

Airflow-Oximetry Combined Signal Based Automatic Detection of Sleep Apnea in Adults

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the degree of

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Certificate of Original Authorship

I, Md Bashir Uddin declare that this thesis is submitted in fulfilment of the requirements for the award of Doctor of Philosophy (PhD), in the School of Biomedical Engineering, Faculty of Engineering and Information Technology (FEIT) at the University of Technology Sydney (UTS).

This thesis is wholly my work unless otherwise referenced or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution.

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(Md Bashir Uddin)

December 2020

To my beloved parents
*(Mrs **Alya Begum** & Late **Ali Asgar Moral**)*
for all your immeasurable love, unlimited support, and endless
encouragement

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Format of Thesis

This thesis by compilation is structured as a single manuscript that comprises a combination of chapters and published/publishable works (i.e., papers). This thesis presents each chapter/paper logically and coherently by the addition of linking text to establish the relationship between one chapter/paper and the next. This thesis by compilation includes:

- An introduction to the basic physiology and terms linked to the research study.
- A chapter or paper that describes a review of the literature.
- A chapter or paper that describes the electroencephalogram spectral power with varying apnea duration.
- A chapter or paper that describes the automatic diagnosis of sleep apnea.
- A chapter or paper that describes the modified algorithm for the diagnosis of sleep apnea.
- A final discussion of the research study and proposed future works.

List of Papers/Publications

This thesis includes the following papers/publications. The status of each paper and its corresponding chapter in the thesis are also included at the last of each paper.

1. **Uddin, M. B.**, Chow, C. M., and Su, S. W. (2018). Classification methods to detect sleep apnea in adults based on respiratory and oximetry signals: a systematic review. *Physiological Measurement*, 39(3), 03TR01. DOI: 10.1088/1361-6579/aaafb8. **(Published) – Chapter 2**
2. **Uddin, M. B.**, Su, S. W., Chen, W., and Chow, C. M. (2019). Dynamic changes in electroencephalogram spectral power with varying apnea duration in older adults. *Journal of Sleep Research*, 28(6), e12850. DOI: 10.1111/jsr.12850. **(Published) – Chapter 3**
3. **Uddin, M. B.**, Chow, C. M., Ling, S. H., and Su, S. W. (2020). *A robust airflow envelope tracking and digitization approach for automatic detection of apnea and hypopnea event*. Paper presented at the 7th IEEE Asia-Pacific Conference on Computer Science and Data Engineering. **(Accepted and Presented) – Chapter 4**
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Contribution of Authors

Md Bashir Uddin is the primary contributor and has contributed to the whole thesis and all papers presented in this thesis. The specific contributions of all authors listed in the previous papers/publications are mentioned below:

Md Bashir Uddin (**Uddin, M. B.**): This author is the primary contributor to all papers/publications listed in this thesis. The main contributions are:

- Performing systematic review of literature.
- Electroencephalogram (EEG) spectral analysis with varying apnea durations.
- Designing an automatic algorithm with subsequent modifications for sleep apnea diagnosis based on airflow (AF) and oximetry (SpO₂) signals.
- Writing, correction, and submission related tasks of all technical papers.

Steven Su (**Su, S. W.**): This author is the secondary contributor to all papers/publications listed in this thesis. The main contributions are:

- Guiding the tasks related to the systematic review of literature.
- EEG spectral power calculation in different frequency bands.
- Reviewing the design processes of the automatic algorithms.
- Modification and corrections to all technical papers listed in this thesis.

Chin Moi Chow (**Chow, C. M.**): This author is the secondary contributor to all papers/publications listed in this thesis. The main contributions are:

- Guiding and modifying the tasks related to the systematic review of literature.
- Guiding the statistical analysis linked to apnea events and EEG spectral powers.
- Correcting the design of the automatic algorithm from the physiological aspects.
- Modification and corrections to all technical papers listed in this thesis.

Steve Ling (**Ling, S. H.**): The main contributions of this author are:

- Guiding the tasks related to the design of the automatic diagnostic algorithm.
- Modification and corrections to some technical papers.

Wenhui Chen (**Chen, W.**): The main contributions of this author are:

- Significant contribution to the statistical analysis for EEG spectral powers.

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Abbreviations

| Abbreviations | Full-Form |
|----------------------|-------------------------------------|
| AASM | American Academy of Sleep Medicine |
| AAT | After apnea termination |
| AE | Abdominal effort |
| AF | Airflow |
| AHI | Apnea hypopnea index |
| ANN | Artificial neural network |
| ANOVA | Analysis of variance |
| AUC | Area under ROC curve |
| BAT | Before apnea termination |
| BHC | Binary hierarchical |
| BMI | Body mass index |
| BS | Backward shifting |
| BS SpO ₂ | Backward shifted oximetry |
| CA | Clustering algorithms |
| CART | Classification and regression trees |
| CO ₂ | Carbon dioxide |
| CPAP | Continuous positive airway pressure |
| CGE | Center of gravity engine |
| CSA | Central sleep apnea |
| dB | Decibel |
| ECG | Electrocardiography |
| EEG | Electroencephalography |
| EMG | Electromyography |
| EOG | Electrooculography |
| FCM | Fuzzy <i>c</i> -means |
| FIR | Finite impulse response |
| FIS | Fuzzy inference system |
| FN | False negative |
| FP | False positive |
| GLM | Generalized linear models |
| HR | Heart rate |
| KM | K-means |

| | |
|----------------------|--|
| KNN | <i>k</i> -nearest neighbors |
| LDA | Linear discriminant analysis |
| LoA | Limits of agreement |
| LRA | Logistic regression analysis |
| LRM | Linear regression model |
| LS-SVM | Least squares support vector machine |
| ML | Machine learning |
| MLP | Multi-layer perceptron |
| MLR | Multiple linear regression |
| MRT | Modified recording time |
| MSA | Mixed sleep apnea |
| NAF | Nasal airflow |
| NN | Neural network |
| NPV | Negative predictive value |
| NREM | Non-rapid eye movement |
| O ₂ | Oxygen |
| O ₂ desat | Oxygen desaturation |
| OLS | Orthogonal least squares |
| OSA | Obstructive sleep apnea |
| PAP | Positive airway pressure |
| PLA | Piecewise linear approximation |
| PNN | Probabilistic neural network |
| PPV | Positive predictive value |
| PSG | Polysomnography |
| PVDF | Polyvinylidene fluoride |
| QDA | Quadratic discriminant analysis |
| RBF | Radial basis function |
| RDI | Respiratory disturbance index |
| REM | Rapid eye movement |
| RERA | Respiratory effort-related arousal |
| RFC | Random forest classifier |
| RIP | Respiratory inductance plethysmography |
| ROC | Receiver operating characteristic |
| RSS | Random subspace |
| SpO ₂ | Oximetry/Oxygen saturation |
| SD | Standard deviation |

| | |
|------|---------------------------|
| SHHS | Sleep Heart Health Study |
| SVM | Support vector machine |
| SWS | Slow-wave sleep |
| TDNN | Time-delay neural network |
| TE | Thoracic effort |
| TN | True negative |
| TP | True positive |
| TST | Total sleep time |
| TRT | Total recording time |

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Abstract

Sleep apnea, a common sleep disorder, can significantly decrease the quality of life and is closely associated with major health risks such as cardiovascular disease, sudden death, depression, and hypertension. It also elicits brain and physiological changes that vary across the night. Conventional diagnosis of sleep apnea using polysomnography (PSG) is costly and time-consuming, requiring manual scoring of sleep stages and respiratory events. Current automatic diagnostic algorithms used to detect sleep apnea vary in approaches with the use of different physiological signals. An effective, reliable, and accurate automatic method for the diagnosis of sleep apnea will be time-efficient and economical.

This thesis is a narration of the work that led to the development of a novel algorithm suitable for the automatic diagnosis of sleep apnea. A systematic literature review of the existing methods (approaches and algorithms) was performed before designing the algorithm. This review presented an overview of methods to diagnose sleep apnea using respiratory and oximetry signals. The review identified the research gaps with indicating the major concerns, challenges, benefits, and limitations of using respiratory and oximetry signals for the diagnosis of sleep apnea.

This thesis examined the electroencephalogram (EEG) spectral powers resulting from apnea duration of varying length and reported the changes in the relative powers in EEG frequency bands before and at apnea termination. The study was carried out for the purpose of justifying the usability of EEG for the automatic diagnosis of sleep apnea. It investigated the spectral power changes in delta, theta, alpha, sigma, and beta frequency bands of EEG as a function of apnea duration from 375 events. The study revealed a significant reduction in EEG relative powers (the low frequency theta, alpha, and sigma powers) both before and at apnea termination. The findings from the EEG spectral analysis suggests that the application of EEG signal in sleep apnea diagnosis is not reliable due to the random variations in spectral powers as well as the major challenges associated with EEG acquisition and its processing. Due to the limitations associated with the EEG for an unattended home diagnosis of sleep apnea, the EEG signal was excluded from the automatic detection approach.

An automatic method that employed an airflow (AF) envelope tracking and subsequent digitization approach for the diagnosis of sleep apnea was developed. The automatic detection process includes the detection of apnea, hypopnea, sleep time, and apnea hypopnea index (AHI). In designing the algorithms, 988 PSG records were randomly selected from a recognized database of the Sleep Heart Health Study (SHHS). The dataset was further divided into a development ($n = 45$) and a validation ($n = 943$) set. Total sleep time (TST) was estimated from the analysis of AF and oximetry (SpO_2) signals. The algorithm detected apnea events by a digitization process,

following the determination of the peak excursion from AF envelopes. Hypopnea events were determined from the AF envelope and oxygen desaturation with a correction to a time lag in SpO₂. The AHI was estimated from the number of detected events divided by the estimated TST. For performance evaluation, the estimated AHI was compared to the SHHS manually scored data. The automatic algorithm showed strong correlations between the estimated and actual AHI. In addition, the Bland-Altman plot showed very good agreements between estimated and actual AHI, with small mean bias and narrow limits of agreement. Binary (two) class diagnosis was reported where positive (sleep apnea) and negative (normal) classes were identified using different AHI cut-offs (≥ 5 , ≥ 15 , and ≥ 30 events/h). In addition, 4 classes (normal, mild, moderate, and severe) of diagnosis were estimated for performance evaluation. The overall 2 class diagnostic accuracies were found to be 90.7%, 91%, and 96.7% for AHI cut-offs ≥ 5 , ≥ 15 , and ≥ 30 events/h respectively. Moreover, good accuracy (78.9%) and kappa (0.70) were observed for 4 class diagnosis. Though the envelope-based automatic approach performed well, some possible limitations were addressed.

A modified method was developed for the automatic diagnosis of sleep apnea where all possible limitations in the previous envelope-based designed method have been addressed and minimised. The modified approach used a sample-to-sample encoding of the AF signal for the precise detection of apnea events. The per-sample encoding approach accurately detected peak excursion by the exact detection of peak and trough amplitudes. Thus, the limitation (incorrect detection of peak excursion due to fluctuations in the upper boundary) found in the envelope tracking method was minimized. In addition, per-sample encoding of SpO₂ signals correctly identified the start and end of each oxygen desaturation phase, whereas a fixed window method may overestimate the duration of desaturations. Moreover, the adjustment of all possible time lags (0, 10, 20, and 30 s) made the modified algorithm more accurate than the envelope tracking method. The overall 2 class diagnostic accuracies were found 93.5%, 92.4%, and 96.6% for AHI cut-offs ≥ 5 , ≥ 15 , and ≥ 30 events/h respectively. Moreover, excellent overall accuracy (83.4%) and kappa (0.77) were observed for 4 class diagnosis. Comparing to envelope-based approach, the overall increments in 2 and 4 class diagnostic accuracies were 1.4% and 4.5% respectively, whereas 4 class kappa significantly improved from 0.70 to 0.77. Thus, the modified algorithm performed significantly better than the envelope-based approach.

The new algorithm overperformed than any other existing methods for the automatic diagnosis of sleep apnea. It is applicable to any portable sleep screeners especially for the home diagnosis of sleep apnea.

