A Novel Synthetic Simulation Platform for Validation of Breathing Rate Measurement

Nandakumar Selvaraj*, Gabriel Nallathambi, and Paul Kettle

***Abstract*— Validation of biosensor algorithms is paramount for regulated medical devices applied to patient monitoring. We present validation of breathing rate (BR) measurement using a patch medical device via a novel synthetic simulation platform, in-hospital data collection and controlled laboratory study. Single-lead ECG and triaxial body acceleration signals with variability and noise are synthetically generated and quantized for a constellation according to the input parameters of heart rate (HR) as a fundamental frequency(f_c) of ECG and reference BR as a modulating frequency (f_r). Synthetic signals are input to the BR algorithms and the performance of output BRs are evaluated for a region-of-interest of the constellation ($f_c/f_r \geq 3 \ \& \ f_c/f_r \leq 8$) accounting the Nyquist and physiological varability. The performances of patch sensor's BR are also evaluated in 13 post-operative patients with reference to a clinical bedside monitor and in 57 subjects carrying out a controlled laboratory protocol with reference to capnography. The synthetic simulations revealed mean absolute error (MAE) of 0.8±0.6 brpm and standard deviation of absolute error of 0.3±0.2 brpm for the BR algorithms of patch sensor. The controlled laboratory testing revealed MAE of 1.7±0.7 brpm (n=57) for stationary conditions. The proposed simulation platform can be useful for developmental refinement or validation of BR measurement prior to testing in humans at clinical or laboratory conditions and applicable for testing other patient monitoring devices with modular modifications.**

***Index Terms*— Wireless Biosensor, Respiratory Monitoring, Synthetic Simulation, Algorithms, Performance Analytics.**

I. INTRODUCTION

Accurate assessment of vital signs and timely notification of critical events are necessary for continuous patient monitoring that can help to detect infections or complications well in advance and prevent mortalities. Recent advancements in wearable medical technologies for 24-hour health monitoring may allow early detection of patient deterioration and curb the healthcare costs. The accuracy and precision of algorithms implemented in such complex embedded medical systems are paramount to earn the acceptance of clinical community; therefore, it is very important to ensure high quality of algorithmic design via rigorous testing and validation during the developmental cycles.

Synthetic simulation is common to generate surrogate data for early stages of algorithmic design, optimization of the development, and test the reliability over a wide range of a target variable [1]. Further, synthetic simulations may allow assessment of the device performance during uncommon corner cases. But a platform/system solution that allows generating synthetic signals, inputting into sensor hardware and firmware or algorithms, and evaluating performance for a constellation of input variables is not common.

Development of intelligent and efficient algorithms particularly for physiological monitoring and critical event detection necessitates a wide distribution of data belonging to both normal and abnormal conditions. However, obtaining a comprehensive continuous medical-grade data from patients is limited during in-house development and for the validation of algorithms [2]. Moreover, gold-standard reference monitors required for clinical validation of emerging wearable technologies are, in many cases, not designed for ambulatory monitoring. Thus, a synthetic simulator system may be useful to overcome many of those limitations.

We present a novel simulation platform for validation of continuous respiratory monitoring via a patch medical device that involves synthetic generation and quantization of single-lead ECG and triaxial body acceleration signals with variability and noise for a constellation of input fundamental and modulating frequencies. These synthetic signals are input to the breathing rate (BR) algorithms of patch sensor, and the performance of output BRs are evaluated for a predefined region-of-interest of the constellation accounting the Nyquist and physiological variability. Furthermore, the performances of patch sensor's BR are also evaluated in 13 post-operative patients with reference to a standard bed-side patient monitor and in 57 subjects carrying out a controlled laboratory protocol with reference to capnography.

II. MATERIALS AND METHODS

A. System under test

The system under test is a FDA cleared VitalPatch [3], a disposable adhesive patch sensor worn on chest with built-in system-on-chip processor, and associated electronics that allows continuous monitoring of single-lead ECG, tri-axial accelerometer, and thermistor data. The firmware algorithms compute and continuously transmit physiologic variables such as heart rate (HR), BR, skin temperature, body posture, fall detection, and step count among others. ECG derived R wave amplitude (RWA) that measures change of cardiac axis during breathing, triaxial accelerometer signals that measures chest wall movements of expansion and compression due to respiratory cycles, and ECG derived respiratory sinus arrhythmia (RSA) that measures respiratory modulations are combined to assess BR as described previously in detail [4].

B. Synthetic Waveform Simulation Platform

A single-lead ECG and triaxial accelerometer waveforms are synthetically generated for a range of HR (30−200

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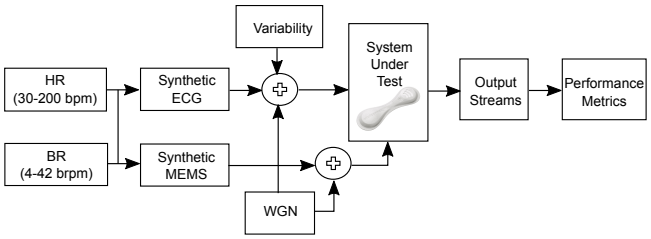

Fig. 1: The proposed synthetic simulation environment.

bpm) and BR (4−42 brpm) as fundamental (f_c) and modulating (f_r) input frequencies respectively, and added with white Gaussian noise (WGN) and variability. These synthetic waveforms are input to a simulator of the patch sensor's algorithms, and the BR outputs are compared with reference BR inputs for performance assessment (Fig. 1).

Generation of synthetic ECG signals: A synthetic ECG waveform can be composed of PQRST individual waves for normal sinus rhythm [5]. Accordingly, the decoupled ECG representation can be approximated by the sum of 5 Gaussian kernels, where each kernel is described by their amplitude, width, central location and HR (a, σ, μ and ω_n respectively). The synthetic model as given in $equation(1)$ below includes a scaling factor [6] that transposes dimensionless ECG representation z to $mV/(rad \times s)$, and provides QRS amplitude and respiratory sinus arrhythmia (RSA) modulations.

$$z(t) = \sum_{i=1}^{n} \frac{w_n \times a_i}{\sigma_i^2} e^{-\frac{(t-\mu_i)^2}{2\sigma_i^2}} \tag{1}$$

To mimic clinical data, a random variability is added to both the amplitude and frequency modulation of ECG for each HR−BR combinations of the constellation. Further, WGN of zero-mean and standard deviation of SD_{wgn} is also added to the ECG as in $equation(2)$.

$$SD_{wgn} = f_{wgn} \times \sqrt{\frac{1}{(n-1)} \sum_{i=1}^{n} (z_i - \mu)^2} \tag{2}$$

where, n is the number of samples, and f_{wgn} is a factor (e.g., 0.1). The ECG signal with added noise is further quantized to 12−bit as in the patch sensor.

Generation of synthetic MEMS signals: The tri-axial accelerometer housed in the printed circuit board of the patch sensor allows capturing human body accelerations within the range of $\pm 4g$ per axis with a resolution $7.8mg$, where $g = 9.81m/s^2$ is the gravitational acceleration. The acceleration signals are calibrated to rotate the coordinate system and obtain the true superior-inferior, anterior-posterior, and left-right acceleration axes. The chest wall movements caused by respiration are captured by the tri-axial accelerometer, and a MEMS based surrogate respiratory signal is generated for BR estimation. In this simulation environment, tri-axial MEMS signals are synthesized according to the input BR. The MEMS signal with added noise is further quantized. The synthetic ECG and MEMS signals are generated for 180s

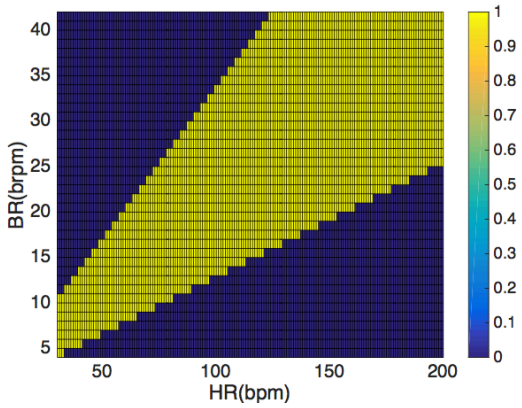

Fig. 2: The color map of HR−BR constellation with the R value corresponding to the region-of-interest for validation.

with all combinations of HR−BR range, and input to the VitalPatch algorithm simulator and BR estimates (Fig. 1).

Region-of-interest (ROI) of the constellation: BR is usually approximated as a linear or piecewise linear function of HR [7], and hence we considered a region of interest in this constellation denoted as R to be a function given $equation(3)$ (Fig. 2), where the ratio of carrier HR frequency (f_c) to the modulating BR frequency (f_r) would satisfy the Nyquist criterion to ensure free from cardiac aliasing [8]. The lower bound threshold ($R = 3$) is chosen to satisfy Nyquist rate and the upper bound threshold ($R = 8$) is chosen to account for a limited physiological variability. The constellation points on the ROI with $R = 1$ in the 2D map is further split into 3 sub-regions of low or shallow range (4−9 brpm), clinical range (10−30 brpm) and higher hyperventilation range (31−42 brpm).

$$R = \begin{cases} 0 & \frac{f_c}{f_r} < 3 \\ 1 & \frac{f_c}{f_r} \geq 3 \& \frac{f_c}{f_r} \leq 8 \\ 0 & \frac{f_c}{f_r} \geq 3 \end{cases} \tag{3}$$

Performance analysis: The last 60s of predicted BR were analyzed to quantify mean absolute error (MAE) and standard deviation of absolute error (SDAE) as the accuracy and precision respectively compared to the reference BR input values. Statistics of BR performance metrics MAE and SDAE were calculated for the full constellation of BR range (4−42 brpm) and the desired 3 sub-regions.

C. Validation in Clinical and Laboratory Settings

The present study analyzed over 50 hours of VitalPatch BR data collected in 13 post-operative cardiac patients compared to a standard patient monitor from hospital settings. The reference BR values of bed-side patient monitor were interpolated to 4s rate as in VitalPatch using their nearest values at 1min rate. The performance of VitalPatch BR is evaluated by MAE and SDAE metrics with reference to the interpolated BR series of the patient monitor.

Furthermore, the present study also conducted data analysis in VitalPatch BR data collected in 57 healthy volunteers

(age: 35±11years) carrying out a protocol in laboratory settings. Each participant wore a VitalPatch sensor on left chest and an oronasal cannula connected to a standard portable capnography monitor (Capnostream20, Oridion) for reference, and underwent various activities including spontaneous breathing, metronome breathing of range 10−30 brpm, postures and activities of daily living (ADL), and walking for about an hour and half. The reference BR values of capnography monitor were down-sampled from a rate of 1s to 4s, and performance analysis was carried out for VitalPatch BR data from controlled settings.

III. Results

A. BR Performance in Simulations

The ROI of HR−BR 2D map had 3237, 138, 2001, 1098 constellation points (combination of HR and BR) with $R = 1$ corresponding to full, low, clinical and high BR range respectively. BR outputs from respective number of simulations are analyzed and determined the performance of BR. The accuracy and precision of VitalPatch BR considering 3237 simulations across full BR range (4−42 brpm) is found to be 0.8±0.6 brpm and 0.3±0.2 brpm referring to MAE and SDAE performance metrics, respectively. The BR performance for clinical BR range (10−30 brpm) show an MAE of 0.5±0.5 brpm and SDAE of 0.2±0.2 brpm. The low and high BR ranges revealed MAE of 1.0±0.2 brpm and 1.2±0.2 brpm, respectively.

B. BR Performance in Clinical Settings

Typical comparisons of BR measured using VitalPatch sensor are shown for specific episodes of arrhythmia and motion from post-operative cardiac patients with reference to bed-side patient monitor (Fig. 3). Despite the spurious intermittent spikes of premature ventricular contractions that substantially affect the respiratory modulations in RRI variability (Fig. 3a), the patch sensor's BR tracks the patient monitor values well with deviations of 1−2 brpm. Fig. 3b represents very poor ECG signal strength (∼100uV) and extensive motion artifacts (compare ECG quality in (a)), where the derived RRI variability seems largely attenuated and having huge spikes where QRS detection may not be possible. Besides, VitalPatchs BR show good correspondence to that of the patient monitor within 1−4 brpm.

The performance analysis of BR in over 50 hours of data in 13 post-operative cardiac patients shows an MAE of 3.5±0.6 brpm and SDAE of 2.8±0.6. The observed error of over 3 breaths on average may be predominantly contributed by the heavy low-pass filtering setting of the patient monitor, whose specifics are not available for comparison. The representative snapshots in Fig. 3 highlight that VitalPatchs BR show essential variability in BR as opposed to heavily low-pass filtered patient monitor response. Besides, the bedside patient monitor was not a standard capnography (note that it is obtrusive) and is prone to inaccuracies (sample data not shown) that may also contribute to the observed performance. Thus, the statistical error estimates are inclusive of patient monitor's deficiencies and inaccuracies.

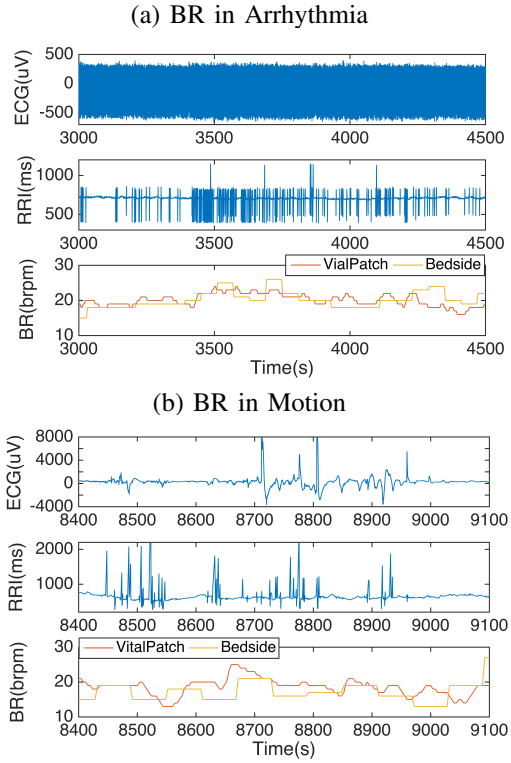

Fig. 3: Comparisons of ECG, R-to-R intervals (RRI) and breathing rate (BR) measured during (a) arrhythmia and (b) motion scenarios in cardiac patients using VitalPatch.

C. BR Performance in Laboratory Settings

The comparison of BR estimates measured from VitalPatch vs the standard capnography monitor during the controlled protocol is illustrated in Fig. 4. VitalPatchs BR estimates show good resemblance in magnitude and trend to the capnography reference during stationary (0−2150s), mild-to-strenuously active time periods of the experimental protocol. The performance analysis of BR measured in 57 subjects at controlled settings revealed MAE and SDAE of 1.7±0.7 brpm and 1.8±0.7 brpm respectively during stationary test periods with metronome and spontaneous breathing. On the other hand, the performance of BR was relative higher with MAE of 3.7±1.2 brpm and 4.1±2.6 brpm for ADL and strenuous activities respectively. Combining stationary and active periods together, the overall performance in laboratory settings is with MAE and SDAE of 3.1±1.2 brpm and 3.1±1.0 brpm, respectively.

IV. Discussion

Accurate biosensor algorithms are critical for medical device regulatory clearances and gaining acceptance in clinical industry. We presented a novel synthetic waveform simulation platform applicable for the development, validation, and testing phases of BR algorithms of embedded medical device. The proposed simulation system for the validation of BR accuracy over an extensive range (4−42 brpm) has been compared with conventional elaborate validation studies in uncontrolled clinical as well as controlled laboratory settings.

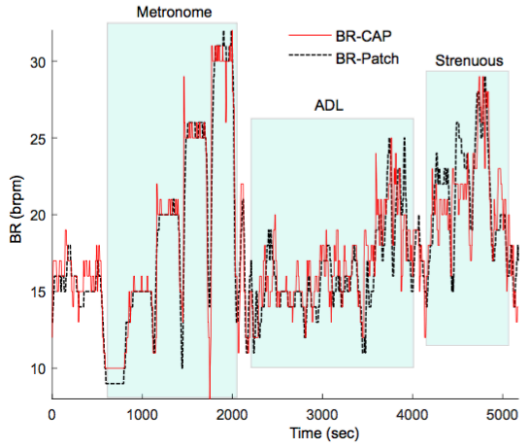

Fig. 4: Representative BR measured using capnography reference vs VitalPatch sensor in laboratory testing.

The synthetic simulations reveal that BR algorithms of patch sensor has MAE of 0.8 brpm with a precision (SDAE) of 0.3 brpm, while the laboratory testing revealed an accuracy (MAE) of 1.7 brpm for stationary conditions. The overall laboratory performance (MAE of 3.1 ± 1.2 brpm) is found to be comparable to that of the clinical performance (MAE of 3.5 ± 0.6 brpm). However, performance comparisons of real data vs simulation data suggests that the BR accuracy in clinical/controlled setting is relatively lower ($1-2$ brpm) than from simulations that could be attributed to many accounted factors such as age, gender, disease conditions, physiological counter mechanisms, body mass and motion that influence the ECG and MEMS signal, and may affect the quality of derived surrogate respiratory signals and BR estimates.

Clinical uncontrolled data collection involved post-operative cardiac patients with varying degrees of complications and mobility as opposed to the laboratory testing that involved only normal subjects and the time durations of active and stationary periods clearly demarcated by visual observation of the protocol that lead to distinguishing the performances in stationary vs active durations. In the present analysis of clinical performance, active vs stationary durations are not differentiated over 50 hours of data in 13 subjects, but objectively separating stationary vs active durations in clinical data is possible by using VitalPatchs activity metric that scales the degree of body movements with reference to gravitational acceleration.

While clinically relevant range of BR in normal adults is generally $16-20$ brpm, the abnormal BR ranges in unhealthy hospitalized adults varies from 14 to 36 brpm [9]. It is recommended that patients with a BR greater than 24 brpm should be monitored closely and reviewed regularly [9]. In our previous clinical study conducted in 76 senior subjects [10], 3σ range of reference BR measured by standard capnography was around 10 to 30 brpm that suggests a typical range for spontaneously breathing healthy controls while performing ADL. It may be possible to capture BR <10 brpm or >30 brpm in patients with respiratory disorders (e.g., sleep apnea and hyperventilation syndromes) or by voluntary forced ventilation/hyperventilation. Since the clinical trial data is often limited in capturing wide range of BR, the proposed simulation platform may be necessary for validation of BR algorithms in outside the BR range from clinical studies.

This simulation platform mimics the use-case of a patient monitoring system with ECG and MEMS sensing for BR assessment by producing input synthetic waveforms for a constellation of underlying control parameters and noise level. Changes in acceleration magnitudes in different axes during different levels of activity and postures are not taken into the current simulation, but can be included in simulations based on data learning from controlled experiments. Thus, the proposed simulation system can be modified further to mimic more realistic data that may allow planning the development and validation phases of algorithmic designs for physiological monitoring. The simulation environment may enhance rapid prototyping by testing the system performances without requiring to commit laborious clinical studies that may lower the developmental cycles and reduce the time-to-market significantly.

In summary, the proposed simulation platform can be useful for validation of BR measurement, and allows modular modifications for incorporating new signal modalities/functionalities that can be applicable for testing other physiological monitoring devices.

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