One research aimed at doing a better assessment in preterm neonates under 32 weeks to improve their respiratory breath. My internship is part of this research topic, especially regarding the Surfactant Replacement Therapy (SRT) to know more about its consequences. My work is based on the analysis of preterm neonates’ respiratory signals before and after SRT.

An experiment aimed at recovering the lung sounds before and after SRT was set up by Arrabella King, the medical student of my team. My internship is based on the analysis of her recordings, in order to distinguish preterm neonates who have had SRT from the others.

### Study design

This is a prospective-observational study, which means neonates involved in this study will have no changes made to their usual care.

**Setting -** The study was conducted at Monash Medical Centre and Monash Children’s Hospital.

**Study population -** The population being studied are preterm neonates less than 32 weeks gestation. Two groups are studied within this population; neonates that require SRT and those that already had SRT.

**Recruitment -** Parents of neonates that fulfil the inclusion criteria were invited to participate in the study during the antenatal or early postnatal period. They were recruited on the wards and an informed consent was obtained from either parent of the child. The recruitment period ran from March 2019 until August 2019.

### Procedure

**Tools -** A Digital Stethoscope (DS) known as Clinicloud (Pty Ltd, Melbourne, Australia) was used to record the samples. It is composed of a diaphragm which functions to capture sounds. Instead of the sound being transmitted via acoustic vibrations, it is converted to electrical signals, which can then be amplified and processed to optimize the information it contains. These electrical signals are converted back to sound waves for listening.[[6]](#endnote-7)

**Recording timeline -** Samples were recorded on babies who need SRT, before and after taking surfactant, exactly on Day 2 and on Day 28 after birth. Day 2 was chosen in spite of Day 1 to allow time to the lungs to remove all their fluids. Day 28 is the time where the diagnostic of Chronic Lung Disease (CLD) is possible.

**Birth**

Days 4 to 6

Day 28

Day 2

Figure … : Recording timeline for preterm neonates with RDS who require a SRT.

Recording

Recording

**Dataset -** The bank of signals is composed of 37 recordings, which all last between 60 and 70 seconds. For safety considerations, only one acquisition has been done in each case. A CHANGER: 106 Recordings, don’t 37 labelled. Longueur entre 23 et 71 secondes, avec pour la plupart autour de 60s.

### Stages of Analysis

The analysis of respiratory sounds is composed of four phases. The preprocessing and the extraction of the features were conducted by the engineering side (Julie Kiewsky) while the statistical study and the interpretation were carried out by the medical side (Arabella King).

**Preprocessing -** The preprocessing part consisted of denoising the signals. A lot of work has been done to remove the crying and reduce the ambient noise. The engineering side was not blind on crying sections.

**Features extraction -** A large number of features were extracted and gathered in an Excel file to allow the medical team to do statistical studies. The engineering side was blinded to patient clinical data, surfactant administration and date of recordings.

**Statistical study & interpretation –** A statistical study was conducted to deduce some properties on the Surfactant Replacement Therapy.

# Pre-processing

The pre-processing was divided into several steps, described below. All the code was done in MATLAB language. The phase of resampling and Butterworth filter were already developed I arrived.

## Purpose

Samples cannot be analyzed without a first phase of treatment. A great diversity and many noises are present, making the distinction and comparison of breath sounds difficult. An almost exhaustive description of these noises is outlined below.

**Variable quality -** For safety considerations, and especially to lessen the risk of infection, only one record has been done, making the quality of the samples very variable.

**Crying -** Newborns’ crying is very common. They often last few seconds, and are present many times in recordings.

**Heartbeat** - Samples being recorded using a stethoscope, the sound of the heart is also there.

**Talks -** The neonates studied are in the NICU. They are premature and with respiratory deficiency, which means that a close eye is kept on them. This is reflected in the recordings by the hustle and bustle of nurses and doctors. In general, the signals recorded on Day 2 are noisier than the ones on Day 28.

**Respiratory supports** - As described in part ..., different respiratory supports exist for newborns suffering from respiratory deficiency. They do not all make the same sound, especially CPAP which are very noisy.

**Stethoscope -** The stethoscope diaphragm movement on the infant chest sometimes creates artefact.

During the allocated time, the removal of all these noises was impossible. It was then necessary to make a choice. Crying removal was a priority because weeping newborns do not breath as they would usually do, and they would greatly distort the results (part …). Respiration being independent of the other noises, a simple filter was set up, to minimize them (part ..)

**Resampling**

The sampling frequency of the Digital Stetoscope is Fs=16000 Hz. A resampling was performed to make it correspond to 2 times the Nyquist Rate.

The Nyquist Theorem specifies that the sampling rate must be at least 2\*fmax. In this case, the bandwidth was chosen to limit the frequencies between 100 and 1000 Hz (voir partie 2.1.2). The Nyquist Rate is then equal to NR=2\*fmax=2000Hz. So the sampling frequency that will be used in the rest of the algorithm is fn=2\*NR=4000Hz.

FAUX : On prend les fréquences de 0 à 2000Hz dans le CS learning

Ce nouvel échantillonnage a été effectué grâce à la fonction resample.

## Crying removing

Explication aim + fait grace à learning

### Labelling

### Analysis of differences between CSs and NCSs

### Threshold Establishing

### Results

VOIR CRYING REMOVING

## Noise Filtering

Explication aim

### Butterworth Filter

### Implementation

### Results

Une fois le signal re échantillonné, the second task was to denoise the recordings.

The noise can be first due to doctors’ conversation, heartbeat or stethoscope imprecision. Le filtrage de ces bruits has been mainly developed by Fatema (an ancient PhD student of Monash University). According to the paper[[7]](#endnote-8) and to some listening tests and discussions in the team, a frequency band of interest between [100Hz, 1000Hz] was chosen. A Butterworth pass-band filter was then designed with the cut-off frequencies above. Ce filtre a la particularité d’avoir un gain proche de 1 in the passband, which means having a [frequency response](https://en.wikipedia.org/wiki/Frequency_response" \o "Frequency response) as flat as possible, ce qui est très intéressant quand on ne veut pas détériorée le signal. L’ordre du filtre a été choisi à 6 après quelques tests pour avoir une sélectivité suffisante. Concernant les fonctions Matlab, butter pour créer le filtre, puis filtfilt pour filtrer le signal ont été appliquées.

D’autres bruits dû aux différentes machines aidant les enfants prématurés à respirer altèrent les signaux. Ces bruits sont particuliers à mon signals bank, c’est donc moi qui ait implémenté ce qui suit. A FAIRE

Parler aussi des discussions des medecins

## Discussion

Mettre signal avant et apres, et commenter toutes les différences.

**Crying removing**

Mettre un signal avant et après pre-processing, entourer les zones de pleurs, mettre différents signaux pour voir les différences. Tout commenter dans les différences. Mettre pourcentage d’accuracy.

Attention toujours pas parfait. Nous avons dû enlever quelques recordings et d’autres influencent surement encore négativement les résultats.

Dire que les résultats qu’on obtient sont quand meme satifaisant

Mentionnée les autres méthodes qu’on aurait pu utiliser : corss validation à la place de ROC, faire sur plusiuers fetaures et pas seulement sur le power ratio.

Le comparer à d’autres études déjà faites à ce sujet. Meme choses chez les enfants tres prematures ?

# Features extraction

Cette partie est dédiée à l’extraction de caractéristiques. Comme dans le cas du pre-processing, je suis partie d’un code contenant déjà certaines fonctionnalités, résumées dans le tableau en annexe … . Mon travail a été de faire des recherches afin de trouver d’autres caractéristiques judicieuses sur ces signaux, et de les implémenter.

Dire que j’étais aveugle aux données, et que le but était de faire le plus de features possibles, pour ensuite voir lesquels étaient significatifs distinguer le SRT des non SRT.

## Methods

Mettre comme features : toutes celles faites avant moi (mean PSD, … en expliquant quelques phrases à chaque fois). Pas disticntion dans de parties, mais plutôt début de paragraphes en gras.

Pour LPC, ne prendre que les derniers parce que les premiers avec le fitrage de 100 à 1200 ne servent à rien (à mieux comprendre)

## Results

Mettre les tableaux en annexe de résultats. Attendre d’avoir les résultats de Belle pour inserer les courbes de statistiques et tout ca.

## Methods

La plupart des caractéristiques extraites se trouvent dans le domaine spectral, bien que quelques-unes soient tirées du domaine temporel et spectro-temporel.

### Temporal Features

Le domaine temporel est assez dangereux à utiliser car les enregistrements n’ont pas tous la même durée, ni ….

Tout de même, le Zero Crossing Rate ainsi que le temps entre chaque respiration (inhalation et exhalation) ont été implémenté.

ZRC : qu’est-ce que c’est et pourquoi c’est utile

Autre

ZeroCrossings: the number of time domain zerocrossings of the signal. ZeroCrossings are useful to detect the amount of noise in a signal.

### Spectral Coefficients

MFCC déjà implémenté

Choisi 2 autres, pourquoi judicieux?

#### Linear Predictive Coefficients - LPC

Linear Predictive Coding with its LPCs (Linear Predictive Coefficients) are a tool used mostly in audio signal processing and speech processing for representing the signal spectral envelope with a reduced number of parameters.

Ces coefficients sont intéressants dans le projet car il donne des informations sur le signal, notamment sur les formants et …. C’est pour cette raison qu’il a été choisi de les implémenter.

**Theorical calculations**

They are based on a prediction of the signal value at time t approximated with linear combination of real signal values in previous moments, which can be expressed as follows (eq. 1):



where t is a discrete time moment, ft is the original signal, ftprime an approximation of the original signal, ak the LPCs 1≤k≤p and p the number of LPCs.

They are calculated so that they minimize the error between the real signal and the one calculated using LPCs over the interval of interest to minimize to mean squared error as defined in (1.3 ) .



where ts is the starting point in time of the interval for which the error is being calculated, te the ending and E the measured error on the interval t∈[ts; te].

To minimize this error, the ak are calculated in such a way that the derivative of E is equal to 0 (…).

avec =0.

Finally, the expression of the LPCs are as follow (…):

METTRE L’EXPRESSION

More details one the calculation of the coefficients can be found on the paper[[8]](#endnote-9).

**Implementation**

L’implémentation se fait simplement avec la fonction lpc sous Matlab. Le choix de 6 coefficients a été retenu car …

#### LSF

IDEM

### Spectral Fit

2 facons diférrentes de ‘représenter’ le periodogramme

#### Gaussian Mixture Model

Qu’est ce que c’est? Pourquoi en avoir choisi 6 ? Qu’est-ce qu’on regarde dessus ? Pourquoi judicieux ?

#### Moving Average F

IDEM

### Perceptual Spectral Features

#### Brightness

The spectral centroid is commonly associated with the measure of the brightness of a sound. It indicates at which frequency the energy of a spectrum is centered upon, by evaluating its center of gravity.

**Theorical calculations**

It is calculated as the weighted mean of the frequencies present in the signal, with their magnitudes as the weights (eq …).

Attention mettre juste somme sur k (pas de N)

Here, F [k] is the amplitude corresponding to bin k in Discrete Fourier Transform spectrum.

**Implementation**

## Results

Donner les résultats des LPC Et LSF avec le vrai signal et les estimations à l’aide des coeffs.

Donner les résultats avec Belle.

## Discussion

# Conclusion

Dans les ouvertures :

* The all system could be used in the features on a phone, so that the doctors can see the results just after or during the auscultation. Need a low computation time
* Peut etre trop loin: check the quality of recordings directly so that the doctors can put the stetoscope at the place where there is less artefact.

**Birth**

Days 4 to 6

Day 28

Day 2

It opposes the surface tension attraction forces to reach a balance, allowing the open and stable alveoli maintenance, the pulmonary compliance reduction (lung ability to open and close), the cells dry upkeep and defenses against infectious agents.[[9]](#endnote-10)



Figure 2: Surfactant role in the respiratory system

REFAIRE le SCHEMA

<https://ib.bioninja.com.au/standard-level/topic-6-human-physiology/64-gas-exchange/pneumocytes.html>

# Vocabulary

Preterm births

Babies born prematurely

Preterm neonates

Newborn=neonate

Premature=preterm=premature infants

# Annex 1

|  |  |  |
| --- | --- | --- |
| **Available tools** | **Advantages** | **Disadvantages** |
| **X-ray** | * Cheap * Bedside * Instant results | * Ionizing radiation |
| **Ultrasound** | * Cheap * Bedside * Instant results * Radiation free | * Training * Infection |
| **Electrical impedance tomography** | * Bedside * Radiation free * Dynamic monitoring * Assess regional changes | * Appliance of electrodes * Technical analysis * Cross sectional only |
| **Respiratory inductive plethysmography** | * Bedside * Radiation free * Dynamic monitoring | * Technical analysis * Sensitive to heat and movement * Influenced by blood flow |
| **Gas techniques** | * No sedation | * Doesn't measure trapped gas * Affected by mask leaks * Alter breathing patterns * Costly |
| **Whole body plethysmography** | * Measures trapped gas | * May require sedation * Bulky machine * Unsuitable for unstable or small neonates |
| **Computed tomography** | * High quality image resolution | * Ionizing radiation * Transfer to machine * Unsuitable for unstable neonates * Costly * Time consuming |

<https://www.nhlbi.nih.gov/health-topics/respiratory-distress-syndrome>

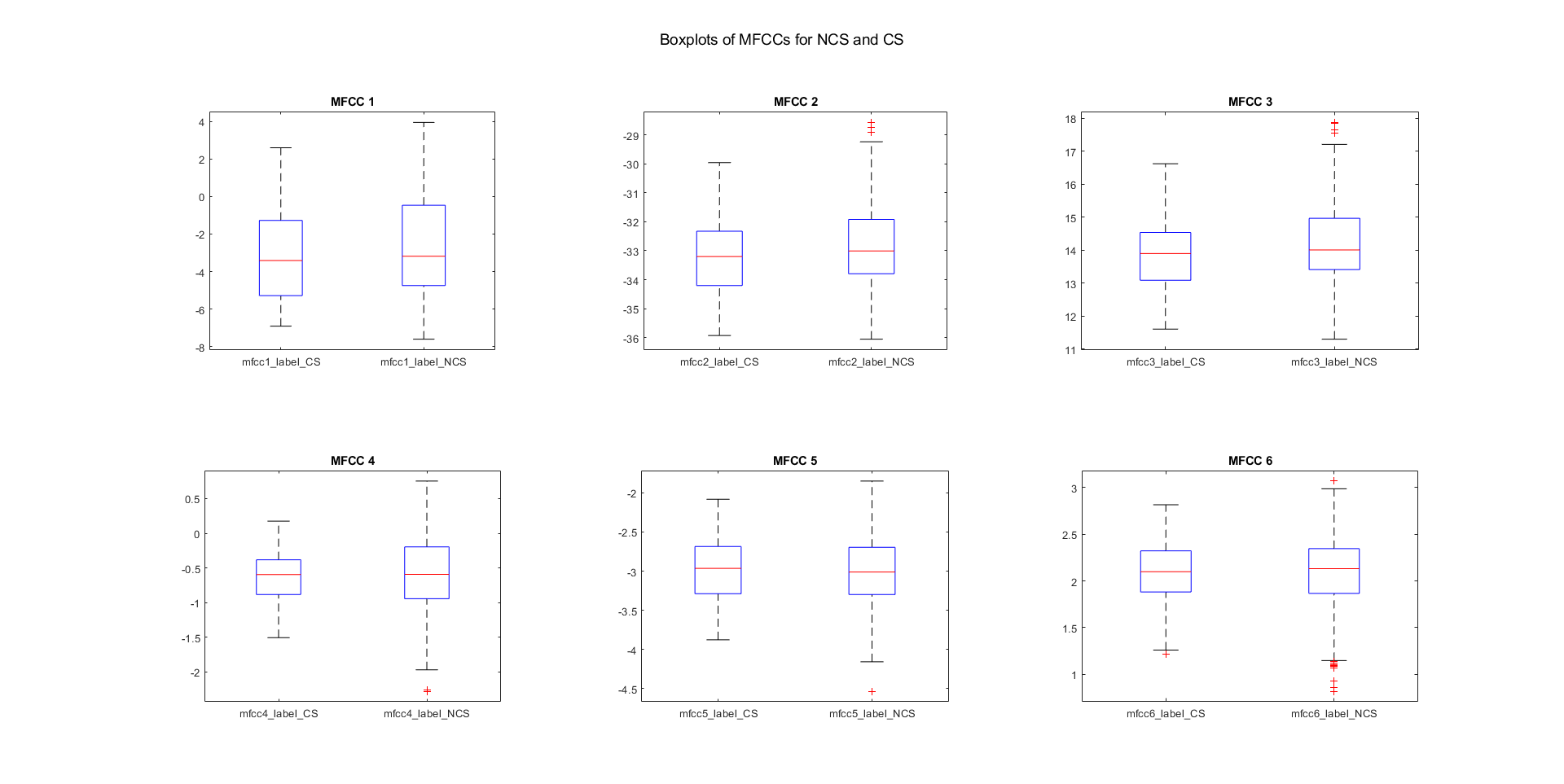
# Annex 2

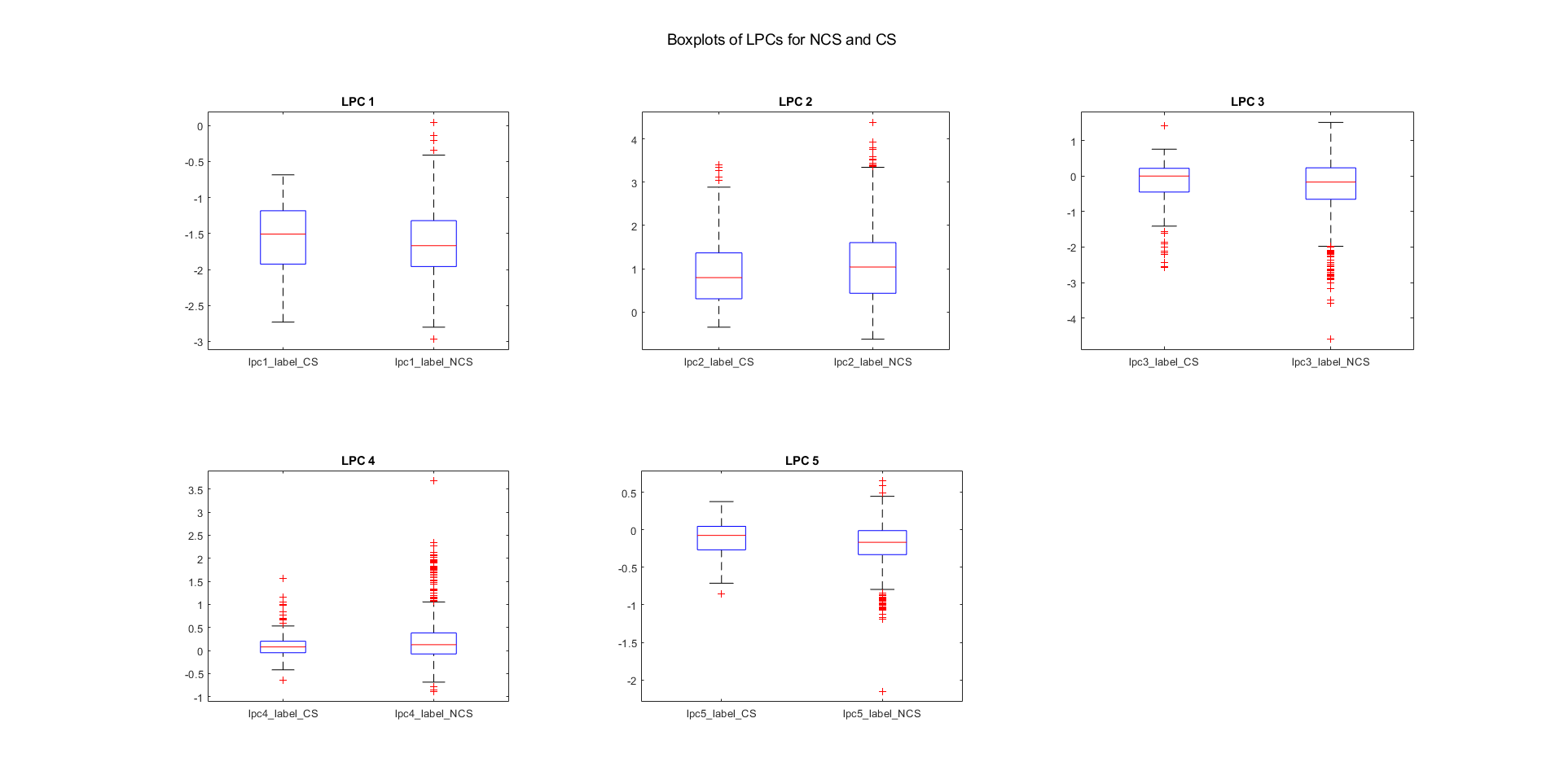
Faire une timeline avec ce que j’ai effectué durant mon stage.

# Annex 3

Boxplots to know what features will be the most appropriate for differentiating CSs and NCSs.

Mettre aussi premiere figure



**

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