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

by Md Bashir Uddin

Thesis submitted in fulfilment of the requirements for the degree of

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under the supervision 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***
4. **Uddin, M. B.**, Chow, C. M., Ling, S. H., and Su, S. W. (2020). A novel algorithm for automatic diagnosis of sleep apnea from airflow and oximetry signals. *Physiological Measurement, 42*(1). DOI: 10.1088/1361-6579/abd238 (**Published**) – ***Chapter 4***
5. **Uddin, M. B.**, Chow, C. M., Ling, S. H., and Su, S. W. (2020). *A per-sample digitized algorithm for automatically detecting apnea and hypopnea events from airflow and oximetry*. Paper presented at the 42nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society.
   DOI: 10.1109/EMBC44109.2020.9176212 (**Published**) – ***Chapter 5***
6. **Uddin, M. B.**, Chow, C. M., Ling, S. H., and Su, S. W. (2020). An algorithm for automatic diagnosis of sleep apnea hypopnea syndrome from per-sample encoding of airflow and oximetry. *IEEE Journal of Biomedical and Health Informatics*. (**Under review**) – ***Chapter 5***

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 (SpO_2) 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.

Contents

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 *c*-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	*k*-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

List of Figures

List of Tables

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 SpO_2. 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 SpO_2 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.