

## Mini-Symposia Title:

New developments in Sleep Bioengineering: 1. Detection and analysis of patterns in disturbed sleep

## Mini-Symposia Organizer Name & Affiliation:

Michael C.K. Khoo, PhD, University of Southern California, Los Angeles, USA and Thomas Penzel, PhD, Charite University

## Mini-Symposia Speaker Name & Affiliation 1:

Diane B. Boivin, MD, PhD, Centre for Study and Treatment of Circadian Rhythms, McGill University, Montreal, Canada.

## Mini-Symposia Speaker Name & Affiliation 2:

Moady Younes, MD, FRCPC, PhD, Dept. of Internal Medicine, University of Manitoba, Winnipeg, Canada.

## Mini-Symposia Speaker Name & Affiliation 3:

Timo Lepannen, PhD, Department of Applied Physics, University of Eastern Finland, Kuopio, Finland.

## Mini-Symposia Speaker Name & Affiliation 4:

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## 5 Mini-Symposia Speaker Name & Affiliation 5:

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## Theme:

- 01. Biomedical Signal Processing
- 02. Biomedical Imaging and Image Processing
- 03. Micro/ Nano-bioengineering; Cellular/ Tissue Engineering &
- 04. Computational Systems & Synthetic Biology; Multiscale modeling
- 05. Cardiovascular and Respiratory Systems Engineering
- 06. Neural and Rehabilitation Engineering
- 07. Biomedical Sensors and Wearable Systems
- 08. Biorobotics and Biomechanics
- 09. Therapeutic & Diagnostic Systems and Technologies
- 10. Biomedical & Health Informatics
- 11. Biomedical Engineering Education and Society
- 12. Translational Engineering for Healthcare Innovation and Commercialization

## Mini-Symposia Synopsis— Max 2000 Characters

Insufficient sleep has been identified as an epidemic of global proportions, with chronic insomnia and sleep apnea being the most prevalent forms of sleep disorders. Due to the close association between sleep regulation and the key physiological organ systems, disruption of sleep continuity can adversely affect cardiorespiratory and metabolic function, leading to associated morbidities such as cardiovascular disease and diabetes. The pathological changes in the cardiorespiratory and metabolic systems can subsequently “feed back” to impact sleep quality. The dynamic interactions between these systems give rise to the spontaneous variabilities evident in measurements of respiration, heart rate, blood pressure and sleep-wake state. Clever analysis of these signals, using novel algorithms and new technologies, can yield insight into the underlying mechanisms for the pathologies that result from these sleep disorders, and also lead to improved diagnostic and therapeutic approaches. In this series of 3 mini-symposia, an interdisciplinary panel of experts in the field will present state-of-the-art advances in our understanding of these complex phenomena and the quantitative tools that have been developed to better characterize them. This series of minisymposia follows in the tradition of similarly themed minisymposia series on sleep that we have organized for EMBC over the past several years, which have attracted considerable interest among EMBC attendees. The first minisymposium session will focus on the detection and analysis of patterns in actigraphy, EEG, and cardiorespiratory signals during disturbed sleep.

Synopsis of Talk #1:  
**Ambulatory recording of sleep-wake patterns in shift workers**

**Diane B. Boivin, MD, PhD,**

*Centre for Study and Treatment of Circadian Rhythms, Douglas Research Centre,  
Department of Psychiatry, McGill University, Montreal, Quebec, Canada.*

Working at night and on rotating schedules disturbs sleep and imposes long periods of wakefulness, often at times when an individual would rather sleep. This situation can generate substantial sleep-wake disturbances and increase the risk of fatigue-related accidents at work or even of road traffic accidents while commuting to and from work. and. The reliable assessment of the sleep-wake cycle in operational settings is critical for the design of practical interventions to minimize fatigue-related errors, incidents, and accidents. Several field studies have used wrist-mounted actigraphy recording to measure the timing, duration, and efficiency of sleep in shift working populations. However, conventional actigraphy does not fully quantify sleep recovery processes. Results from several field studies of shift workers will be presented. These will show the impact of circadian misalignment and extended waking on sleep and vigilance parameters. Ambulatory assessments of the sleep-wake cycle and sleep stages organisation will be discussed. Future research should target the development of new wearable devices to reliable and easily quantify sleep stages in ambulatory settings.

Synopsis of Talk #2:  
**New methods of evaluating sleep from EEG: beyond Rechtschaffen and Kales**

**Magdy Younes, MD, FRCPC, PhD**

*Department of Internal Medicine, University of Manitoba, Winnipeg, Manitoba, Canada.*

INTRODUCTION

There is substantial evidence that short sleep duration and improper circadian timing of sleep are associated with a number of negative health outcomes. However, at this time there is little evidence that the third dimension of sleep (i.e., sleep depth or intensity) is important for health outcomes. There is a need for a reliable and valid biological metric of sleep depth/intensity to determine if this dimension of sleep also contributes to the impact of sleep and sleep deficiency upon health consequences.

Non-REM sleep depth is currently divided into three discrete stages, N1, N2 and N3 (R&K system). It is, however, clear that sleep does not progress in a stepwise manner. Rather, transition from stage wake (W) to the lightest sleep (N1) is gradual, reflecting different degrees of sleep propensity, and EEG in stage N2 ranges from a pattern that is similar to wake patterns to one that is similar to that in N3. Changes in sleep propensity during wakefulness or in sleep depth during stage N2, as a result of interventions are missed when the current R&K system is used. Furthermore, sleep staging by the R&K criteria is highly subjective resulting in substantial inter-rater variability.

THE ODDS RATIO PRODUCT (ORP)

The odds-ratio-product (ORP) is a recently-introduced measure derived from the relation of EEG power in different frequencies to each other. It is a continuous metric ranging from 0 (very deep sleep) to 2.5 (full wakefulness).

The EEG is analyzed in consecutive 3-second epochs. Fast Fourier transform is applied to the C3 and C4 EEG signals. Sum of powers is calculated in four frequency ranges; 0.33-2.33 Hz, 2.67-6.33 Hz, 7.0-14.0 Hz, and 14.3-35.0 Hz. Power in each range is assigned a rank (0 to 9) based on its decile within the range encountered in reference clinical sleep studies. The four ranks are concatenated in order of the frequency ranges to produce 10,000 four-digit labels (0000 to 9999) that describe the relative powers in the four frequency bands. The probability of any pattern occurring during arousals or in epochs manually scored wake was determined in the development files by reference to a look-up table. Probability (0 to 100%) is divided by 40 (% of epochs scored wake in development files), resulting in a range from 0 (never occurs during wakefulness or in arousals) to 2.5 (never occurs during epochs scored asleep).

VALIDATION

- 1) Within every individual ORP decreases progressively from stage wake to stage N3.
- 2) Average ORP during stage wake (within the sleep study) decreases following sleep deprivation or restriction, indicating that it is sensitive to sleep propensity.
- 3) ORP decreases progressively as very early stage N2 progresses to deep stage N2, where the EEG is just shy of containing 6 seconds of delta waves per 30-second epoch, the threshold for scoring N3.
- 4) Average ORP in N2 decreases following sleep deprivation or restriction.
- 5) ORP increases across the night in response to declining homeostatic drive.
- 6) ORP increases transiently in a graded manner in response to noise pulses of different intensities.
- 7) Most importantly, correlation between current ORP and probability of a spontaneous arousal occurring within the next 30 seconds is almost perfect ( $r^2 = 0.98$ ).

POTENTIAL APPLICATIONS

A) *Identification of mechanism of sleep fragmentation:* Sleep fragmentation results either from excessive arousal stimuli originating within or external to the body or from light sleep where even normal (weak) stimuli can result in arousal. At present it is not possible to distinguish between the two mechanisms. Knowledge of the relation between ORP and frequency of spontaneous arousals in normal subjects (#7 above) would make it possible to determine whether excessive arousals in a given subject are due to light sleep (central mechanism) or peripheral stimuli.

B) *Determination of sleep adequacy:* To the extent that an increase in ORP from beginning to end of the night (#5, above) reflects the restorative function of sleep, the change in ORP across the night may be used to determine if the patient slept enough for his individual requirements.

Synopsis of Talk #3  
**Neural network analysis of sleep recordings – potential to fully automatized diagnosis of obstructive sleep apnea**

**Timo Leppänen, PhD**

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Diagnostics Imaging Center, Kuopio University Hospital, Kuopio, Finland*

### *Introduction*

Currently, the diagnosis of obstructive sleep apnea (OSA) and accurate identification of sleep stages are based on time-consuming and expensive processes via manual scoring of sleep stages and respiratory events. Thus, there exists a need for reliable automatic analysis methods for assessment of OSA severity and detection of sleep stages, making polygraphic (PG) and polysomnographic (PSG) studies more readily available with lower costs. As neural network analysis is gaining ground in the field of advanced diagnostics it could also provide a solution for automated sleep staging and OSA diagnosis.

The aim of this presentation is to present different neural network approaches developed in our research group e.g. for automatic estimation of OSA severity and identification of sleep stages. Additional neural network approaches for estimation of the severity of OSA-related sleepiness and probability for co-morbidities may also be presented.

### *Methods*

We have developed a neural network approach to estimate the apnea-hypopnea index (AHI) based only on blood oxygen saturation (SpO<sub>2</sub>) signals recorded during PGs. SpO<sub>2</sub> signals of 1692, 99, and 198 suspected OSA patients were used for training, validation, and testing, respectively.

This idea was further elaborated by developing a neural network for AHI estimation for stroke and transient ischemic attack (TIA) patients. The neural network was trained with 1379 SpO<sub>2</sub> signals from PGs of suspected OSA patients and tested with 77 SpO<sub>2</sub> signals from PGs of acute stroke and TIA patients.

For sleep staging, PSGs of 804 suspected OSA patients were used to train and optimize a combined convolutional and long short-term memory neural network. The training was conducted utilizing a single channel (F4-M1) and a

two-channel (F4-M1 + EOG) inputs. An independent test set of 87 patients was used for testing.

To further elaborate this idea, a combined convolutional and recurrent neural network was developed to identify sleep stages automatically from the photoplethysmogram (PPG) obtained by a pulse oximeter. PPG signals of 894 suspected OSA patients were utilized.

### *Results*

A neural network estimated AHI with a median absolute error of 0.78 events/hour. 90.9% of patients were classified into the correct OSA severity category based on the estimated AHI values.

In stroke and TIA patients, the median absolute error of estimated AHI was 1.45 events/hour. Furthermore, the neural network identified moderate-to-severe OSA with high sensitivity (92.3%) and specificity (96.1%).

For the suspected OSA patients, the neural networks achieved sleep staging accuracies of 82.9% ( $\kappa=0.77$ ) and 83.8% ( $\kappa=0.78$ ) with a single EEG channel and two channels (EEG+EOG), respectively. The sleep staging accuracy decreased with increasing OSA severity.

Based on PPG, the neural network achieved 80.1% epoch-by-epoch accuracy with kappa ( $\kappa$ ) of 0.65 for 3-stage classification (wake/NREM/REM). For 4-stage (wake/N1+N2/N3/REM) and 5-stage (wake/N1/N2/N3/REM) classification, the neural networks achieved 68.5% ( $\kappa=0.54$ ), and 64.1% ( $\kappa=0.51$ ) accuracies, respectively. The total sleep time was overestimated with a mean (SD) error of 7.5 (55.2) min.

### *Conclusions*

Neural network analysis has great potential for automatic analysis of PGs and PSGs. It could provide more effective and personalized pathways for the sleep staging and the diagnosis and severity assessment of OSA, significantly reducing the costs and time required for manual analysis of PG and PSG recordings.

Synopsis of Talk #4:

**Changes in tidal volume and stroke volume during overnight PSG: results of first clinical study using portable electrical impedance tomography (EIT)**

**Eung Je Woo, PhD**

*Department of Biomedical Engineering, Kyung Hee University, Seoul, Republic of Korea*

During a conventional overnight PSG test, multiple signals are acquired from a patient during natural sleep: nasal pressure, oronasal thermistor, respiratory efforts, SpO<sub>2</sub>, snoring sound, EEG, EMG, ECG, and others. These signals are interpreted or scored to detect respiratory events and produce the apnea hypopnea index (AHI). The AHI is used to suggest a treatment method for the patient. Considering the complicated cardiopulmonary physiology behind the respiratory events, it would be desirable to continuously acquire the signals of tidal volume and stroke volume noninvasively from the patient during natural sleep. Recruiting 14 sleep apnea patients, we conducted the first clinical study of measuring tidal volume and stroke volume signals using a portable electrical impedance tomography (EIT) device during overnight PSG tests in a sleep lab. Verifying the quality of the acquired data, we will show how tidal volume and stroke volume changed during various respiratory events of obstructive, central, and mixed types. Quantitation of hypopnea will be tried based on the quantitative nature of the measured tidal volume signal. We will try to understand the cardiopulmonary coupling phenomena during the respiratory events using the acquired tidal volume and stroke volume signals. More clinical studies will be proposed to show the clinical usefulness of the new method.