Internship Report

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# Glossary

SRT :

RDS :

CS : Crying Segment

NCS: Non-Crying Segment

# 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 the first two months of my internship, I first met her every week by videoconference. From August, she returned  [partially](https://www.linguee.fr/anglais-francais/traduction/partially.html) to work which allowed me to see her more often.

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 most often with her.](https://www.researchgate.net/institution/Monash_University_Australia)

## 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)

The neonates’ immaturity affects many areas, 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. Surfactant is a liquid produced by the lungs that plays a key role by reducing the surface tension between liquid and air in each alveolus. 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.[[4]](#endnote-5)



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>

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. [[5]](#endnote-6)

### 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.

First and foremost, all enfants who have breathing problems need **respiratory supports**. Different aids 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

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 **surfactant replacement therapy (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[[6]](#endnote-7). *When should it be used? What dose to inject?* Indeed, it is not always well seen to put a foreign substance in a very fragile baby. 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

### The 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). Indeed, lung acoustics reflect lung volume and then their analysis is essential to know more about the treatment consequences. My internship 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.

### The Experiment

#### Available Tools

Different tools can be used to record the sound of the lungs, which all has advantages and disadvantages. The tool choice is very important, on the one hand for the smooth running of the experience and the health of the baby, and on the other hand for the sound recorded quality. Arrabella made a state of the art of these various tools summarized in the table in Annex 1.

There is no « gold standard” device to asses lung parameters[[7]](#endnote-8), but the **Digital Stethoscope (DS)** known as Clinicloud (Pty Ltd, Melbourne, Australia) was finally chosen. 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 can be converted back to sound waves for listening.[[8]](#endnote-9)

A stethoscope is normally used by a doctor to listen. But respiratory deficiency diagnoses are very difficult and remain rather subjective, depending on the doctors’ experience and ability. Even if electronic auscultation has yet to find clinical acceptance, the electrical signals of the stethoscope will be recorded so that they can be analyzed.

#### Considerations and Constraints

The signals quality depends on the conditions in which the sound is recorded. Recording respiratory signals on premature newborns creates a number of constraints, which will then have to be taken into account.

**Population:** The samples need to be recorded for neonates delivered at Monash Medical Center during the recruitment period (from March to August 2019), with a gestational age between 24 and 32 weeks inclusive whose parents have given informed consent to involvement in the study.

**Safety considerations:** Premature newborns are very fragile beings. To lessen the risk of infection, the medical team need to take all the precautions that are necessary. Indeed, the Digital Stethoscope has the potential to introduce pathogens into the neonates' environment. To limit the risk of contamination and because the experience should not encroach on the health of the baby, only one recording is allowed. The quality of the sound can therefore be very variable.

**Ambient noise**: A close eye is kept on preterm neonates, especially when they have a respiratory deficiency. For this reason, the hustle and bustle of nurses and doctors are often present. The respiratory support used by the baby will also have a significant impact on his breathing sound. And finally, although premature newborns cry less than neonates at term, crying sections are heard in almost all recordings.

### The Sound Analysis

#### Breathing Sounds Generalities, A FAIRE

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4518345/>

* Ses caractéritiques avec des nombres
  + Breath sound has three characters; frequency, intensity, and timbre or quality.
* Niveau de la recherche là-dedans

#### Adventitious lung sounds: Wheezes Crackles Squeak Pleural rub Stridor

#### The Recordings

Recordings will be done 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 was chosen because it is at this point that we can determine if the child has a Chronic Lung Desease (CLD).

**Birth**

Days 4 to 6

Day 28

Day 2

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

Recording

Recording

The bank of signals is composed of twenty recordings, all between 24 and 32 weeks of gestation, who have a Respiratory Distress Syndrome and who requires a Surfactant Replacement Therapy.

As explained in section 1.3.2.2, the signals have a variable quality, which depends on the ambient noise. In general, the signals recorded on Day 2 are noisier than the ones on Day 28.

FAIRE UN SCHEMA COMME MATTHIEU AVEC LES RECORDINGS ET LEUR NOMBRE ET D’OU ILS PROVIENNENT. Rq : Je n’ai eu acces à ca qu’a la fin de mon stage car il fallait être blinded.

#### The Stages of Analysis

My goal was to assist the medical team in the analysis of the raw audio recordings. I was blinded to patient clinical data, surfactant administration and the timing of recordings. But label on the respiratory supports? The analysis of the raw recordings involves three stages.

The **preprocessing** part is essential in this study. Depending on the type of baby's respiratory support, on the neonates’ crying and on background noise due to the doctors' discussions, the quality of recordings is very variable, but should not influence the results.

The **features extraction** is then the heart of the project, as that will allow to deduce some properties on the Surfactant Replacement Therapy. A large number of features were extracted and gathered in an Excel file to allow the medical team to do statistical studies.

Finally, a **classification** was do ne to predict outcomes like CLD or no CLD.

# Pre-processing

The pre-processing part was essential in this project due to the signals bank diversity. Crying sections, heartbeats, artefact created by the movement of the stethoscope diaphragm on the infant chest, breathing supports and noises due to talks and machine beeps are factors to consider before extracting features. Indeed, they change from one recording to another and can influence the respiratory sounds detected. Attention ne mettre que ce que je traite

## Methods

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.

### 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.

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

### Crying removing

#### Learning features on crying sections

Base d’apprentissage et base de test

**Labelling the crying sections thanks to annotators**

The first step was to label the signals with ‘Crying sections’ (CS) and ‘Non-Crying sections’ (NCS). This was done by 3 annotators on the entire signal basis. Independently, Lindsay, Arrabella and I listened to the different samples and annotated them on Audacity. The labels were extracted as text files.

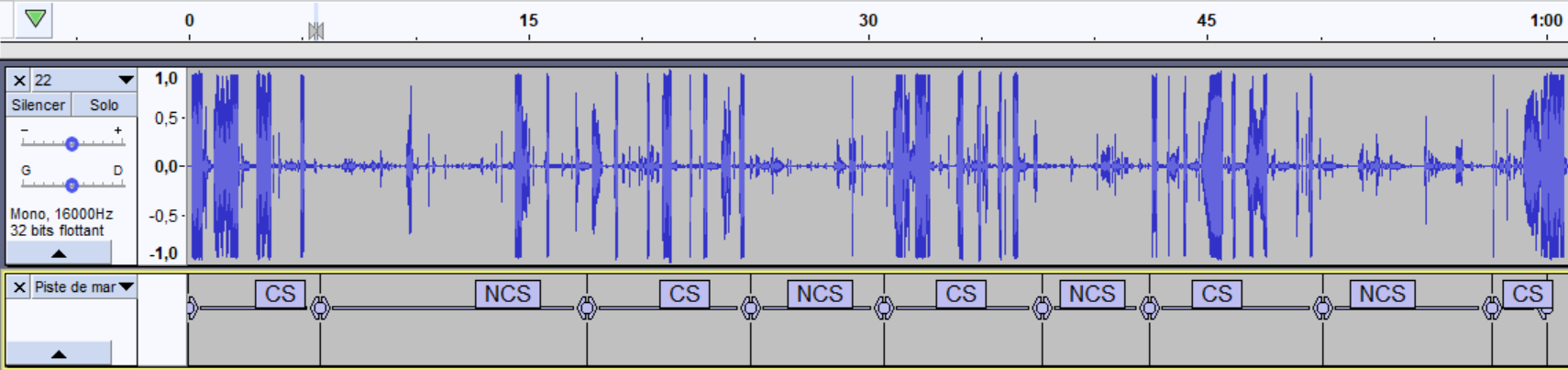


Figure 4: Julie's annotations of signal 22 on Audacity

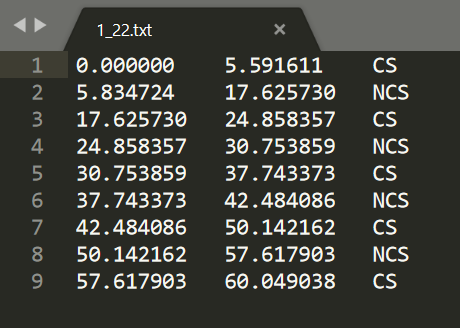


Figure 1: Text file generated by Audacity after Julie's annotations on signal 22

Each text file follows a strict name structure: ObersatorID\_SampleID. Every line corresponds to a CS or NCS, with the beginning and end time of the section (cf figure 5).

These files are read one by one in MATLAB, with the aim of creating a vector of 0 and 1, respectively corresponding to the NCS and CS labels. In order to reduce the computation time, a moving average with a 1-second window and a 25% overlap was applied. The window was chosen based on the duration of CS, which is often more than 1 second.

The level of agreement between the annotators was then measured on each signal using Fleiss’ KAPPA. It is a statistical measure which assesses the [reliability of agreement](https://en.wikipedia.org/wiki/Inter-rater_reliability) between a fixed number of raters when assigning [categorical ratings](https://en.wikipedia.org/wiki/Categorical_rating) to a number of items. In the project, three raters (Arabella, Lindsay and I), two categorical ratings (CS/NCS) and sixty items (60 sections of 1 second) were used to find a Fleiss’ KAPPA coefficient for each signal. A KAPPA coefficient equal to 0 means no agreement, while 1 means perfect agreement. The detailed calculation of this coefficient can be seen in annex … . It was implemented on Matlab using a function in the Matlab File Exchange [[9]](#endnote-10) . Mettre sa valeur ici?

Finally, each CS with a 2/3 or 3/3 agreement has been retained. The figure 5 illustrates the final annotated labels of signal 22.

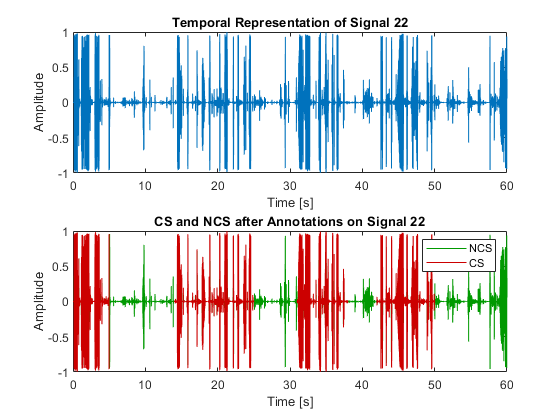


Figure 5: Annotated CS and NCS of Signal 22

**Analysis of differences between CS and NCS**

Once the theoretical labeling of the signals has been done, it is necessary to learn how to detect CSs. In order to know which characteristics will be most appropriate for the detection of CSs, a first study has been done. It is based on box plots illustrating the differences between NCS and CS on different common characteristics in signal processing (voir annex 3). faire liste des features?

Finally, with the help of the spectrogram, it was decided that the Power Ratio could be enough to differentiate the CS and NCS. Indeed, the difference is …. (cf figure …), IIICIIIIII

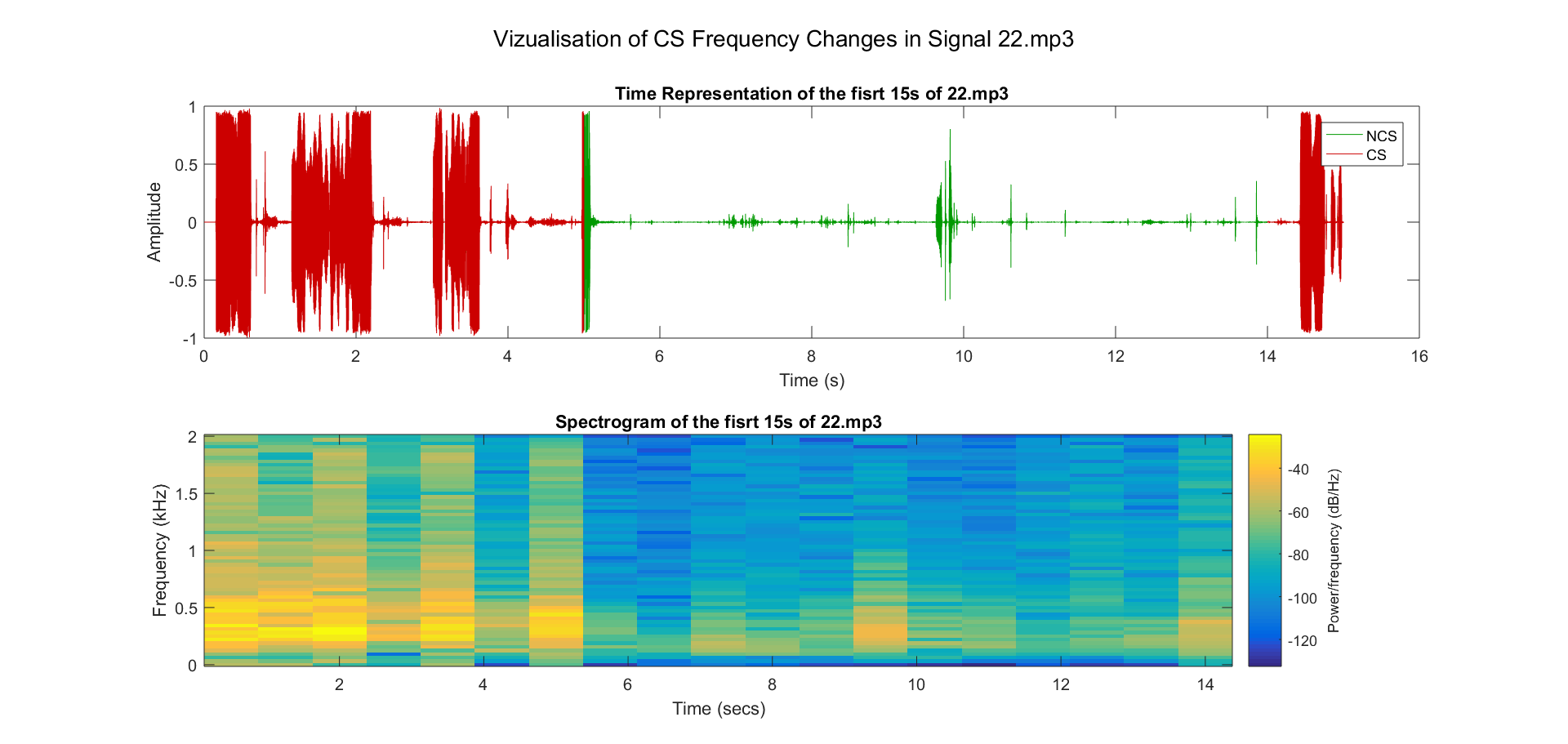
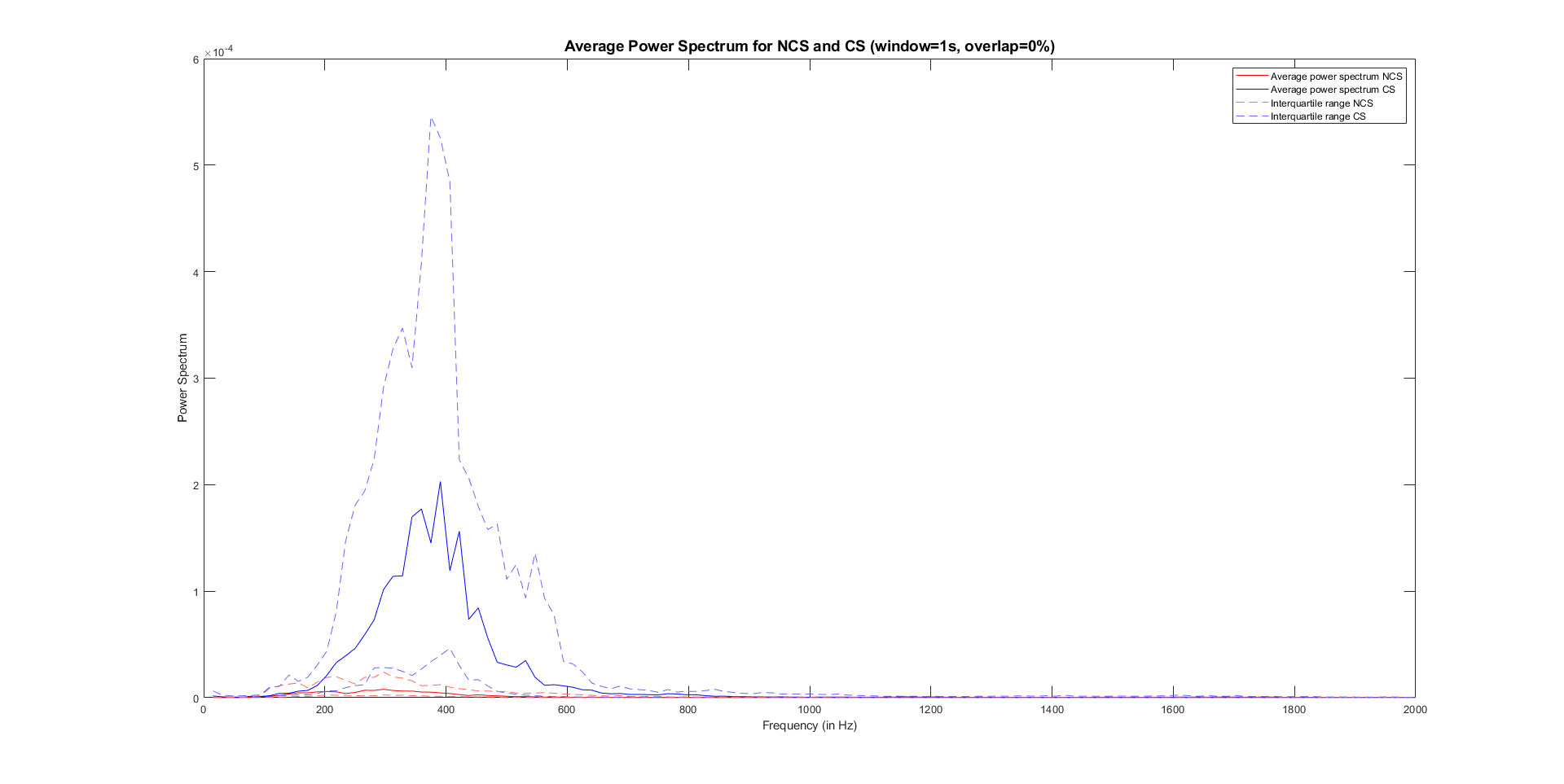


Figure 6: Vizualisation of CS Frequency Changes in the first 15s of Signal 22

On a extrait de segments CS et NCS differentes features : + spectrogram

Cela a permis de voir ou est-ce qu’on pouvait avoir les plus grandes différences. On a choisi de garder le mean power ratio. A METTRE MIEUX EN PLUS GRAND LES TEXTES



**Cross validation**

[**https://machinelearningmastery.com/k-fold-cross-validation/**](https://machinelearningmastery.com/k-fold-cross-validation/)

**Sources:** Page 184, [An Introduction to Statistical Learning](http://amzn.to/2FkHqvW), 2013.

Cross-validation is a statistical method used to estimate the skill of machine learning models.

**k-Fold Cross-Validation**

Cross-validation is a resampling procedure used to evaluate machine learning models on a limited data sample. The procedure has a single parameter called k that refers to the number of groups that a given data sample is to be split into.

The general procedure is as follows:

1. Shuffle the dataset randomly.
2. Split the dataset into k groups
3. For each unique group:
   1. Take the group as a hold out or test data set
   2. Take the remaining groups as a training data set
   3. Fit a model on the training set and evaluate it on the test set
   4. Retain the evaluation score and discard the model
4. Summarize the skill of the model using the sample of model evaluation scores

Importantly, each observation in the data sample is assigned to an individual group and stays in that group for the duration of the procedure. This means that each sample is given the opportunity to be used in the hold out set 1 time and used to train the model k-1 times. (**Sources:** Page 184, [An Introduction to Statistical Learning](http://amzn.to/2FkHqvW), 2013)

**Configuration of k**

The k value must be chosen carefully for your data sample. **Representative**: The value for k is chosen such that each train/test group of data samples is large enough to be statistically representative of the broader dataset.

<https://en.wikipedia.org/wiki/Cross-validation_(statistics)>

Exhaustive cross-validation: Exhaustive cross-validation methods are cross-validation methods which learn and test on all possible ways to divide the original sample into a training and a validation set.

#### Removing the crying sections

2 seuils

Cross validation (with leanring base and validation base)

### Noise Filtering

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[[10]](#endnote-11) 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) 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

## Results

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

## Discussion

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

# 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.

## 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[[11]](#endnote-12).

**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

# Classification

## Methods

## Results

## Discussion

# Conclusion

**Birth**

Days 4 to 6

Day 28

Day 2

# 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>

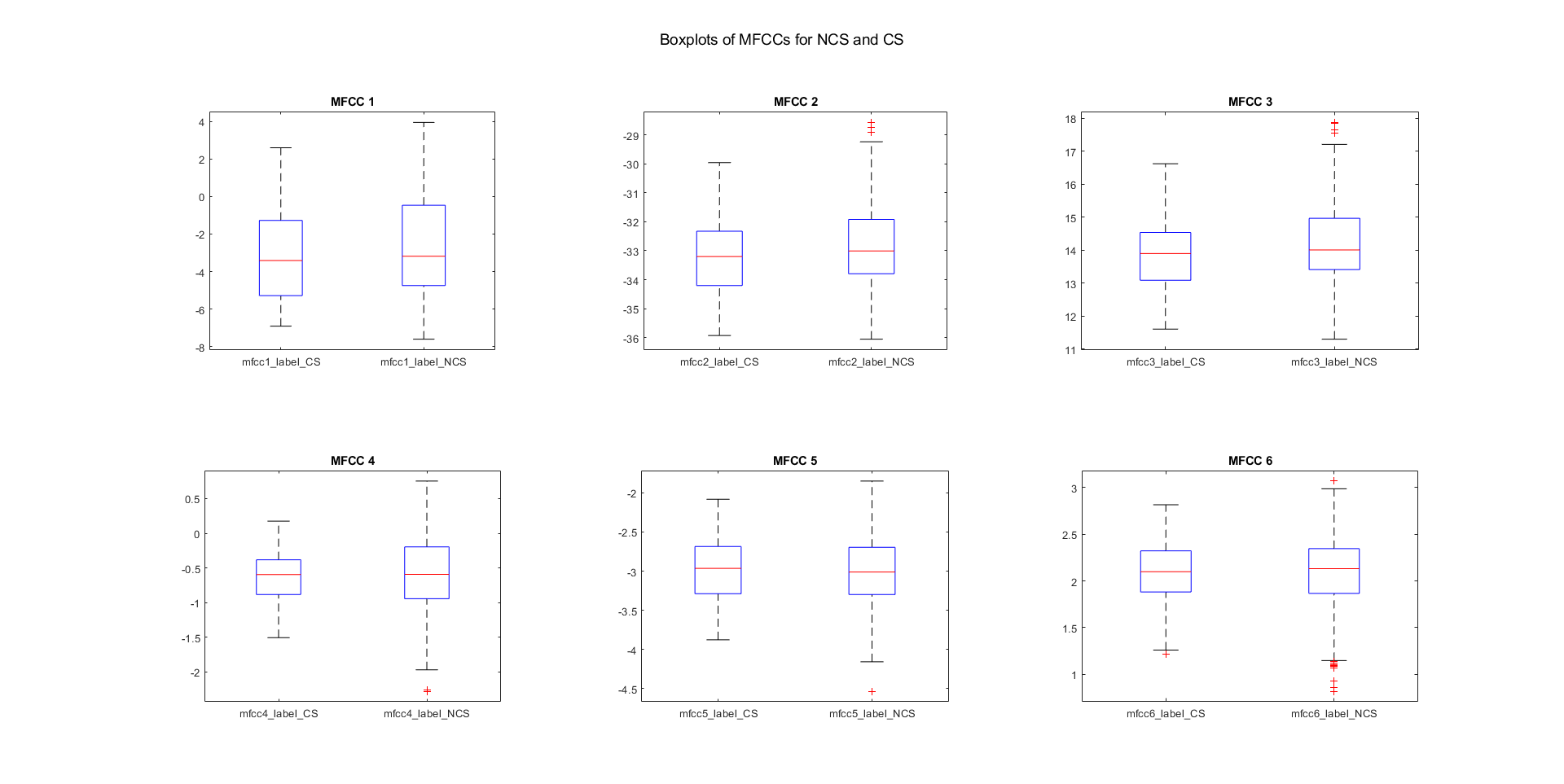
# Annex 2

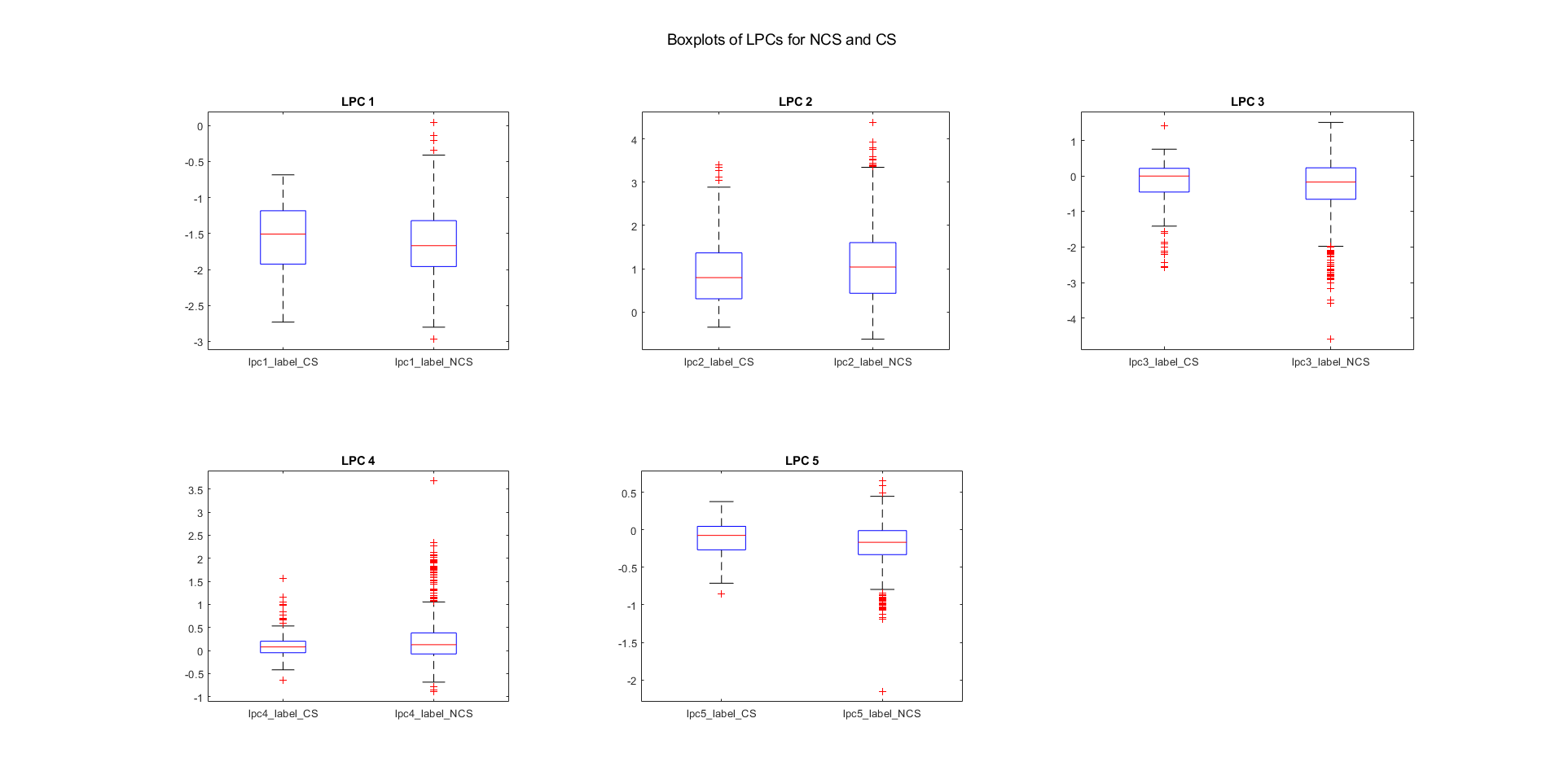
Faire une timeline avec ce que j’ai effectué durant mon stage.

# Annex 3

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

Mettre aussi premiere figure



**

# References

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