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# Abstract

Abstract text

# Chapter 1

## Introduction

A recent study estimated that over 900 million adults globally are affected by the common group of respiratory sleep disorders called Sleep-disordered breathing (SDB) [1], or in particular, Sleep Apnea, which clinical manifestations include sleepiness, fatigue, cardiovascular disease, and hypertension. SDB is even linked to higher cases of diabetes, stroke occurrences and increased morbidity [2, 3, 4]. Diagnosis of the disorder relies on detecting repeated respiratory events in which airflow is either reduced (hypopnea) or entirely paused (apnea) during sleep [2, 5]. These events can further be categorized into obstructive or central origin, depending on if the apnea happens due to a physical blockage of the upper airway or if caused by the brain failing to signal breathing resulting in missing breathing effort. In case the event shows features of both, it is classified as a mixed. Dividing the number of events by the total sleep time (TST) gives the Apnea-Hypopnea-Index (AHI), which indicates the severity of the disorder.

Gold standard for detecting SDB in Polysomnography (PSG) which captures physical and biological signals like heart (electrocardiogram, ECG) and brain (electroencephalogram, EEG) activity, airflow, peripheral oxygen saturation (SpO<sub>2</sub>), chest and abdominal movements, sleeping position, and blood volume changes (photoplethysmographie, PPG). This approach comes with a few downsides: Firstly, due to the vast amount of sensors and specialized equipment, setup and analysis of the full PSG is costly, requires human experts and might impact sleep quality. Secondly, looking only at a single night might have low diagnostic meaningfulness [6] and the analysis of multiple nights is needed. All this contributes to the fact that an estimated 93% of women and 82% of men with at least moderate SDB are undiagnosed [7].

In 2000, PhysioNet started interest in the topic of less complex apnea detection by holding a competition on their Apnea-ECG Dataset that only consists of labeled ECG recordings split into one-minute epochs. Although presented

models reached high performances, later studies showed poor generalizability for these models and indicated that the dataset doesn't fully cover the broad spectrum of apneic events [8]. Therefore, in the last decades, a wide range of sleep disorder datasets and apnea detection architectures were published that focused on generalizability. For instance, Olsen et al. [9] used bidirectional GRUs on ECG data to achieve a sensitivity (Se) of 68.7%, a precision (Pr) of 69.1%, and an F1-score of 66.6% on their self-defined event-level metric and an AHI-correlation of  $R^2 = 0.829$ . Xie et al. [10] later validated Olsens model on the SOMNIA dataset and achieved an F1-score of 70.8% using the PSG-computed hypnogram and an F1-score of 0.631 with their Multi-Task model that computed sleep stages based on ECG and respiratory effort (RE) only [11]. Also using ECG and RE, Fonseca et al. [12] achieved intraclass correlation coefficient of 0.91 across different datasets.

Using the signal on which sleep apnea is mainly defined on, Airflow, also helps to increase performance greatly. Li et al. [13] achieved an F1-score of 85.7% on classifying one-minute segments of Airflow and ECG. Later, Yook et al. [14] used Airflow and SpO2 together to achieve an F1-score of 93% on classifying 10-second segments converted into scalograms. Downsides to this approach includes that the nasal cannula, a thin tube placed under the nostrils, might be uncomfortable during sleep and hard to set up properly.

One of the more simple signals to set up and record while sleep is PPG, which can be obtained through the use of a pulse oximeter that illuminates the skin to measure changes in light absorption. These devices come in a range of forms such as wrist-worn, like most modern smart-watch already have, or finger-worn, mounted typically on the index finger, which can also calculate SpO2. Lazazzera et al. [15] used PPG and SpO2 signals to achieve a Sensitivity of 76.9% and Specificity of 73.2%, although their dataset only consisted of 96 patients without any kind of co-morbidity. With the same input signals, Wu et al. [16] trained a transformer-based model on a dataset containing patients with co-morbidities and were able to validate their performance on PPG and SpO2 signals measured by a Smart Ring resulting in an F1-score of 64.9%.

In this work, we present an event-level apnea detection model that relies solely on signals obtained by easy to use recording hardware, namely PPG and SpO2, and show the importance of correct sleep stage identification.

# Chapter 2

## Methods

### 2.1 Dataset

The data we used in this work came from the Multi-Ethnic Study of Atherosclerosis (MESA) [17], a large-scale sleep study aimed to investigate correlations between sleep quality, cardiovascular health, SDB, and other factors across different ethnic groups. Over 6,800 men and women from six different US communities were approached in the initial examination. For the final sleep exam ten years later, 288 participants were ineligible<sup>1</sup>, roughly 2,700 were not contacted, and roughly 1,500 refused to participate. From the 2,261 participants undergoing the sleep exam, 2,060 had full-night PSG recordings, 2,156 had actigraphy data, and 2,240 completed a sleep questionnaire.

For the sleep event scoring, we used the automatic Somnolyzer system **TODO: cite**, which scored events based on the recommended criteria from the American Academy of Sleep Medicine (AASM) **TODO: cite**: apnea events were defined as a 90% or greater reduction in airflow for at least 10 seconds, while hypopnea events were defined as a 30% or greater reduction in airflow for at least 10 seconds, with either a  $\geq 3\%$  oxygen desaturation or an associated arousal. **TODO: obstructive vs central vs mixed?**

As SDB events manifest differently across sleep stages, we used a modified version of the hypnogram prediction model from Bakker et al. [18], that used only PPG signals, ensuring that our model works doesn't depend on signals outside of the finger-worn PPG sensor setup. Comparing the predicted hypnogram<sup>2</sup> with the Somnolyzer hypnogram, we achieved a Cohen's Kappa of 0.55,

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<sup>1</sup>due to undergoing apnea treatment, living too far away, or other reasons

<sup>2</sup>Bakker's model combined N1 and N2 stages into one, resulting in four stages: Wake, N1/N2, N3, and REM. For calculating the Kappa, Somnolyzer scorings were adjusted to the same format

Fold	N	Age (years)	BMI ( $kg/m^2$ )	Sex (N male)	TST (h)
1	470	$70 \pm 9$ [55, 90]	$29 \pm 5$ [19, 48]	228 (48.5%)	$6.2 \pm 1.36$ [1.7, 10]
2	470	$70 \pm 9$ [54, 90]	$29 \pm 6$ [17, 56]	208 (44.3%)	$6.2 \pm 1.36$ [1.6, 10]
3	470	$69 \pm 9$ [55, 90]	$29 \pm 5$ [16, 50]	229 (48.7%)	$6.2 \pm 1.47$ [0.7, 10]
4	470	$69 \pm 9$ [55, 90]	$28 \pm 5$ [17, 50]	210 (44.7%)	$6.2 \pm 1.32$ [0.9, 10]
Full	1880	$69 \pm 9$ [54, 90]	$29 \pm 6$ [16, 56]	875 (46.5%)	$6.2 \pm 1.38$ [0.7, 10]

Table 2.1: Demographic distribution and sleep times of the MESA dataset subset. Format for Age, BMI, and TST is mean  $\pm$  std [min, max].

showing moderate agreement.

Filtering the MESA participants for those with PPG and SpO2 data, Somnolyzer scorings, and available predicted hypnograms, we ended up with a dataset size of 1,880 participants. Table 2.1 shows the demographic distribution and sleep times of our dataset subset together with the generated folds. To assess SDB severity, the AHI is often categorized into four classes. These so called severity classes are defined as follows: Normal ( $AHI < 5$ ), Mild ( $5 \leq AHI < 15$ ), Moderate ( $15 \leq AHI < 30$ ), and Severe ( $AHI \geq 30$ ). Table 2.2 shows their distribution. The amount of different apnea classes is shown in table 2.3.

## 2.2 Signals and Preprocessing

We used the PPG and SpO2 signals from the MESA dataset, which were recorded at 256Hz and 1Hz, respectively. A third input to the model is the hypnogram from Bakker et al. [18], which was predicted at  $\frac{1}{30}$ Hz and on PPG only, ensuring that the model still relies solely on data it can retrieve from the PPG sensor in the real world. The PPG signal has been denoised using a lowpass filter with a cutoff frequency of 5Hz.

To analyse the importance of correct sleep stage information, we also tested a version of the model that uses the "ground-truth" Somnolyzer hypnogram instead of the predicted one.

Fold	AHI	Severity Class			
		normal	mild	moderate	severe
1	$22.2 \pm 18.3$ <b>[0.4, 100]</b>	61	153	136	120
2	$22.0 \pm 18.3$ <b>[0.3, 93]</b>	61	151	134	124
3	$21.3 \pm 17.1$ <b>[0.4, 95]</b>	61	151	138	120
4	$22.0 \pm 18.3$ <b>[0.4, 107]</b>	61	150	140	119
Full	$21.9 \pm 18.0$ <b>[0.3, 107]</b>	244	605	548	483

Table 2.2: AHI and severity class distribution accross folds and full dataset subset. **TODO: better use [25%,75%] interval instead of [min, max]?** Format for the AHI is mean  $\pm$  std [min, max].

Fold	obstructive apnea	central apnea	mixed apnea	hypopnea
1	15k (24%)	4k (7%)	1k (2%)	42k (67%)
2	16k (26%)	4k (6%)	1k (2%)	42k (66%)
3	15k (24%)	3k (6%)	1k (2%)	41k (67%)
4	17k (26%)	4k (6%)	1k (2%)	42k (66%)
Full	63k (25%)	16k (6%)	5k (2%)	167k (67%)

Table 2.3: Total number of apnea events per fold and in total. Important to note is the imbalance of the different apnea types, especially the underrepresentation of central and mixed apnea.



## PPG Preprocessing

To deal with the high temporal resolution of the PPG signal, we tested three different preprocessing methods that would transform the 256Hz signal into a 1Hz signal with multiple dimensions:

- **Statistical:** On a 1Hz basis we extracted the mean, standard deviation, minimum, maximum, and mean peak interval of the PPG signal, resulting in a 5-dimensional representation of the PPG signal. Due to the nature of PPG showing the heartbeats at 1Hz, we used a sliding window of 5s around the 1Hz point to calculate the statistics.
- **Variational Autoencoder:** The Variational Autoencoder (VAE) is an unsupervised generative model that learns to encode the input data into a lower-dimensional latent space and then reconstruct it back to the original space. The VAE consists of an encoder and a decoder, where the encoder maps the input data to a distribution in the latent space, and the decoder samples from this distribution to reconstruct the input. Using the same sliding window approach as in the statistical method, we trained the VAE to reconstruct the middle 1s from the 5s input window. With that, the encoder learns to compress the input into a lower temporal dimension while preserving the relevant information. For training the main SDB detector model, this encoder is used to transform the 256Hz PPG signal into a 1Hz signal with 8 dimensions.
- **In-model Convolution Stack:** While the prior methods calculated the 1Hz representation of the PPG signal before training the model, we also tested a method that would use a stack of convolution to learn the 1Hz representation during training. The convolution stack consists of five *double conv blocks* **TODO: is the name ok so?**, which are composed of two 1D convolution layers with a kernel size of 3 or 5 **TODO: write letters out or not?**, each followed by a batch normalization layer and ReLU activation. Between these blocks are max pooling layers with a kernel size of 4 resulting in the downsampling of the signal to 1Hz, while bringing the number of channels up from 1 to 8. **TODO: should I explain the whole model and every single line in more detail in the appendix?**

Each preprocessing method brings the PPG signal down to 1Hz with multiple dimensions, which is then stacked together with the 1Hz SpO2 signal and the

hypnogram that was upsampled to 1Hz. The input to the detection model is therefore a 1Hz signal with  $2 + d$  dimensions, with  $d$  being the number of dimensions from the selected PPG preprocessing method(s).

## 2.3 Model Architecture

The core of the detection model is an adapted version of the U-Net architecture, originally proposed for 2D image segmentation by Ronneberger et al. [19]. The U-Net architecture improves an encoder-decoder structure by adding skip connections between the corresponding encoder and decoder layers, which allows the model to learn both low-level and high-level features **TODO: stolen formulation**. The adapted model uses 1D convolutions on the temporal dimension instead of 2D convolutions on the width and height of images. The output of the U-Net has the same resolution as the input, which allows the model to classify each second as either part of an event or of normal breathing. This in turn allows us or the user to analyse the prediction on a event level, instead of just the AHI level, which can be important, as studies showed links between apnea event duration and health that go beyond the AHI severity classifications [20]. **TODO: create a model figure. how detailed should it be? show the complete u-net? TODO: channel sizes and temp resolution through the data flow**

### Attention mechanisms

Our model can leverage three types of attention:

- **Self-Attention in the bottleneck:** The self-attention mechanism, originally proposed by Vaswani et al. [21], computes relevance vectors for each input feature through their query (Q) and key (K) matrices. By multiplying this vector with the value matrix (V), the model learns long-range dependencies throughout the sequence, making it possible to focus on the important parts of the input data. The self-attention mechanism is computed as:

$$\text{Attention}(Q, K, V) = \text{softmax} \left( \frac{QK^T}{\sqrt{d_k}} \right) V \quad (2.1)$$

where  $d_k$  is the dimension of the key matrix and the softmax function normalizes the attention scores, ensuring that they sum to 1. Using Self-Attention can increase model complexity greatly due to their quadratic

complexity, which is why we apply it in the bottleneck, where the temporal resolution is at its lowest.

- **Attention gates:** Originally proposed for the task of medical pancreas image segmentation by Oktay et al. [22], attention gates are employed at the skip connections of the U-Net and help the model highlight important regions while suppressing irrelevant ones. They work by learning a gate that refines the skip connection (encoder) features before concatenation. This gate is computed from the same incoming skip connection features and the decoder features from the layer below. **TODO: add the formula?**
- **Squeeze-and-Excitation (SE) blocks:** The SE block, proposed by Hu et al. [23], is a lightweight attention mechanism that computes channel-wise feature importance. It works in two parts: First, the squeeze operation creates feature maps across the spatial dimensions using global average pooling, resulting in a 1D vector for each channel. Then, in the excitation part, two fully connected linear layers with ReLU activation transform this vector and multiply it with the input, effectively weighting the channels by importance. **TODO: add the formula?**

**TODO: talk about complexity impact? quadratic in time, quadratic in channels**

## 2.4 Training and Evaluation

### Cross-Validation

To ensure statistical validity, we used a fixed seed of 42 and a 4-fold cross-validation approach balanced for AHI severity class. In k-fold cross-validation, the dataset is split into k equal parts (called folds). One then selects one fold as the test set and train the model on the remaining k-1 folds. This process is repeated k times, each time with a different fold as the test set, and the results are averaged to obtain a more reliable estimate of the model’s performance. This approach helps to mitigate the risk of overfitting and provides a more robust evaluation of the model’s generalization ability. As seen in Tables 2.1, 2.2, and 2.3, the folds are not only balanced for AHI severity class, but also show a good distribution of demographic data.

## Training Parameters and Setup

The training targets are one-dimensional vectors with the same length as the input sequence, where each second is labeled as either 0, indicating normal breathing, or 1, indicating an apnea event. The final layer of the model is a sigmoid activation function, that maps each second to an event probability value between 0 and 1. During training, we optimize the binary cross-entropy loss<sup>3</sup> (BCE) between the predicted probabilities and the true labels. The BCE loss is defined as: **TODO: formula** The loss is then averaged over each batch and parsed to the optimizer, in our case the Adam optimizer with a learning rate of 0.001 **TODO: explain Adam maybe?**.

As for batching, we used randomly selected 32 30-minute segments from four different recordings each to mitigate batch overfitting on sleep patterns of a single participant **TODO: table with memory usage**.

During testing, we used a sliding window approach, where each recording was split into 30-minute segments with a 2-minute overlap **TODO: graphic explaining this**. Model predictions were then concatenated, disregarding each first and last minute to create the final prediction for the whole night. This approach allows us to predict recordings of arbitrary length, on which metrics like the AHI can be calculated.

Each fold has been trained on a single NVIDIA A40 GPU with 48GB VRAM with a time limit of 2 days for 30 epochs.

## Evaluation Metrics

Several metrics are employed to measure the performance of the model, that can be divided into three categories:

### A. Event-level metrics

To assess the model performance on an event level, regardless of the length of the night, we use the event-level metrics. They are calculated by extracting events from the predicted probabilities by thresholding the probabilities and counting each consecutive sequences of 1s as a single event. To mitigate outliers, we disregarded events shorter than 3 seconds and combined consecutive events that

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<sup>3</sup>specifically, we use PyTorch's **TODO: do I need to cite?** `nn.BCEWithLogitsLoss()`, which combines the sigmoid activation and BCE loss into one class, as it is more stable than doing these operation in sequence.

are less than 3 seconds apart into one event **TODO: is this correct for the final results?**.

Olsen et al. [9] defined scoring rules on the event-level that are defined as follows: A predicted event, that overlaps with a true event, gets classified as a true positive (TP). If a predicted event has no overlapping true event, it gets counted as a false positive (FP). If a true event doesn't overlap with any predicted event, it gets counted as a false negative (FN). Note that there are no true positives (TP) on the event-level. In this work, we use a more strict version of their rules, that were adjusted by Xie et al. [10], and in which each event can only be used for scoring one time. Meaning that if a predicted event overlaps with multiple true events, only one true event gets counted as TP, while the others are counted as FN. The same applies the other way around, where a true event can only be counted as TP once and other overlapping predicted events are counted as FP. A visual example can be seen Figure **TODO: Add figure from Jiali paper**. From this, we can now compute the following metrics:

Metric	Calculation	Meaning
Recall (Rec)	$\frac{TP}{TP+FN}$	What % of real events got detected?
Precision (Pr)	$\frac{TP}{TP+FP}$	What % of predicted events where real events?
F1-score	$2 * \frac{Pr * Re}{Pr + Re}$	Harmonic mean of Precision and Recall

As these metrics depend on the selection for a proper threshold, we **TODO: we or we'll?** show these metrics as a function of the threshold **TODO: also AUC under F1-curve?? unusual as normally AUC for TPR and FPR which uses TN**.

## B. AHI-level metrics

Dividing the total number of apnea events by the TST (in hours) gives us the most common metric for SDB severity, the AHI. We compare the predicted AHI ( $AHI_{pred}$ ) and the Somnolyzer AHI ( $AHI_{true}$ ) using the following metrics:

- Plotting  $AHI_{pred}$  against  $AHI_{true}$  shows their correlation which can also be expressed in the **Root Mean Square Error** (RMSE) and the **TODO:**

$R^2$ , what is up with Olsens Paper?  $mx+b$ . RMSE is calculated as:

$$RMSE = \sqrt{\frac{1}{n} \sum_{i=1}^n (AHI_{pred} - AHI_{true})^2} \quad (2.2)$$

where  $n$  is the number of samples (or AHIs in our case).

- The **Bland-Altman plot** is another way to visualize agreement by plotting the difference between the two AHI values against their mean **TODO: should I cite these?**. This allows us to see the bias, defined as the mean difference, and limits of agreement, defined as the bias  $\pm 1.96$  times the standard deviation of the differences. The limits of agreement are the range in which 95% of the differences between the two AHI values are expected to fall.
- The **Spearman’s rank correlation coefficient** ( $\rho$ ) ignores the actual values of the AHIs and only looks at their ranks. This is useful for measuring the strength of the monotonic relationship between the two AHI values, regardless of their actual values **TODO: formula?**. The coefficient ranges from -1 to 1, where -1 indicates a perfect negative correlation, 0 indicates no correlation, and 1 indicates a perfect positive correlation.
- Finally, we also calculated the **Intraclass Correlation Coefficient** (ICC) **TODO: what is it? which one do we use? how is it computed maybe?**

### C. Severity-class-level metrics

The last set of metrics we used is the severity-class-level metrics, which are calculated on the AHI severity classes. As mentioned, the boundaries for the severity classes are defined as follows: Normal ( $AHI < 5$ ), Mild ( $5 \leq AHI < 15$ ), Moderate ( $15 \leq AHI < 30$ ), and Severe ( $AHI \geq 30$ ). As small errors in the AHI around these hard thresholds can lead to a wrong classification, we used near-boundary double-labeling (NBL), which allows us to assign two classes for AHIs that fall in the range of about 2.5 around the boundaries. Exact values can be found in **TODO: appendix**.

Using these four classes we can plot the confusion matrix and compute model **Accuracy** (Acc), defined as the number of correctly classified patients divided by the total number of patients, and the **Cohen’s Kappa** ( $\kappa$ ) **TODO: what is it? how is it computed?**.

Finally, this matrix can be binarized to assess the discrimination ability between normal to abnormal (mild-severe), mild to moderate, and moderate to severe SDB. **TODO:** should I create a table explaining all (Acc, Sen, Spe, PPV, NPV, LR+, LR-) metrics again or is LR enough?

## Chapter 3

# Results

- Baseline Model vs PPG Preprocessing vs Attention Model Results
- PlethPre reduced training time of detection model by 3x
- Significance of SpO2 and the Hypnogram (No SpO2/Hypnogram, Only PPG Baseline Model)
- AHI correlations and Severity class results



## Chapter 4

# Discussion

- Discussion and Implications (Is this way applicable in the real world)
- Limitations
- Further work

## Chapter 5

# Conclusion

- Summerization of paper
- Significance of work
- Outlook

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