Multiparameter Physiological Analysis in Obstructive Sleep Apnea Simulated With Mueller Maneuver

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***Abstract*—Sleep apnea is a common condition that poses serious health risks. Current state-of-the-art technology for diagnosing and assessing sleep apnea is obtrusive, expensive, and lacks integration/analysis of important cardiovascular and respiratory parameters. This paper evaluates a novel unobtrusive multiparameter sleep apnea monitor, namely, the Biopeak chest belt monitor, and describes a collection of associated algorithms for the detection of sleep apnea and assessment of the extent of the resulting physiological disturbance. The system uses dry electrodes to acquire electrocardiogram, respiratory, and stroke volume data and analyzes multiple physiological parameters from it. In a pilot investigation on eight healthy subjects simulating a total of 66 obstructive sleep apnea (OSA) events with Mueller maneuvers, the proposed system achieves an accuracy of 95.6%, a specificity of 97.2%, and a sensitivity of 93.8% for identifying these events. Moreover, the response of the simulated OSA events on the multiple physiological parameters conforms to earlier published work. We thus conclude that the proposed chest belt system has potential to be used for reliable sleep apnea detection and comprehensive evaluation of cardiovascular and respiratory parameters in sleep apnea.**

***Index Terms*—Bioimpedance, chest belt monitor, electrocardiogram, Mueller maneuver, obstructive sleep apnea, respiration, stroke volume.**

I. Introduction

SLEEP apnea is a sleep anomaly characterized by episodes of cessation in breathing or abnormally low breathing, during sleep [1]. Generally, three kinds of apneas are defined, namely, central sleep apnea (CSA), obstructive sleep apnea (OSA), and mixed sleep apnea [2]. Researchers have found that among sleep apnea patients, the prevalence of CSA, OSA, and mixed sleep apnea is 1%, 84%, and 15% respectively [3].

Sleep apnea or sleep disordered breathing (SDB) is a dangerous condition whereby the lungs and thus other organs of the body are deprived of oxygen. This can lead to an increased risk of cardiovascular disease, stroke, high blood pressure, arrhythmias, memory loss, and sleep deprived driving accidents [4]–[10].

In addition to serious health risks, sleep apnea also has significant economic impact. For example, it is estimated that patients with SDB consume health care services at approximately twice the rate of control subjects prior to diagnosis, for a period of about ten years [11], [12].

It is estimated that in adults, 4% males and 2% females suffer from sleep apnea [13]. Moreover, studies have shown that about 1.8% of children in the age range of 3–11 years suffer from SDB, for example, [14]. The prevalence of sleep apnea in adolescents is considered to be similar to that in younger children.

Given severe health risks, substantial economic impact, and considerable prevalence, the diagnosis and assessment of sleep apnea is a topic of great research interest.

The current gold standard for diagnosing sleep apnea is polysomnography (PSG) whereby several physiological signals such as electrocardiogram (ECG), electroencephalogram (EEG), electromyogram (EMG), respiration, and blood oxygen saturation are acquired and analyzed during sleep [15], [16]. However, PSG is a highly obtrusive test in which multiple electrodes and sensors are attached to a patient's chin, scalp, eyelids, chest, and finger during sleep. Moreover, the patient has to undergo sleep testing in a sleep clinic under the supervision of a sleep technologist. Consequently, PSG is a cumbersome and expensive test, and has long wait times associated with it.

Last but not least, despite recording a multitude of signals, PSG does not seem to provide detailed information about the impact of sleep apnea on the cardiovascular dynamics – it is primarily used to detect sleep apnea events [15], [16]. Since we know that sleep apnea increases the danger of cardiovascular disease, stroke, high blood pressure, and lethal arrhythmias [4]–[10], studying its effect on the cardiovascular system could be of paramount importance in risk stratification and selection of treatment protocols for patients.

Due to high costs, long waiting periods, and comfort-related problems associated with PSG, home and portable monitoring of sleep related disorders is gaining rapid popularity

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[17]. For example, the Alice PDx portable sleep diagnostic system from Philips is designed for OSA screening [18]. However, it is bulky and obtrusive whereby gel electrodes and multiple leads are required for ECG data acquisition. Moreover, no information is available about the kinds of analysis (especially cardiovascular assessment) this system undertakes for assessing sleep apnea. The Zeo Sleep Manager is worn around the head to monitor quality of sleep using indices such as deep sleep, light sleep, wakefulness, and rapid eye movement [19]. The main disadvantage of the Zeo Sleep Manager is that it cannot measure any cardiovascular parameter such as an ECG. Sleep Check is a nasal cannula-based system that measures respiratory airflow pressure for detecting sleep apnea and classifying it as obstructive, central, and hypopnea [20]. Again, although it may detect pauses in breathing, it cannot provide any cardiovascular information for SDB.

A number of research articles in the area of sleep monitoring are focused toward the assessment of cardiovascular and respiratory parameters in sleep apnea or employing these parameters for sleep apnea detection. These studies have mostly been performed on sleep apnea patients or on healthy subjects/sleep apnea patients simulating sleep apnea with breathing maneuvers like the Mueller maneuver.

Researchers have found that in sleep apnea patients, ECG-based heart rate (HR) and heart rate variability (HRV) are altered during wakefulness [21]–[23] and sleep [21], [22], [24]–[28]. Moreover, studies have also found that OSA events induce changes in ECG R-peak amplitudes [25], [26], [28], [29]. The changes induced in HRV and ECG R-peak height due to sleep apnea have also been utilized for its automatic detection [25]–[29]. As a step beyond R-peak height assessment, researchers have also studied the morphology of the ECG signal for automatic detection of apnea events. For example, Khandoker *et al*. [30] used multiscale wavelet analysis on 5 s epochs of ECG signals to identify episodes of OSA and hypopnea. Maier *et al*. [31] studied the phase shift between areas of QRS complexes obtained from different ECG leads of a Holter monitor to detect OSA events.

Parameters such as stroke volume (SV) and cardiac output (CO), which characterize cardiac efficiency [32], have also shown to provide vital cardiovascular insights into the evaluation of SDB. Garpestad *et al*. [33] showed that SV and CO measured using echocardiography drop significantly following OSA episodes during sleep. Orban *et al*. [34] found comparable results (again with echocardiography) for healthy subjects simulating OSA by performing Mueller maneuvers. Viscor *et al*. [35] assessed SV using bioimpedance to demonstrate similar results for Mueller maneuvers performed by sleep apnea patients.

Analysis of respiratory signals acquired using various measurement protocols shows promise in the detection and assessment of sleep apnea [36]. For example, Nakano *et al*. [37] employed Fourier power spectrum analysis on a single channel PSG airflow record to accurately detect SDB. Kowallik *et al*. [38] found that breath-to-breath variability measured from the PSG airflow signal correlates with apnea-hypopnea index in OSA patients. Masa *et al*. [39] analyzed shapes of the respiration signals obtained from PSG thoracoabdominal bands to successfully detect OSA events during sleep. Várady *et al*. [40] analyzed the phase shift between respiratory signals acquired from PSG thoracoabdominal bands for detection of OSA events.

In yet another study, Townsend *et al*. [41] detected central apnea episodes without analyzing any cardiovascular or respiratory signals. Rather, they conducted pattern analysis on motion and orientation signals produced by an array of sensors embedded between the mattress and box spring of the patient's bed to detect central apneas.

Our survey of the literature indicates that there is a push toward portable and home monitoring of sleep apnea [17]–[20]. Moreover, research in this area highlights the importance of assessing cardiovascular and respiratory parameters in sleep apnea [21]–[40], which may help in effective diagnosis and management, risk stratification, and formulation of treatment regimens for patients with SDB. However, to the best of our knowledge, no device manufacturer or research article reports the integration of cardiovascular (ECG + SV) and respiratory data acquisition and analysis into a single unobtrusive portable/wearable system for sleep apnea monitoring.

In this article, we present an unobtrusive, compact, portable, ergonomically designed, and easy to use wearable chest belt monitoring system for multiparameter physiological analysis in sleep apnea. A Canadian company called Biopeak Corporation has developed this monitor, which comprises dry gel-free electrodes and associated hardware/software for high quality ECG, bioimpedance-based SV and respiratory data acquisition [42].

We have developed a set of algorithms that enable this chest belt monitor to assess multiple cardiovascular and respiratory parameters. More specifically, we apply a moving window analysis to extract multiple physiological parameters such as HRV, ECG R-peak height, and respiratory variability from the acquired data. We then combine these parameters to create integrated physiological metrics (IPMs). The IPMs are used for automatically detecting simulated apnea events. Additionally, we evaluate changes in multiple physiological parameters such as SV and breathing peak height in the neighborhood of these events.

To test the performance of the chest belt monitor and the developed algorithms, we undertook a pilot investigation on eight healthy subjects who simulated OSA events by performing 66 Mueller maneuvers. Receiver operating characteristic (ROC) analysis shows that the IPM comprising mean and standard deviation (SD) of ECG R-peak height achieves an accuracy of 95.6%, specificity of 97.2%, and sensitivity of 93.8% for simulated OSA detection. Moreover, statistically significant differences are found in ECG parameters, SV, and respiratory measures in the neighborhood of these OSA events, which conform to earlier published work [22], [33]–[35], [38].

Our results are encouraging and show that the proposed chest belt monitoring system has potential to be used for

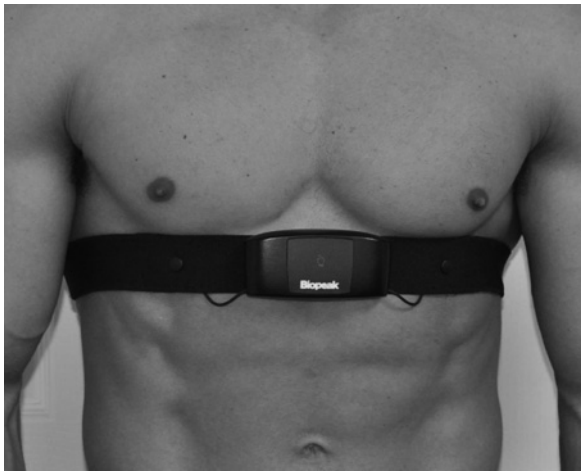

Fig. 1. Biopeak chest belt system acquiring data from healthy male subject. It comprises two active rigid electrodes on inner surface of belt (not seen). These electrodes are connected to central unit, which attaches to outer surface of belt as shown.

reliable detection of sleep apnea events and evaluation of a variety of cardiovascular and respiratory parameters during sleep apnea.

II. Data Acquisition System

A. Biopeak Monitor

Fig. 1 shows the Biopeak monitor, acquiring data from a healthy male subject. It comprises an elasticized belt with nylon-coated adjusters. It thus fits conveniently and snugly on to the chest under the breast region.

The inner surface of the belt comprises two small dry rigid active electrodes, which are used for ECG and tetrapolar bioimpedance measurements. Additionally, each active electrode has an embedded temperature sensor for continuous skin temperature monitoring.

The electrodes are connected to the central unit, which attaches to the outer surface of the chest mounted fabric belt. An accelerometer is also provided inside the central unit for movement and orientation measurement. Moreover, the central unit includes a microcontroller, memory, rechargeable battery, a universal serial bus (USB) port, Bluetooth, and other related hardware/software.

The above renders the chest belt as a compact standalone wearable multiparameter physiological data acquisition, storage, and transmittal system. The continuous multiparameter waveform data that the chest belt acquires, stores, and transmits, includes ECG, galvanic skin response, bioimpedance, temperature, and 3-D acceleration. The waveform data acquisition frequency of the Biopeak monitor is 600 Hz.

The waveform data stored on the central unit of the belt can be transmitted to a personal computer (PC) and other devices using a USB cable or Bluetooth protocol for further analysis. We have developed a set of algorithms pertinent to sleep apnea, in MATLAB (Natick, MA, USA), for an offline analysis of the chest belt data on a PC.

III. Experimental Study

A. Pilot Investigation

We undertook a pilot instigation to evaluate the performance of the Biopeak monitor and the developed algorithms for assessing multiple cardiovascular and respiratory parameters during simulated OSA events. The study comprised eight healthy subjects ($N_T = 8$, Age Range: 26–63 years) of which six were males ($N_M = 6$, Age Range: 26–45 years) and two were females ($N_F = 2$, Age Range: 41–63 years). The range of the body mass index (BMI) of these subjects was 21–25. To the best of our knowledge, no subjects had any history of cardiovascular/respiratory disease or SDB. The University of Ottawa Research Ethics Board approved the study and written informed consent was obtained from all participants before enrolling them in the study.

All eight subjects were monitored with the chest belt while they performed Mueller maneuvers to simulate OSA events. Seven subjects performed eight Mueller maneuvers each whereas one subject performed ten Mueller maneuvers resulting in a total of 66 Mueller maneuvers ($MM = 66$) for the entire population ($N_T = 8$). For all subjects, a time gap of approximately three minutes was provided between each Mueller maneuver. The subjects performed the Mueller maneuvers sitting upright in a chair, exhaling completely, closing their mouth with their palm, and pinching their nose with their index finger and thumb to stop breathing. They resumed normal breathing when they could not comfortably hold their breath anymore. Subjects were asked to try and keep the duration of each Mueller maneuver in the range of 15–25 s, keeping in mind their own comfort. This resulted in Mueller maneuvers of varied durations. For each subject, we recorded the start and end time of the data acquisition session with the belt. Moreover, we recorded the start and end time of each Mueller maneuver per session. Each data collection session lasted about thirty minutes during which the belt continuously monitored all data described in Section II-A.

IV. Data Preprocessing

For this paper, we analyze the ECG and bioimpedance data recorded by the Biopeak monitor for all subjects. The measured ECG and bioimpedance waveform data is preprocessed to derive information about R-peak height, R-R interval (RRi), breathing peak height, interbreath interval (IBI), and SV.

The ECG data is filtered using a second order zero phase band-pass filter with a pass-band frequency range of 1–50 Hz to remove high frequency phenomena and facilitate R-peak detection. This is followed by identifying ECG R-peaks using the MIT/PhysioNET MATLAB QRS onset detector software [43], [44]. Based on the identified R-peaks, RRis are computed in seconds and R-peak heights are computed in millivolts (mV) for all subjects.

A respiratory signal is derived by filtering the bioimpedance signal with a second order zero phase band-pass filter that has a pass-band frequency range of 0.07–0.7 Hz. To further smooth the derived respiratory signal, a cubic smoothing spline function is fitted to it. Then a zero crossing algorithm is employed on the fitted spline function for identifying breathing

1. Scale the physiological time series $X = [x_1, x_2, ..., x_N]$ to create a time series $S = [s_1, s_2, ..., s_N]$. Each element of S is defined as,
$$s_j = (x_j - \bar{X})/\sigma_X, j = 1, 2, ..., N,$$
where $\bar{X}$ is mean of X, and σ_X is the standard deviation (SD) of X. This step makes the series mean equal to zero, normalizes it on SD, and makes it dimensionless.
2. Transform the scaled time series $S = [s_1, s_2, ..., s_N]$ into a Gaussian time series $G = [g_1, g_2, ..., g_N]$ where,
$$g_j = \frac{1}{\sqrt{2\pi}} e^{-\frac{s_j^2}{2}}, j = 1, 2, ..., N.$$
This step accentuates the events or changes in the series.
3. If $G_A = [g_{A1}, g_{A2}, ..., g_{AN}]$ and $G_B = [g_{B1}, g_{B2}, ..., g_{BN}]$, are two Gaussian time series, define $IPM = [ipm_1, ipm_2, ..., ipm_N]$ as,
$$ipm_j = log\,(g_{Aj} \times g_{Bj}), j = 1, 2, ..., N.$$
The IPM is created by taking log product of two or more Gaussian series. This is a generic and common procedure for combining two or more series.
4. High pass filter *IPM* using cut-off frequency of 0.0045 Hz to remove baseline drift (low frequency phenomenon).
5. Smooth *IPM* using a cubic smoothing spline function to remove high frequency fluctuations (noise).
6. Interpolate(up sample)*IPM* at sampling frequency 5 Hz to increase its time resolution for more accurately locating apnea events.

Fig. 2. Algorithm for constructing IPM.

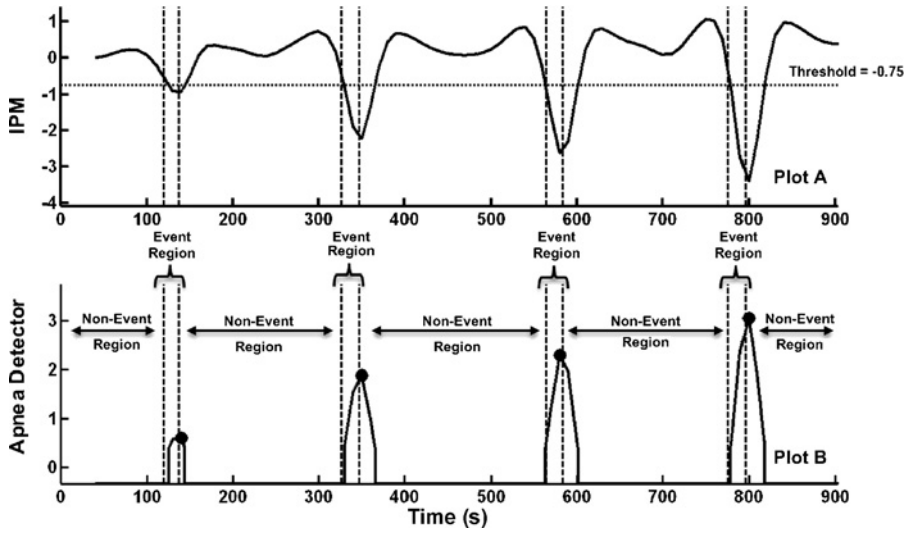

Fig. 3. Illustration of automatic apnea event detection. Solid line in Plot A shows first 900 s of IPM comprising mean and SD of ECG R-peak height for Subject 2. Dashed vertical lines show start and end of four simulated OSA events. Threshold of -0.75 on IPM (dotted horizontal line, Plot A) yields apnea detector shown with solid line in Plot B. Apnea detector picks up all four simulated apnea events (Mueller maneuvers) correctly (large dots, Plot B).

peaks. Based on the identified breathing peaks, IBIs are computed in seconds and breathing peak heights are computed in ohms for all subjects. Since the respiratory signal is derived from the bioimpedance signal measured in ohms, the breathing peak height is also reported in ohms.

The first step in computing SV involves filtering the bioimpedance signal using a second order zero phase band-pass filter, which has a pass-band frequency range of 0.7–10 Hz. The beat-to-beat SV is then derived in ohms from the filtered bioimpedance signal using ECG R-peak alignment. Finally, ohmic SV data is multiplied by an empirical constant (specific to the monitor) to determine SV in milliliters (ml) for all subjects. We note that the SV numbers reported in ml in this paper have not been clinically validated. However, this is not a problem since the focus of this research is to study relative changes in SV (and other parameters) and not the absolute values.

Based on the recorded start and end times of Mueller maneuvers, all preprocessed data is visually inspected and manually annotated to specify the start and end times of all Muller maneuvers ($MM = 66$) for all subjects ($N_T = 8$).

0. Initialize $TP = 0$; $FP = 0$; $TN = 0$; $FN = 0$; threshold = +20
1. Automatically detect apnea events using IPM.
2. If a detected apnea event lies in an event region (± 10 s), $TP = TP + 1$. Repeat for all detected apnea events in all event regions.
3. If a detected apnea event lies in a non-event region, $FP = FP + 1$. Repeat for all detected apnea events in all non-event regions.
4. If an apnea event is not detected in a non-event region, $TN = TN + 1$. Repeat for all non-detected apnea events in all non-event regions.
5. If an apnea event is not detected in an event region, $FN = FN + 1$. Repeat for all non-detected apnea events in all event regions.
6. Decrement the threshold by -0.25.
7. Repeat Steps 1-6, until a threshold of -20 is reached.
8. Compute $Sensitivity = TP / (TP + FN)$; $Specificity = TN / (FP + TN)$; $Accuracy = (TP + TN) / (P + N)$.

Fig. 4. Receiver operating characteristic (ROC) analysis algorithm. TP: true positive. FP: false positive. TN: true negative. FN: false negative. P: positives. N: negatives. Please also refer to Fig. 3.

V. Automatic Apnea Detection

A. Moving Window Analysis

For studying physiological changes over time, a window of size 20 s is moved in steps of 10 s from the beginning to the end on the preprocessed ECG, respiratory, and SV data. The following parameters are computed inside each window instant: 1) mean R-peak height, 2) SD of R-peak height, 3) root mean square successive difference (RMSSD) [45] of R-peak height, 4) wavelet spectral density (WSD)[46] of R-peak height, 5) mean RRi, 6) SD of RRi, 7) RMSSD of RRi, 8) WSD of RRi, 9) mean breathing peak height, 10) SD of breathing peak height, 11) Mean IBI, 12) SD of IBI, and 13) Mean SV. This creates synchronized multiple physiological time series reporting a 20 s assessment of the above parameters every 10 s for all subjects. A window size of 20 s is chosen because we expect the simulated OSA events (Mueller maneuvers) to be of about 20 s in duration on average. There are two main reasons for this expectation: 1) it is documented in literature that Mueller maneuvers generally have a duration range of 15–25 s [47], [48], and 2) we instructed our subjects to try and make the Mueller maneuvers to last for about 15–25 s each. However, we would like to mention that the window size that we employ can be readily changed and the analysis undertaken again, based on the expected time duration of the events we are trying to capture. A step size of 10 s is chosen because it is 50% of the chosen window size and will thus provide appropriate time resolution for studying physiological changes over time in the given scenario.

B. Integrated Physiological Metric

For automatically detecting simulated apnea events (Mueller maneuvers), integrated physiological metrics (IPMs) are created using various combinations of the 13 physiological time series outputted from the moving window analysis. The main steps in constructing an IPM involve scaling the desired physiological time series, converting them into Gaussian time series, and computing the log product of these Gaussian time series.

The algorithm for constructing an IPM is presented in Fig. 2. The physiological time series X of Step 1 is one of the 13 physiological time series outputted from the moving window analysis, for example, the time series of ECG R-peak heights, RRis, SV, etc. The series X is scaled by subtracting its mean value from it and dividing it by its SD – this gives a scaled dimensionless time series S, which has a zero mean. We note that the mean and SD used for this scaling are computed on the entire duration of the physiological time series X. In our pilot investigation, whereby seven subjects performed eight Mueller maneuvers each while one subject performed 10 Mueller maneuvers, the durations of all physiological time series outputted from the moving window analysis were well within 1 h. Thus, we assumed these series to be stationary whereby they would have a stable baseline. As a result, the mean and SD used to scale these series were computed on their full duration. For actual nighttime monitoring of sleep apnea, the physiological times series X may have duration of 8 h or more. In that case, the assumption of stationarity may not hold for the series. One approach to scale such a series could be to divide it into sections of 1 h each, and then scale each section separately based on the section mean and SD.

In Step 2, the scaled time series S is transformed into a Gaussian time series $\mathbf{G}$. The Gaussian series $\mathbf{G}$ is essentially the same series as S but with its fluctuations magnified. In this manner (Steps 1–2), 13 Gaussian series can be created from the 13 physiological time series outputted from the moving window analysis.

An IPM is constructed by taking the log product of two or more (up to 13) Gaussian time series (Step 3). Once an IPM is constructed, it is high-pass filtered to bring the baseline value to a horizontal level or to remove low frequency phenomena (Step 4). Then the IPM is smoothed to remove any spikes and outliers or high-frequency noise (Step 5).

Finally, the IPM is interpolated (up sampled) using a sampling frequency of 5 Hz or 0.2 s (Step 6). We recall that the sampling rate of the series outputted from the moving window analysis is 10 s (or 0.1 Hz) and thus this is the sampling rate of the constructed IPM. The final step of re-sampling the IPM at 5 Hz (Step 6) improves its time resolution from 10 s to 0.2 s. This increases the automatic apnea detection algorithm's likelihood of picking up the apnea events with greater temporal accuracy. Steps 1–6 create a stable IPM with satisfactory time resolution and render it fit for robust automatic apnea detection.

We note that a window size of 20 s and a step size of 10 s removed high frequency components but preserved information pertinent to the Mueller maneuvers. This was followed by creating the IPM and then improving its time resolution to 0.2 s using interpolation (up sampling). If we had employed a moving window of step size 0.2 s from the beginning, we would not have eliminated high frequency phenomena or efficiently isolated simulated sleep apnea events.

C. Apnea Detection and ROC Analysis

Fig. 3 shows how the IPM comprising mean R-peak height and SD of R-peak height is used to automatically detect four simulated OSA events (Mueller maneuvers) for Subject 2. The dashed vertical lines show the start and end of the four OSA events. The first step involves defining a threshold on the IPM, which is -0.75 in this case (dotted horizontal line, Plot A, Fig. 3). Next, indices of all data points that lie below the given threshold are found and stored. Then all data points in the IPM are set to zero except the data points that lie below the threshold. The resulting time series is then multiplied by -1 to reverse its polarity and normalized by subtracting its mean value from it to construct an apnea detector (solid line, Plot B, Fig. 3). Finally, a zero crossing algorithm is used to find peaks (OSA events) in the apnea detector (large dots, Plot B, Fig. 3). The above procedure is repeated for different thresholds.

We note that automatic apnea detection is an offline method. During monitoring, the Biopeak belt stores all data inside its central unit. Once monitoring is complete, this data is transferred to a PC for analysis and automatic apnea detection. This protocol will suit home and remote monitoring of sleep apnea well. For example, patients can sleep at home at night with the Biopeak monitor attached to them as it records data. Next day, they can take the monitor to the clinic for getting the data analyzed.

To evaluate the performance of the automatic apnea detection algorithm, an ROC analysis is undertaken whereby different IPMs are tested with varying thresholds for detecting all Mueller maneuver events (MM = 66). The threshold is varied from + 20 to -20 in steps of -0.25 for all IPMs tested. These values are chosen empirically based on inspecting the various IPMs constructed and their maxima and minima. The ROC analysis algorithm used in this paper is presented in Fig. 4.

We note that the ROC analysis parameters, namely, specificity, sensitivity, and accuracy, are routinely used to assess a clinical diagnostic test's efficacy [49]. Since detection of apnea events can be considered equivalent to a diagnostic test, it is in this sense that the terms specificity, sensitivity, and accuracy are used in this paper. The ROC analysis that we undertake maximizes sensitivity, specificity, and accuracy of detection of the simulated OSA events, based on changing the threshold from + 20 to -20 in steps of -0.25 on various IPMs. The threshold at which an IPM achieves the maximum sensitivity, specificity, and accuracy is chosen as the optimum threshold for that IPM.

An error of ± 10 s is permitted to the automatic apnea detection algorithm. That is, if an apnea event is detected up to 10 s before it actually started or if it is detected up to 10 s after it actually ended, it is counted as a correct detection. The reason for permitting a ± 10 s error to the apnea detection algorithm is that the IPMs are constructed using windowing operation involving a step size = 10 s, that is, data is analyzed every 10 s (Section V-A). As a result, a lag or lead of 10 s from the actual boundaries of an OSA event is expected from the automatic apnea detection algorithm.

VI. Correlation Analysis

To study the relationship among various physiological parameters measured by the Biopeak monitor, Pearson's linear correlation analysis is performed between each pair of physiological time series outputted from the moving window analysis for all subjects ($N_T = 8$). A correlation matrix with $C\ (n, 2) = n!/(2!\ (n - 2)!)$ elements is produced, where n is the number of physiological parameters assessed. Thus, for $n = 13$ (the number of parameters evaluated in the moving window analysis), a correlation matrix with 78 unique elements (or correlations) is created.

VII. Event-Related Analysis

To study the effect of simulated OSA events (Mueller maneuvers) on the cardiovascular and respiratory parameters, an event-related analysis is undertaken on the preprocessed ECG, respiratory, and SV data. Here, based on the manually annotated OSA events, three distinct regions are defined namely *before, during,* and *after*. *Before* is defined as the time interval corresponding to 16 heartbeats preceding the start of a Mueller maneuver. Similarly, *after* is defined as the time interval corresponding to 16 heartbeats following the end of a Mueller maneuver. Finally, *during* is defined as the actual duration for which a Mueller maneuver lasts (varying durations for entire population).

For all subjects ($N_T = 8$) and all Mueller maneuvers ($MM = 66$), all 13 parameters listed in the moving window analysis section (Section V-A) are assessed *before, during,* and *after* the Mueller maneuvers. Bar charts with error bars and Student T-Test analysis (two-tailed distribution, two sample unequal variance) are employed for assessing whether statistically significant differences exist in these physiological parameters *before, during,* and *after* the Mueller maneuvers.

VIII. Results

Visual inspection confirmed that the QRS detection software identified all ECG R-peaks correctly. Moreover, the respiratory and SV data appeared free of noise or outliers.

The mean duration of the recordings from all subjects ($N_T = 8$) was 33 ± 5 minutes. Moreover, the mean duration of all Mueller maneuvers (MM = 66) was 24 ± 7 s. The mean respiratory disturbance index (RDI) [15] for the population ($N_T = 8$) was $15.34 \pm 1.77\ h^{-1}$. For each subject, RDI was calculated by dividing the number of Mueller maneuvers with the duration of the recording in hours. Then, the mean and standard deviation of the RDIs for all subjects ($N_T = 8$) was computed. The Biopeak monitor measured the mean HR as 75 ± 10 beats per minute, breathing rate as 15 ± 1 breaths per minute, and SV as 67 ± 18 ml, for the entire population ($N_T = 8$).

Fig. 5 shows the entire ECG waveform data along with the identified R-peaks (top panel) and SV waveform data (bottom panel) for Subject 3. The dashed vertical lines show the start and end times of the eight Muller maneuvers (simulated OSA events). Very clear and distinct drops are observed in ECG

TABLE I

CORRELATION MATRIX SHOWING PEARSON'S CORRELATIONS BETWEEN ALL 13 PHYSIOLOGICAL PARAMETERS ASSESSED USING THE BIOPEAK CHEST BELT FOR ALL SUBJECTS ($N_T = 8$). CORRELATIONS GREATER THAN OR EQUAL TO 50% OR LESS THAN OR EQUAL TO −50% APPEAR IN BOLD FONT AND ARE UNDERLINED

$N_T = 8$	Mean R-Peak Height	SD R-Peak Height	RMSSD R-Peak Height	WSD R-Peak Height	Mean RRi	SD RRi	RMSSD RRi	WSD RRi	Mean Breathing Peak Height	SD Breathing Peak Height	Mean IBI	SD IBI	Mean SV
Mean R-Peak Height													
SD R-Peak Height	**-50%**												
RMSSD R-Peak Height	-13%	**71%**											
WSD R-Peak Height	8%	**52%**	**85%**										
Mean RRi	27%	-39%	-36%	-33%									
SD RRi	-3%	34%	23%	22%	-9%								
RMSSD RRi	5%	32%	28%	29%	6%	**73%**							
WSD RRi	20%	21%	28%	35%	11%	**56%**	**82%**						
Mean Breathing Peak Height	3%	40%	40%	45%	-24%	19%	27%	34%					
SD Breathing Peak Height	-17%	42%	30%	31%	-21%	21%	27%	28%	**82%**				
Mean IBI	-25%	31%	11%	5%	0%	26%	18%	17%	24%	24%			
SD IBI	-37%	38%	14%	6%	-18%	20%	14%	6%	8%	19%	**54%**		
Mean SV	29%	10%	30%	41%	-30%	11%	9%	9%	39%	20%	-9%	-4%	

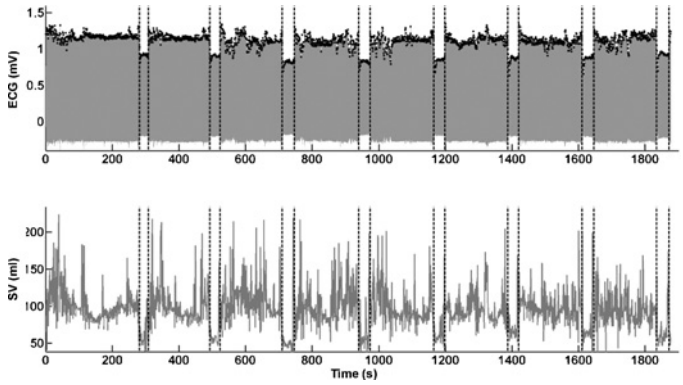

Fig. 5. ECG waveform data (gray plot, top panel) with identified R-peaks (black dots, top panel) and SV waveform data (gray plot, bottom panel) for Subject 3. The dashed vertical lines show the start and end times of all the eight simulated OSA events (Mueller maneuvers).

R-peak heights during each of the eight Mueller maneuvers. Similarly, the SV data also shows drops during the Mueller maneuvers, though it has more fluctuations as compared to ECG R-peak heights in the nonevent regions.

The Pearson's correlation matrix examining the relationship between the 13 physiological parameters assessed with the chest belt system is presented in Table I. The highest correlation is observed between RMSSD and WSD of the ECG R-peak height (85%). A negative correlation of -50% is observed between mean and SD of the ECG R-peak height. Other correlations that are greater than or equal to 50% are observed between RMSSD and WSD of RRi (82%), mean and SD of breathing peak height (82%), SD and RMSSD of RRi (73%), SD and RMSSD of R-peak height (71%), SD and WSD of RRi (56%), mean and SD of IBI (54%), and SD and WSD of R-peak height (52%).

TABLE II

SUMMARY OF THE ROC ANALYSIS − THRESHOLD, ACCURACY, SPECIFICITY, AND SENSITIVITY FOR DIFFERENT CONSTITUENTS OF THE IPM FOR DETECTING SIMULATED OSA EVENTS FOR ALL SUBJECTS ($N_T = 8$, MM = 66)

Metrics in IPM	Threshold	Accuracy	Specificity	Sensitivity
Mean + SD of R-Peak Height	−0.75	95.6%	97.2%	93.8%
All 13 Parameters	−4.00	84.8%	90.8%	78.1%
All Non-ECG Parameters	−2.25	64.8%	83.3%	44.1%

The results of the ROC analysis comparing the performance of various metrics inside the IPM for automatically detecting simulated OSA events (MM = 66) are presented in Fig. 6 and Table II. Best accuracy of 95.6%, specificity of 97.2%, and sensitivity of 93.8% is achieved for a threshold of −0.75 when the IPM comprises mean and SD of the ECG R-peak height (Fig. 6, Table II). When all 13 physiological parameters are combined inside the IPM, the accuracy, specificity, and sensitivity reduce to 84.8%, 90.8%, and 78.1% respectively for a threshold of −4.00. Finally, when all non-ECG parameters (mean & SD of breathing peak height, mean & SD of IBI, and mean SV) are used to form the IPM for detecting simulated OSA events, an accuracy of 64.8%, specificity of 83.3%, and sensitivity of 44.1% is achieved for a threshold of −2.25.

The performance of the automatic apnea detection algorithm in terms of the RDI is presented in Table III. For each subject,

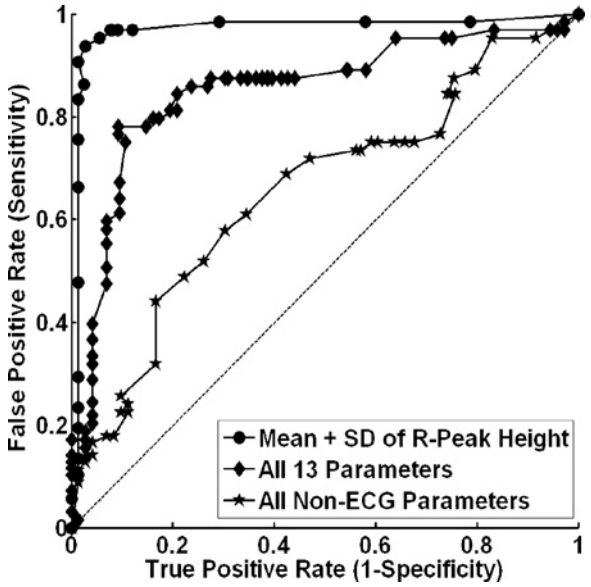

Fig. 6. ROC analysis comparing the performance of various metrics inside the IPM for automatically detecting simulated OSA events for the entire population ($N_T = 8$, MM = 66). Best performance is achieved when IPM comprises mean and standard deviation of the ECG R-peak height (accuracy = 95.6%, specificity = 97.2%, sensitivity = 93.8%, for a threshold of −0.75).

based on the optimum threshold determined by the ROC analysis for a particular IPM, the number of simulated apnea events picked up by the algorithm is counted. This number is then divided by the duration of the subject's recording in hours for computing the apnea detection algorithm-based RDI. This procedure is repeated for all subjects to determine the mean (± SD) of the population RDI estimated by the automatic apnea detection algorithm for various IPMs and corresponding optimum thresholds. Results are compared with the actual mean (± SD) RDI of the population. Best results are obtained for a threshold of −0.75 when the IPM comprises mean and SD of the ECG R-peak height whereby the apnea detection algorithm-based RDI is 14.84 ± 2.12 h^{-1} as compared to the actual RDI of 15.34 ± 1.77 h^{-1}. The apnea detection algorithm-based RDI drops to 13.36 ± 3.30 h^{-1} vis-à-vis the actual RDI of 15.34 ± 1.77 h^{-1} when the IPM comprises all 13 physiological parameters for a threshold of −4.00. Finally, when all non-ECG parameters (mean and SD of breathing peak height, mean & SD of IBI, and mean SV) are used inside the IPM for a threshold of −2.25, the apnea detection algorithm-based RDI further reduces to 9.34 ± 3.89 versus the actual RDI of 15.34 ± 1.77 h^{-1}.

Best results for automatic detection of simulated OSA events are obtained when the IPM comprises mean and SD of the ECG R-peak height (Fig. 6, Tables II and III). This shows that the greatest impact of the Mueller maneuvers is on the ECG R-peak height. The electrical activity of the heart can be represented by considering it to be a dipole [50]. During a Muller maneuver the orientation of this dipole changes. As a result, the voltage (or R-peak height) measured by the Biopeak monitor also changes. We note that other kinds of apneas, for example, central or mixed, could impact other physiological parameters (such as RRi or SV) to a greater extent. Therefore, using an IPM, which combines various

TABLE III
COMPARISON OF RDIS ESTIMATED BY THE AUTOMATIC SLEEP APNEA DETECTION ALGORITHM WITH THE ACTUAL RDIS FOR DIFFERENT CONSTITUENTS OF THE IPM AND THE CORRESPONDING OPTIMUM THRESHOLDS FOR THE ENTIRE POPULATION ($N_T = 8$, MM = 66)

Metrics in IPM	Threshold	Actual RDI (Mean ± SD)	Estimated RDI (Mean ± SD)
Mean + SD of R-Peak Height	−0.75	15.34 ± 1.77 h^{-1}	14.84 ± 2.12 h^{-1}
All 13 Parameters	−4.00	15.34 ± 1.77 h^{-1}	13.36 ± 3.30 h^{-1}
All Non-ECG Parameters	−2.25	15.34 ± 1.77 h^{-1}	9.34 ± 3.89 h^{-1}

physiological parameters, gives us a better opportunity to reliably detect different kinds of apneas. In this particular study involving simulated OSA events only, the ECG R-peak height shows the greatest responsiveness to these events. Hence the ROC analysis shows the best performance of the IPM when it comprises mean and SD of the ECG R-peak height.

In Table IV, we present results of our IPM-based automatic OSA detection algorithm in light of results published in relevant earlier work. Our results are promising – the performance of our automatic apnea detection algorithm is slightly better than previous work. We note that as compared to our method, all previous work employed more obtrusive means for acquiring data (column seven, Table IV). Moreover, our method allows for analyzing a larger variety of physiological parameters for apnea detection as compared to earlier work (column eight, Table IV).

The results of the event-related analysis for all the 13 physiological parameters *before, during,* and *after* the simulated OSA events are presented in Fig. 7. The mean and WSD of the ECG R-peak height show statistically significant drops *during* the simulated OSA events. Moreover, the SD and RMSSD of the R-peak height show significant rises around the OSA events. The mean RRi drops (or the mean HR increases) significantly around the OSA events. The RMSSD and WSD of RRi characterizing HRV drop significantly *during* the simulated OSA events. The SD of the breathing peak height shows a statistically significant rise *during* the OSA events. The mean IBI rises (or the mean breathing rate decreases) significantly *during* the OSA events. The SD of IBI, characterizing respiratory or IBI variability increases significantly *during* the OSA events. Finally, the mean SV shows a statistically significant fall and rise around the simulated OSA events. Only two parameters, namely SD of RRi and mean breathing peak height do not show any statistically significant changes *during/around* the simulated OSA events.

A comparison of results from the event-related analysis with results published in some earlier papers is presented in Table V. We note that the statistically significant drops and rises that we observe *during/around* simulated OSA events are in good agreement with previous work. Again, the data acquisition method employed by previous studies is more obtrusive as compared to those utilized in this research (column seven, Table V). Moreover, we study the response of a greater variety of physiological parameters in

TABLE IV

COMPARISON OF EVENT-RELATED ANALYSIS WITH EARLIER PUBLISHED WORK

Authors	No. of Subjects (N_T)	Health Status	No. of Recordings	No. of Apnea Events	Data Analyzed	Data Acquisition Method	Parameters Analyzed	Accuracy	Specificity	Sensitivity
de Chazal et al. [26]	32	OSA/Mixed Apnea Patients	70	50	ECG	Bedside Monitor With Gel Electrodes	ECG R-Peak Amplitude, RRi	89.7%	90.7%	88.1%
Zywietz et al. [27]	32	OSA/Mixed Apnea Patients	70	50	ECG	Bedside Monitor With Gel Electrodes	ECG RRi	92.0%	92.7%	90.8%
Suhas et al. [29]	30	Healthy Subjects/ OSA Patients	241	178	ECG	Bedside Monitor With Gel Electrodes	ECG R-Peak Amplitude	79.0%	74.0%	84.0%
Ahmad et al. (Pilot Study)	8	Healthy Subjects Simulating OSA	8	66	ECG, Respiration, SV	Portable/Wearable Biopeak Chest Belt With Dry Electrodes	ECG R-Peak Amplitude, RRi, Breathing Peak Amplitude, IBI, SV	95.6%	97.2%	93.8%

TABLE V

COMPARISON OF EVENT-RELATED ANALYSIS WITH EARLIER PUBLISHED WORK

Authors	No. of Subjects (N_T)	Health Status	No. of Recordings	No. of Apnea Events	Data Analyzed	Data Acquisition Method	Parameters Analyzed	Parameters Showing Statistically Significant Changes During/Around Apnea Events (P<0.05)
Aydin et al. [22]	60	Healthy Subjects/ OSA Patients	60	NS	ECG	Holter With Gel Electrodes	ECG RRi	OSA ⇒ HRV ↑↓
Viscor et al. [35]	15	Mitral Regurgitation Patients Simulating OSA	15	150	SV	Bedside Bioimpedance Monitor With Gel Electrodes	SV	OSA ⇒ SV ↓↑
Kowallik et al. [38]	43	Healthy Subjects/ OSA Patients	43	NS	Respiration	Bedside Airflow Monitor	IBI	OSA ⇒ IBI Variability ↑
Ahmad et al. (Pilot Study)	8	Healthy Subjects Simulating OSA	8	66	ECG, SV, Respiration	Portable/Wearable Biopeak Chest Belt With Dry Electrodes	ECG R-Peak Amplitude, RRi, Breathing Peak Amplitude, IBI, SV	OSA ⇒ R-Peak Height ↓, R-Peak Height Variability ↑, HR ↑, HRV ↓, Breathing Peak Height Variability ↑, Breathing Rate ↓, IBI Variability ↑, SV ↓↑

NS: Not Specified

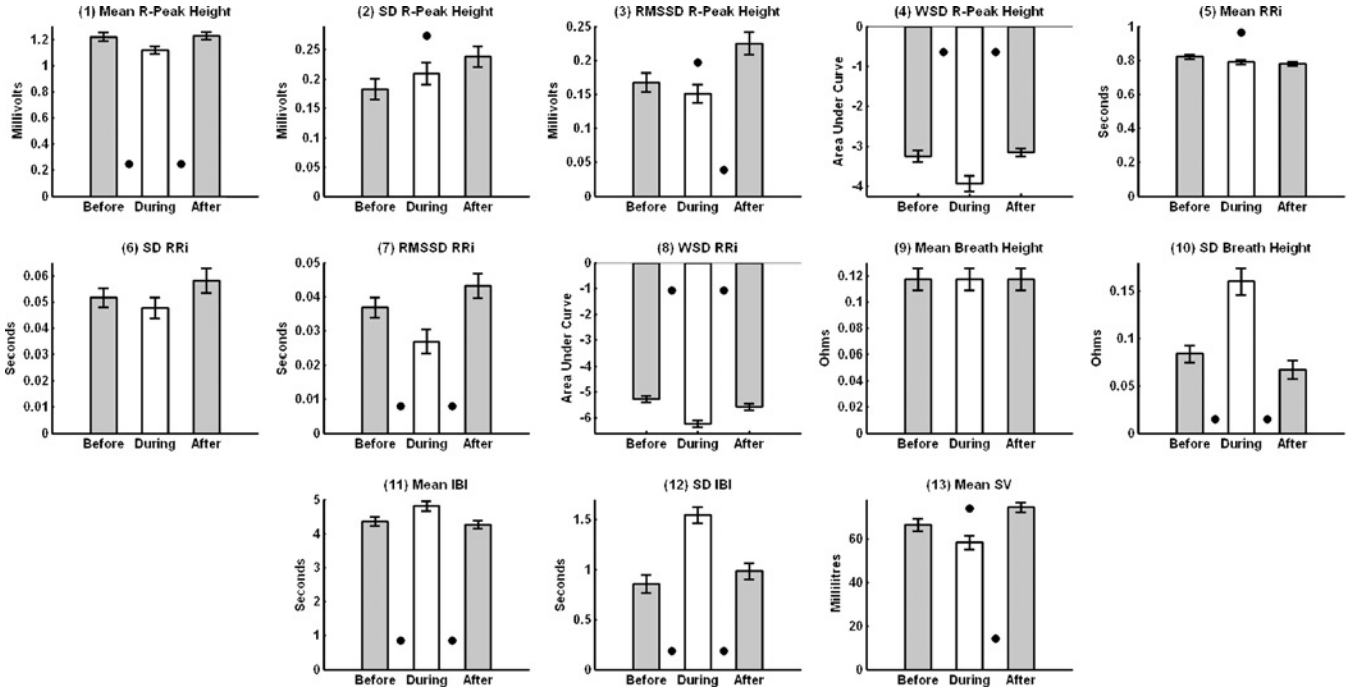

Fig. 7. Bar plot and student t-test analysis of all 13 physiological parameters *before, during,* and *after* simulated OSA events for all subjects (MM = 66, $N_T = 8$). Bars represent the mean value whereas error bars represent standard error of mean (SEM). Dots signify a $P < 0.05$ for student t-test. Dot lying in between adjacent bars shows that there is a statistically significant difference between *before* and *during* or *during* and *after*. Dot in line with central bar shows that there is a statistically significant difference between *before* and *after*. No dots in these regions signify that there are no statistically significant differences.

the neighborhood of apnea events in comparison with earlier publications (column eight, Table V).

We note that other previous work also studied automatic apnea detection from a single lead ECG signal, for example, [25], [30], [31]. Similarly, researchers also explored the response of apnea on various physiological parameters, for example, [23], [34]. However, three combined features of our method makes it novel vis-à-vis previous work.

1) The use of an integrated unobtrusive wearable chest belt device with dry electrodes for acquiring all data as opposed to obtrusive gel electrodes with leads connected to a separate device box employed in earlier work.
2) The availability and study of a richer variety of physiological parameters (cardiovascular plus respiratory) for automatic apnea detection as compared to much fewer parameters analyzed in previous studies.
3) The ability to assess response of multiple physiological parameters in the neighborhood of apnea events with the event-related analysis in contrast to previous work that only studied a limited number of parameters.

IX. Conclusion

In this paper, we presented the Biopeak monitor and a collection of associated algorithms for assessing multiple physiological parameters in sleep apnea. This was the first study in which a comprehensive cardiovascular and respiratory evaluation of sleep apnea (a total of 13 parameters) was integrated into a single unobtrusive portable/wearable chest belt system with dry electrodes. Moreover, a combination of two distinct sleep apnea assessment methods, namely, the moving window and event-related analyses were proposed. The IPM derived from the moving window analysis was used for automatically detecting simulated sleep apnea events whereas the event-related analysis focused on studying the effect of these events on cardiovascular and respiratory parameters. A pilot investigation on healthy subjects ($N_T = 8$) who simulated OSA events with Mueller maneuvers ($MM = 66$) produced excellent results. We thus conclude that the proposed chest belt monitoring system shows promise to be used unobtrusively for robust recognition of sleep apnea events and assessment of a variety of cardiovascular and respiratory parameters in sleep apnea.

Our results point toward three potential benefits for sleep monitoring. First, a portable/wearable monitor like the Biopeak monitor promises to bring sleep apnea testing to the comfort of people's homes. Second, its ergonomic design and dry electrodes enable it to be worn comfortably for several nights to accomplish long-term sleep monitoring and assessment. Finally, the proposed algorithms for detection of sleep apnea and assessment of its cardiovascular and respiratory response help in risk stratification of patients and formulation of their treatment protocols.

As a simplistic first approach for automatic apnea detection, IPMs were created using unweighted products (Fig. 2). However, different types of sleep apneas (for example, OSA, central, and mixed) could have varying impact on various physiological parameters. Our future work will thus involve using a correlation matrix such as Table I and principal component analysis (PCA) for constructing IPMs with weighted physiological parameters. This promises to increase consistency and reliability of the detection of various kinds of sleep apnea events. The ROC analysis gives us an objective means of comparing the performance of various IPMs for automatically detecting sleep apnea events.

Our results are promising; however, we note that this research was performed on a small sample size of healthy subjects simulating OSA with Mueller maneuvers. Future work will therefore be focused on employing this chest belt system and associated algorithms for monitoring a larger population of sleep apnea patients and healthy subjects during sleep. We are also planning trials whereby healthy subjects and sleep apnea patients will be monitored with the proposed system as they perform other maneuvers such as Valsalva maneuver and breath hold. The above will enable us to test the efficacy and feasibility of the proposed system for night monitoring as well as assessment of other kinds of apneas, namely central and mixed.

The Biopeak monitor also records body movement and orientation data using an embedded accelerometer. For this paper, we did not analyze the accelerometer data acquired by the belt. In our future work, we will integrate the body movement and orientation data with the existing physiological parameters to provide a richer variety of information for reliable diagnosis and evaluation of sleep apnea.

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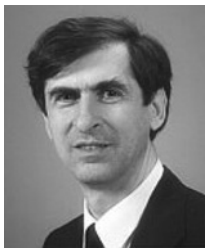

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