UNSUPERVISED ENSEMBLING OF MULTIPLE SOFTWARE SENSORS: A
NEW APPROACH FOR ELECTROCARDIOGRAM-DERIVED RESPIRATION
USING ONE OR TWO CHANNELS

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ABSTRACT. While several electrocardiogram-derived respiratory (EDR) algorithms have been proposed to extract breathing activity from a single-channel ECG signal, conclusively identifying a superior technique is challenging. We propose viewing each EDR algorithm as a software sensor that records the breathing activity from the ECG signal, and ensembling those software sensors to achieve a higher quality EDR signal. We refer to the output of the proposed ensembling algorithm as the ensembled EDR. We test the algorithm on a large scale database of 116 whole-night polysomnograms and compare the ensembled EDR signal with four respiratory signals recorded from four different hardware sensors. The proposed algorithm consistently improves upon other algorithms, and we envision its clinical value and its application in future healthcare.

1. INTRODUCTION

Respiration is the primary physiological activity of the human body, which is the process of converting glucose to energy on the cellular level. Breathing, on the other hand, is the physical process that transfers gases between cells and the environment. In the clinic, the respiratory signal (or breathing signal) is a broad term that refers to any signal containing information related to the breathing process. Respiratory signals provide clinicians with important information concerning the breathing process, including tidal volume [15], respiratory rate, and the variability of the breathing pattern [3]. The respiratory rate quantity can be accessed by counting the number of breaths a patient takes in a one-minute period [31] [34]. On the other hand, effectively assessing breathing pattern variability requires more signal processing [4]. These quantities can be used to monitor respiratory health or to predict respiratory failure [12].

On the respiratory signal recording side, the gold standard amongst respiratory signals is the spirogram collected by the spirometry. However, spirometry is uncomfortable and not ideal for long-term monitoring [13]. Besides the spirometer, a variety of hardware and software sensors for measuring respiration have been proposed [23]. Compared to the spirogram, the information obtained from these sensors might be limited, and obtaining a reliable respiratory signal is challenging. In this paper, we focus on the respiratory signal that can be extracted from the electrocardiographic (ECG) signal, which is an ensembled software methodology for estimating breathing activity through easy-to-use, mobile-capable, and non-invasive ECG sensors. It is based on the fundamental physiological fact – when the patient inhales (resp. exhales), transthoracic electrical impedance increases (resp. decreases), and the amplitude of the ECG signal decreases (resp. increases) and the ECG morphology changes.

Deriving the respiratory signal from a multiple- or single-channel ECG has been attempted using a number of methods [25] [17] [6]. Traditionally, the EDR signal is obtained
by interpolating the time series of RS amplitudes as follows:

\[ EDR (r_i/f_s) := E(r_i) - E(s_i), \]

where \( E \in \mathbb{R}^n \) is the discrete-time ECG signal having length \( n \) and a sampling rate of \( f_s \) Hz, \( r_i \) is the sample index of the \( i \)-th R peak, and \( s_i \) is the sample index of the subsequent S peak. Another method involves estimating the area of each QRS complex [6, Chapter 8]. Principal component analysis (PCA), independent component analysis, and kernel principal component analysis (kPCA) have also been used to obtain an EDR signal [19, 16, 39, 37]. Recently, an EDR algorithm based on the diffusion maps [7] algorithm was proposed [22].

While many EDR approaches exist, the superiority of one particular technique is debated. For example, one comparison article advocates for the method based on RS amplitudes [38], while another advocates for the method based on measuring QRS areas [29]. Since it is difficult to conclude which EDR algorithm is optimal, it is natural to consider fusing all such sensors together; that is, combining available EDR algorithms to obtain a breathing activity signal that is generally better than existing EDR signals. In other words, we can view each EDR algorithm as a software sensor for the breathing activity, and try to combine these software sensors to obtain a better one. This idea, which is similar to the concept of ensemble learning in machine learning [30], has lead to this work.

In this work, we provide two main contributions. First, we introduce and test multiple nonlinear sensor fusion approaches to deriving the respiratory signal from a two-channel ECG signal. Second, we show that the existing approaches to estimating the respiratory signal from a single- or two-channel ECG signal can be combined, or ensembled, to enhance the quality of the breathing activity estimation. In other words, a multitude of initial EDR estimates, viewed as the outputs of different software sensors measuring breathing activity from the ECG signal, are ensembled to yield a respiratory signal that is of superior quality. We refer to the proposed EDR signal as the ensembled EDR.

2. Methods

We provide a detailed description of our proposed ensembled EDR algorithm that extracts breathing activity from a two-channel ECG signal. The flowchart of the algorithm is shown in Figure 1. Implicit in the description of this algorithm is the corresponding algorithm that should be employed when only a single-channel ECG signal is available. We will make the distinction between the single- and two-channel algorithms clear when necessary.

2.1. Step 1: Pre-processing. The raw ECG signal is first upsampled to a sampling rate of 1000 Hz. Measurement noise and powerline interference in the ECG signal are surpressed by applying a bi-directional, third-order Butterworth lowpass filter with a cutoff frequency of 40 Hz. Baseline wandering is estimated and subsequently removed by applying a median filter with a window size of 200 ms to each channel of the ECG signal. This step also moderately suppresses the P and T waves. We detect the QRS complexes in each channel of the ECG signal by applying a standard high-accuracy QRS detector [24]. We apply a standard beat matching algorithm [10] to ensure that all of the QRS complexes detected in the first channel are also present in the second channel, and vice versa; the extraneous detections are removed. When using only one ECG channel, we perform beat-matching after applying two different QRS complex detection algorithms to the same ECG channel. Denote the pre-processed two-channel ECG signal as a pair of vectors \( E_1, E_2 \in \mathbb{R}^n \), where \( n = f_s \times T \) is the number of samples, \( f_s = 1000 \) Hz is the sampling rate of the signal, and
Figure 1. We visually portray the main steps in the proposed ensembled EDR algorithm, in which multiple EDR signals (estimated using diverse methods) are fused to form a stronger one. In the middle, we show the individual EDR estimates which, while different, share the information that can be extracted by the ensembling method. Our algorithm can achieve a superior estimate when one or two ECG leads are available. When there are two ECG leads, various estimates for the respiratory signal are made on each lead individually and on both leads simultaneously. All of the estimates are then ensembled to obtain the final EDR signal. We note that this method can in theory be extended when more ECG leads are available.

\( T \) is the duration of the recording in seconds. Suppose there are \( N \) detected R peaks in the ECG signal. Let \( r^{(1)}_i \) denote the location in samples of the \( i \)th R peak in the first channel, and let \( r^{(2)}_i \) denote the location in samples of the \( i \)th R peak in the second channel. For the purpose of analyzing the traditional EDR signal, the S peak following each R peak is
determined by

\[ s_i^{(k)} = \arg \min_{r_i^{(k)} + 1 \leq t \leq r_i^{(k)} + 60} E_k(t), \]

where the window length of 60 samples, corresponding to a 60 ms duration, is chosen according to normal electrophysiology. By defining a window around each R peak that extends 30 samples (ms) to the left and 60 samples (ms) to the right, we are able to capture the entire QRS complex, recalling that the P and T waves have been suppressed. For each channel \((k = 1 \text{ and } k = 2)\), we collect the segments containing QRS complexes and stack them as rows in a matrix:

\[ X_k(i, j + 31) := E_k \left( r_i^{(k)} + j \right), \quad -30 \leq j \leq 60, \]

where the resulting matrix is \( X_k \in \mathbb{R}^{N \times p} \), where \( p = 91 \). Note that the row ordering of \( X_k \) encodes the temporal information.

2.2. Step 2: Estimating the respiratory signal. We build a variety of estimates for the respiratory signal; these estimates, resulting from several techniques, are viewed as software sensors for the breathing activity. When only one ECG channel is available, we consider the traditional approach based on RS amplitudes [1], the geometric approach (PCA), and the manifold learning approach (diffusion maps) to obtain a pool of EDR signals. When two ECG channels are available, we apply various sensor fusion approaches, including canonical correlation analysis [18], an extension [33] of alternating diffusion [20, 36], and another variant of alternating diffusion based on the dynamic Laplacian [14]. Subsequently, these estimated respiratory signals from various software sensors are fused to obtain a new EDR signal, the ensembled EDR.

2.2.1. Traditional approach. The first estimate for the respiratory signal is the traditional EDR signal. We set

\[ R_{1, j}^{\text{trad}} = E_1(r_i^{(1)} + j) - E_1(s_i^{(1)}), \]

\[ R_{2, j}^{\text{trad}} = E_2(r_i^{(2)} + j) - E_2(s_i^{(2)}), \]

so that after piecewise cubic spline interpolation at a sampling rate of 10 Hz, the assigned \( N \) points \( \{ R_{1, i}^{\text{trad}}(r_i^{(1)} / f_s) \}_{i=1}^N \) and \( \{ R_{2, i}^{\text{trad}}(r_i^{(2)} / f_s) \}_{i=1}^N \) yield interpolated vectors \( R_{1, \text{rad}} \), \( R_{2, \text{rad}} \in \mathbb{R}^{10T} \). This interpolation is applied to all the subsequent EDR estimates, and thus, for brevity, is omitted.

2.2.2. Geometric approach. The next two estimates are obtained via principal component analysis (PCA). Let \( p_1, \ldots, p_5 \in \mathbb{R}^p \) be the top five principal components of the matrix \( X_1 \) (that is, the top five eigenvectors of the corresponding \( p \times p \) covariance matrix), and let \( q_1, \ldots, q_5 \in \mathbb{R}^p \) be the top five principal components of the matrix \( X_2 \). We then set

\[ R_{1, j}^{\text{PCA}} = \sum_{k=1}^p X_1(i, k)p_j(k), \quad j = 1, \ldots, 5 \]

\[ R_{2, j}^{\text{PCA}} = \sum_{k=1}^p X_2(i, k)q_j(k), \quad j = 1, \ldots, 5 \]
Details about this method can be found in [19, 28]. We mention that the number five is chosen in an ad hoc way. A different number of principal components can be considered.

2.2.3. Manifold learning approach. Next, we apply a nonlinear manifold learning method called the diffusion maps algorithm [7], which can be viewed as a generalization of the kernel PCA approach [39]. We build self-tuning affinity matrices $W_1, W_2 \in \mathbb{R}^{N \times N}$ by setting

$$
W_l(i, j) = \frac{1}{2} \exp \left[ -\sum_{k=1}^{p} \frac{(X_l(i, k) - X_l(j, k))^2}{\sigma_l^{(i)}} \right] + \frac{1}{2} \exp \left[ -\sum_{k=1}^{p} \frac{(X_l(i, k) - X_l(j, k))^2}{\sigma_j^{(j)}} \right],
$$

where $\sigma_l^{(i)}$ is the median of the squared Euclidean distances from the $i$-th row of $X_l$ to all other rows. We then perform $\alpha$-normalization with $\alpha = 1$ to mitigate any non-uniform densities (see [7] for details). We calculate

$$
W_l^{(\alpha)} = D_l^{-1/2} W_l D_l^{-1/2},
$$

where $D_l \in \mathbb{R}^{N \times N}$ is a diagonal matrix satisfying $D_l(i, i) = \sum_{j=1}^{N} W_l(i, j)$. We then calculate the isotropic diffusion kernel by setting

$$
P_l = \left( D_l^{(\alpha)} \right)^{-1/2} W_l^{(\alpha)} \left( D_l^{(\alpha)} \right)^{-1/2},
$$

where $D_l^{(\alpha)} \in \mathbb{R}^{N \times N}$ is a diagonal matrix satisfying $D_l^{(\alpha)}(i, i) = \sum_{j=1}^{N} W_l^{(\alpha)}(i, j)$. We obtain the top five non-trivial eigenvectors $\phi_l^{(i), \ldots, \phi_l^{(5)}} \in \mathbb{R}^N$ of $P_l$, and we set $\varphi_l^{(i)} \in \mathbb{R}^N$ to be the vector

$$
\varphi_l^{(i)} = \left( D_l^{(\alpha)} \right)^{-1/2} \phi_l^{(i)}.
$$

Finally, we set

$$
R_{1,j}^{DM} \left( \frac{r_1^{(1)}}{f_s} \right) = \varphi_l^{(1)}(i), \quad j = 1, \ldots, 5
$$

$$
R_{2,j}^{DM} \left( \frac{r_2^{(2)}}{f_s} \right) = \varphi_l^{(2)}(i), \quad j = 1, \ldots, 5.
$$

Again, we mention that a different number of eigenvectors can be considered.

2.2.4. Linear sensor fusion approach. First, let $u_1, \ldots, u_5 \in \mathbb{R}^p$ denote the top five left-singular vectors of the matrix $X_1^\top X_2$, and let $v_1, \ldots, v_5 \in \mathbb{R}^p$ denote the top five right-singular vectors of the same matrix [18]. We set

$$
R_{1,j}^{CCA} \left( \frac{r_1^{(1)}}{f_s} \right) = \sum_{k=1}^{p} X_1(i, k) u_j(k), \quad R_{2,j}^{CCA} \left( \frac{r_2^{(2)}}{f_s} \right) = \sum_{k=1}^{p} X_2(i, k) v_j(k)
$$

for all $i = 1, \ldots, N$ and $j = 1, \ldots, 5$. 
2.2.5. Nonlinear sensor fusion approaches. To perform the extended alternating diffusion algorithm\cite{33}, we calculate
\begin{align}
K_1 &= (D_1^{(α)})^{-1}W_1^{(α)}, \\
K_2 &= (D_2^{(α)})^{-1}W_2^{(α)}
\end{align}
(15)
\begin{align}
A &= K_1K_2^T - K_2K_1^T, \\
S &= K_1K_2^T + K_2K_1^T
\end{align}
(16)
Let $a_1, \ldots, a_5$ be the eigenvectors of the anti-symmetric matrix $A$ that correspond to the five non-conjugate eigenvalues of largest magnitude. Set
\begin{align}
R_{AD}^{(i,j)}\left(\frac{r_i^{(1)} + r_i^{(2)}}{2f_s}\right) &= \Re a_j(i), \\
R_{AD}^{(i,j)}\left(\frac{r_i^{(1)} + r_i^{(2)}}{2f_s}\right) &= \Im a_j(i)
\end{align}
(17)
for all $i = 1, \ldots, N$ and $j = 1, \ldots, 5$, where $\Re$ and $\Im$ denote the real and imaginary parts, respectively. Let $b_1, \ldots, b_5$ be the top five eigenvectors of the symmetric matrix $S$, and set
\begin{align}
R_{AD}^{(i,j)}\left(\frac{r_i^{(1)} + r_i^{(2)}}{2f_s}\right) &= b_j(i)
\end{align}
(18)
for all $i = 1, \ldots, N$ and $j = 1, \ldots, 5$.

Finally, we introduce a decomposition of the discrete dynamic Laplacian\cite{14}. We let $c_1, \ldots, c_5 \in \mathbb{R}^N$ be the top five non-trivial eigenvectors of the operator
\begin{align}
K_1 + K_2 = \frac{2}{f_s}
\end{align}
(19)
and set
\begin{align}
R_{DL}^{(i,j)}\left(\frac{r_i^{(1)} + r_i^{(2)}}{2f_s}\right) &= c_j(i)
\end{align}
(20)
for all $i = 1, \ldots, N$ and $j = 1, \ldots, 5$.

2.3. Step 3: Ensembling the estimated respiratory signals. Prior to combining all 52 estimates for the respiratory signal, we normalize them. For each $i = 1, \ldots, N$ and each estimate $R \in \mathbb{R}^{[10T]}$, set
\begin{align}
\bar{R}(i) &= \frac{R(i) - \sum_{k=-49}^{50} R(i+k)}{\sqrt{\sum_{l=-49}^{50} \left( R(l) - \sum_{m=-49}^{50} R(l+m) \right)^2}}
\end{align}
(21)
This procedure corresponds to locally $z$-scoring the signal.

We proceed with ensembling the estimates using a method that can be extended to include any type of EDR signal. Consider the initial matrix $M^{(0)} \in \mathbb{R}^{[10T] \times 52}$, whose columns are the 52 EDR estimates. Then, we compute the time-lagged representations $M^{(t)} \in \mathbb{R}^{([10T]-t) \times 52}$, given by
\begin{align}
M^{(t)}(i,j) := M^{(0)}(i+t, j)
\end{align}
(22)
for all $i = 1, \ldots, [10T] - t, j = 1, \ldots, 52$, and $t = 0, \ldots, 9$. We define a matrix $B$, whose rows are given by
\begin{align}
\text{row}_i B := \left[ \text{row}_{i+9} M^{(0)} \ldots \text{row}_{i+1} M^{(8)} \text{row}_i M^{(9)} \right]
\end{align}
(23)
for all $i = 1, \ldots, [10T] - 9$. Note that $B$ has 520 columns. Let $U \in \mathbb{R}^{[10T] - 9}$ be the top left-singular vector of $B$. We view this time series as the final estimate for the respiratory signal, the ensembled EDR. Note that the first entry represents the estimated
respiratory volume at time 1.0 seconds; to compensate for this lag, we add 9 null values at the beginning of the signal $U$, whose effective sampling rate is 10 Hz.

The rationale underlying the use of singular value decomposition (SVD) for fusing the estimates is as follows. Geometrically, $U$ represents the direction (in the high-dimensional space $\mathbb{R}^{\lceil 10T-9 \rceil}$) at which the power of all of the estimates is maximized. In other words, $U$ represents the common information between all of the estimates.

In some cases, only one ECG lead is available. In these cases, we do not have access to any of the estimates of the respiratory signal that require two ECG channels. However, we can still use the procedure described above, only now $M^{(0)} \in \mathbb{R}^{(\lceil 10T-9 \rceil) \times 11}$, and subsequently $M^{(0)}$, consist only of the 11 signal-channel estimates. The rest of the steps remain unchanged.

2.4. Material. The ECG signals featured in our experiment are from a set of 116 standard overnight polysomnograms which were recorded to confirm the presence of sleep apnea syndrome in subjects suspected of sleep apnea at the sleep center in Chang Gung Memorial Hospital (CGMH), Linkou, Taoyuan, Taiwan. The Institutional Review Board of CGMH approved the study protocol (No. 101-4968A3). All recordings were acquired on the Alice 5 data acquisition system (Philips Respironics, Murrysville, PA). All subjects had an apnea-hypopnea index less than 5. We use both leads of the ECG recording, which, before upsampling, were sampled at 200 Hz. To evaluate the effectiveness of our estimate for the respiratory signal, we compare it to the \texttt{FLOW}, \texttt{CFLOW}, \texttt{THO}, and \texttt{ABD} signals, where \texttt{FLOW} is the patient flow signal recorded from the thermistor, \texttt{CFLOW} is the patient flow signal recorded from the nasal cannula, \texttt{THO} is recorded from the chest band with the piezosensor, and \texttt{ABD} is recorded from the abdominal band with the piezosensor.

2.5. Evaluation. To evaluate the performance of our algorithm and compare it to the performance of other algorithms, we employ the following procedure. We randomly select eight non-overlapping 30-minute segments from each subject’s polysomnogram. The total number of 30-minute segments is 928. Using the two (or one, as appropriate) ECG leads, we build our proposed ensembled EDR on each 30-minute segment. Let $U$ denote the ensembled EDR for one 30-minute segment, and let $V$ denote either the \texttt{FLOW} signal, the \texttt{CFLOW} signal, the \texttt{THO} signal, or the \texttt{ABD} signal. For each integer lag parameter $\tau$ in the range $-10 \leq \tau \leq 10$, we consider the shifted time series

$$U^{(\tau)}(i) := U(i + \tau)$$

and calculate the absolute value of the Pearson correlation coefficient $\rho_{\tau}$ between the first two minutes of $U^{(\tau)}$ and $V$ (ignoring any null values in $U^{(\tau)}$). Our final measure of similarity between $U$ and $V$ is

$$\gamma = \max_{-10 \leq \tau \leq 10} \left[100 \times \rho_{\tau}\right].$$

The parameter $\tau$ allows us to account for any delay between the ECG-derived respiratory signal and the respiratory signal as measured through the various sensors. The metric $\gamma$ is inherited from a previous work which examined the use of kernel PCA for building an EDR signal [39].

Inspired by a previous work [2], we introduce a second evaluation metric to quantify the extent to which our ensembled EDR signal can accurately measure time-varying respiratory rate. Effectively, it is a comparison between the time-frequency representations (TFR) of $U^{(\tau^*)}$ and $V$, where $\tau^*$ is maximum argument of (25). We use the de-shape synchrosqueezing transform (dsSST) [21] to calculate both TFRs. The dsSST is designed
to remove harmonics in the spectrogram that result from the non-sinusoidal nature of the breathing pattern. (These harmonics are not relevant when assessing instantaneous respiratory rate.) We use a window size of 200 samples, a Gaussian window with bandwidth 0.15, a soft log parameter of 0.03, a hop of 1, and 300 DFT points in the dsSST. The columns of both TFRs are $\ell_1$-normalized and compared using the 1-Wasserstein distance [8, Equation 4.3], yielding the metric $\eta$. Note that the 1-Wasserstein distance is the $L_1$ distance between cumulative density functions.

To examine how the signal length affects the performance of our new ECG-derived respiratory signal, we repeat the above experiment using the first 2, 5, and 15 minutes of each selected 30-minute segment. We remark that $\rho_t$ is calculated using only the first two minutes of $U(\tau)$ and $V$ because this way, we can accurately assess the effect of using different signal lengths to estimate the respiratory signal.

3. Results

We begin by examining the case when only one ECG lead is available. In this case, we compare the signal $U$ obtained by fusing 11 single-channel respiratory signal estimates to the traditional EDR signal and to the EDR signal obtained via PCA (the first principal component). In Table 1, these signals are compared to the accompanying $\text{FLOW}$, $\text{CFLOW}$, $\text{THO}$, and $\text{ABD}$ signals in the polysomnogram. Higher $\gamma$ values indicate a more accurate recovery of the respiratory signal. We carry out four assessments on ECG signals of lengths 2, 5, 15, and 30 minutes. (Note that the 2-minute signal is the first two minutes of the corresponding 5-minute signal, and so on.) The ensembled EDR signal in the one-channel scenario (Table 1) obtains a higher $\gamma$ index compared with the other individual methods. The evaluation by the OT distance, the $\eta$ index, is shown in Table 2. The smaller OT distance indicates a better recovery of the respiratory signal in the sense of instantaneous respiratory rate recovery. It is shown that the proposed ensembled EDR consistently performs better.

Next, we examine the case when two ECG leads are available. In this case, the signal $U$ is obtained by fusing 52 estimates for the respiratory signal made on either one of the two leads or on both leads simultaneously (see Section 2.3). Of these 52 preliminary EDR signals, a number of them are obtained using novel methods from the field of nonlinear sensor fusion. In Table 3, we compare both $U$ and these novel two-channel estimates with the accompanying $\text{FLOW}$, $\text{CFLOW}$, $\text{THO}$, and $\text{ABD}$ signals. The ensembled EDR signal in the two-channel scenario (Table 3) obtains a significantly higher $\gamma$ value compared with all other one- and two-channel methods. The evaluation by the $\eta$ index is shown in Table 4, and the proposed ensembled EDR consistently performs better.

We carry out the following statistical tests to examine how the length of the signal affects the optimality of our ensembled estimate for the respiratory signal. We focus on the two-channel ensembled EDR algorithm only. The results of this test are shown in Table 5. For each target respiratory signal ($\text{FLOW}$, $\text{CFLOW}$, $\text{THO}$, or $\text{ABD}$) and each evaluation metric ($\gamma$ or $\eta$), we carry out Friedman’s test to evaluate the null hypothesis that the signal length has no effect on the evaluation metric (for the chosen target respiratory signal). The alternative hypothesis is that the signal length has a statistically significant effect on the evaluation metric (for the chosen target respiratory signal). If the null hypothesis is rejected, we carry out an additional multiple comparisons test (using Tukey’s honestly significant difference criteria) to identify which signal lengths were optimal. After the procedure, we found that using signals 5 minutes in length yielded better $\gamma$ values when the target respiratory signal was either the $\text{FLOW}$, $\text{THO}$, or $\text{ABD}$ signal. Moreover using signals of 5 minutes in length
yielded better $\eta$ values when the target respiratory signal was CFLOW. In all other cases, no statistically significant effects were observed.

| FLOW | Traditional EDR ($\tilde{R}^{\text{ad}}_1$) | PCA ($\tilde{R}^{\text{PCA}}_1$) | Diffusion Maps ($\tilde{R}^{\text{DM}}_1$) | Single-channel ensemble |
|------|---------------------------------------|---------------------------------|---------------------------------------------|------------------------|
| 2 minutes | 57.18 ± 25.39↑ | 57.83 ± 24.93↑ | 57.73 ± 24.44↑ | 60.67 ± 24.91 |
| 5 minutes | 57.28 ± 25.54↑ | 57.85 ± 25.13↑ | 57.15 ± 25.62↑ | 59.92 ± 24.92 |
| 15 minutes | 57.28 ± 25.54↑ | 57.68 ± 25.07↑ | 55.93 ± 24.54↑ | 60.09 ± 24.81 |
| 30 minutes | 57.28 ± 25.54↑ | 57.48 ± 25.18↑ | 54.00 ± 25.03↑ | 58.85 ± 25.31 |

| CFLOW | Traditional EDR ($\tilde{R}^{\text{ad}}_1$) | PCA ($\tilde{R}^{\text{PCA}}_1$) | Diffusion Maps ($\tilde{R}^{\text{DM}}_1$) | Single-channel ensemble |
|------|---------------------------------------|---------------------------------|---------------------------------------------|------------------------|
| 2 minutes | 72.46 ± 18.86↑ | 73.58 ± 18.27↑ | 72.73 ± 18.81↑ | 75.54 ± 17.23 |
| 5 minutes | 72.49 ± 18.92↑ | 73.60 ± 18.32↑ | 71.98 ± 20.23↑ | 74.93 ± 18.18 |
| 15 minutes | 72.49 ± 18.92↑ | 73.58 ± 18.19 | 71.21 ± 19.47↑ | 74.91 ± 18.00 |
| 30 minutes | 72.49 ± 18.92↑ | 73.37 ± 18.27 | 69.68 ± 20.46↑ | 74.14 ± 19.26 |

| THO | Traditional EDR ($\tilde{R}^{\text{ad}}_1$) | PCA ($\tilde{R}^{\text{PCA}}_1$) | Diffusion Maps ($\tilde{R}^{\text{DM}}_1$) | Single-channel ensemble |
|------|---------------------------------------|---------------------------------|---------------------------------------------|------------------------|
| 2 minutes | 69.95 ± 25.75↑ | 70.89 ± 25.91↑ | 70.63 ± 26.74↑ | 73.40 ± 26.56 |
| 5 minutes | 70.10 ± 25.82↑ | 70.90 ± 26.08↑ | 70.02 ± 27.61↑ | 73.36 ± 26.73 |
| 15 minutes | 70.10 ± 25.82↑ | 70.70 ± 25.96↑ | 69.56 ± 26.64↑ | 73.45 ± 26.13 |
| 30 minutes | 70.10 ± 25.82↑ | 70.45 ± 25.96↑ | 67.27 ± 27.00↑ | 72.23 ± 26.81 |

| ABD | Traditional EDR ($\tilde{R}^{\text{ad}}_1$) | PCA ($\tilde{R}^{\text{PCA}}_1$) | Diffusion Maps ($\tilde{R}^{\text{DM}}_1$) | Single-channel ensemble |
|------|---------------------------------------|---------------------------------|---------------------------------------------|------------------------|
| 2 minutes | 72.37 ± 26.10↑ | 73.83 ± 25.85↑ | 73.65 ± 26.58↑ | 76.30 ± 25.76 |
| 5 minutes | 72.41 ± 26.18↑ | 73.90 ± 25.88↑ | 72.99 ± 27.54↑ | 75.99 ± 26.15 |
| 15 minutes | 72.41 ± 26.18↑ | 73.69 ± 26.01↑ | 71.72 ± 26.40↑ | 76.02 ± 25.55 |
| 30 minutes | 72.41 ± 26.18↑ | 73.55 ± 25.97 | 69.64 ± 27.18↑ | 75.00 ± 26.09 |

**Table 1.** Performance of the proposed single-channel ensembled ECG-derived respiratory (EDR) signal evaluated by the $\gamma$ index. Entries in the table are the mean ± standard deviation of all $\gamma$ indices. A statistically significant improvement by the single-channel ensembled EDR (as evaluated by a one-sided Wilcoxon signed rank test with significance level $p < 0.05$) is indicated by the marker ↑.

In Figure 2, we show a short segment of the ensemble of 52 EDR signals next to the accompanying FLOW, CFLOW, THO, and ABD signals. In Figure 3, we show a comparison of the traditional EDR signal obtained from the first ECG lead, the EDR signal obtained from the first ECG lead using the DM algorithm, the single-channel ensembled EDR signal obtained from the first ECG lead, and the two-channel ensembled EDR signal. Compared with the EDR signal from the DM algorithm and the ensemble EDR signal, it is clear that the traditional EDR signal oscillates in an irregular way; specifically, the oscillatory pattern changes from one to another.
In this work, we demonstrate that ensembling multiple EDR signals can lead to a better estimate for the respiratory signal, which we call the ensemble EDR signal. We mention that the ensembling idea for the EDR signal could be extended to other biomedical time series. We also demonstrate the novel application of several sensor fusion techniques for extracting the amplitude modulation of a two-channel ECG signal, including canonical correlation analysis, alternating diffusion maps, and the discrete dynamic Laplacian. In the single-channel case, the traditional EDR signal is fused with the EDR signal obtained via PCA and the EDR signal obtained via the diffusion maps algorithm to achieve an estimate for the respiratory signal which exceeds all individual estimates. In the two-channel case, the traditional EDR signals from both leads are fused with 50 other EDR signals to obtain one final, superior estimate (see Figure 1).

### 4. Discussion

Table 2. Performance of the proposed single-channel ensembled ECG-derived respiratory (EDR) signal evaluated by the OT distance, the $\eta$ index. Entries in the table are the median ± median absolute deviation of all $\eta$ values. A statistically significant improvement by the single-channel ensemble EDR (as evaluated by the one-sided Wilcoxon signed rank test with significance level $p < 0.05$) is indicated by the marker †.

| Flow | Traditional (R_{trad}^{1}) | PCA (R_{PCA}^{1}) | Diffusion Maps (R_{DM}^{1}) | Single-channel ensemble |
|------|-----------------------------|--------------------|-----------------------------|-------------------------|
| CFLON | 4.85 ± 1.87† | 4.85 ± 2.06† | 4.87 ± 2.04† | 4.71 ± 1.99 |
| 2 minutes | | | | |
| 5 minutes | 4.90 ± 1.88† | 4.90 ± 1.98† | 4.83 ± 2.03† | 4.66 ± 1.94 |
| 15 minutes | 4.90 ± 1.88† | 4.88 ± 1.95† | 4.84 ± 1.97† | 4.73 ± 2.03 |
| 30 minutes | 4.90 ± 1.88† | 4.85 ± 1.81† | 4.96 ± 1.83† | 4.65 ± 1.93 |

| Flow | Traditional (R_{trad}^{1}) | PCA (R_{PCA}^{1}) | Diffusion Maps (R_{DM}^{1}) | Single-channel ensemble |
|------|-----------------------------|--------------------|-----------------------------|-------------------------|
| CFLON | 0.78 ± 0.39† | 0.77 ± 0.43† | 0.77 ± 0.36† | 0.71 ± 0.32 |
| 2 minutes | | | | |
| 5 minutes | 0.77 ± 0.38† | 0.75 ± 0.41 | 0.75 ± 0.34 | 0.72 ± 0.31 |
| 15 minutes | 0.77 ± 0.38† | 0.77 ± 0.43 | 0.82 ± 0.42 | 0.81 ± 0.35 |
| 30 minutes | 0.77 ± 0.38† | 0.78 ± 0.45 | 0.88 ± 0.46 | 0.84 ± 0.39 |

| Flow | Traditional (R_{trad}^{1}) | PCA (R_{PCA}^{1}) | Diffusion Maps (R_{DM}^{1}) | Single-channel ensemble |
|------|-----------------------------|--------------------|-----------------------------|-------------------------|
| THO | 1.42 ± 0.93† | 1.32 ± 0.86† | 1.30 ± 0.82† | 1.10 ± 0.66 |
| 2 minutes | | | | |
| 5 minutes | 1.40 ± 0.93† | 1.28 ± 0.86† | 1.33 ± 0.82† | 1.08 ± 0.65 |
| 15 minutes | 1.40 ± 0.93† | 1.31 ± 0.86 | 1.44 ± 0.99† | 1.18 ± 0.70 |
| 30 minutes | 1.40 ± 0.93† | 1.31 ± 0.86 | 1.59 ± 1.06† | 1.30 ± 0.78 |

| Flow | Traditional (R_{trad}^{1}) | PCA (R_{PCA}^{1}) | Diffusion Maps (R_{DM}^{1}) | Single-channel ensemble |
|------|-----------------------------|--------------------|-----------------------------|-------------------------|
| ABD | 0.96 ± 0.49† | 0.98 ± 0.48† | 0.94 ± 0.45† | 0.82 ± 0.37 |
| 2 minutes | | | | |
| 5 minutes | 0.96 ± 0.49† | 0.94 ± 0.46† | 0.86 ± 0.40† | 0.81 ± 0.37 |
| 15 minutes | 0.96 ± 0.49† | 0.99 ± 0.48† | 0.98 ± 0.51† | 0.90 ± 0.35 |
| 30 minutes | 0.96 ± 0.49† | 1.00 ± 0.52 | 1.20 ± 0.72† | 1.00 ± 0.43 |
A NEW EDR FROM ENSEMBLING SOFTWARE SENSORS

Table 3. Performance of the proposed two-channel ensembled ECG-derived respiratory (EDR) signals evaluated by the $\gamma$ index. Entries in the table are the mean ± standard deviation of all $\gamma$ indices. A statistically significant improvement by the single-channel ensembled EDR was observed in all cases (as evaluated by a one-sided Wilcoxon signed rank test with significance level $p < 0.05$).

|   | Canonical Correlation ($R_{CCA}^{1}$) | Alternating Diffusion ($R_{AD}^{1,2}$) | Dynamic Laplacian ($R_{DL}^{1}$) | Two-channel ensemble |
|---|--------------------------------------|---------------------------------------|---------------------------------|----------------------|
|   |                                      |                                       |                                 |                      |
| 2 minutes | 57.95 ± 24.90 | 60.00 ± 24.20 | 60.29 ± 24.71 | 62.98 ± 24.64 |
| 5 minutes | 57.99 ± 25.14 | 59.04 ± 25.08 | 59.49 ± 25.29 | 62.79 ± 24.56 |
| 15 minutes | 57.82 ± 25.08 | 58.16 ± 24.67 | 58.11 ± 24.75 | 62.47 ± 24.36 |
| 30 minutes | 57.66 ± 25.12 | 58.05 ± 24.00 | 57.84 ± 24.96 | 61.60 ± 24.62 |

In this work, we use manifold learning methods such as the diffusion maps algorithm to recover the topology of the manifold which underlies the set of observed QRS complexes. When the manifold is nonlinear, one significant challenge to extracting respiratory dynamics is that this information can be spread non-linearly across multiple eigenvectors of the graph Laplacian. To be specific, it is not guaranteed that the first non-trivial eigenvector will contain (or be the sole container of) the respiratory information. See [22] for an extensive discussion. This problem is also present when we attempt to use linear methods such as PCA to recover a nonlinear manifold. However, when the underlying manifold of QRS complexes is low-dimensional (an assumption we make based on a priori physiological knowledge), an embedding of that manifold can be constructed using a small number of eigenvectors of the graph Laplacian [27], where the spectral convergence in the $L^\infty$ sense with a convergence rate is provided in [9]. We accept that there will be a distortion of the underlying manifold incurred when we use only five eigenvectors of the graph Laplacian to
accomplishing this step will be explored in future work. One issue that we do not address in this work is the linearity of the interpolation step. In principle, the interpolation should be done along the surface of the manifold. Algorithms for accomplishing this step will be explored in future work.

We see that as the length of the ECG signal increases past five minutes, the $\gamma$ values for most methods decrease and the $\eta$ values for most methods decrease. The tests shown in Table 5 support this observation. While asymptotical analysis of the diffusion and other such operators guarantees an improved recovery of the manifold underlying the set of QRS complexes when the number of observed QRS complexes increases, we believe that the decrease when using signals longer than five minutes is due to non-stationarity in the time series. The extent to which stationarity (or a lack of stationarity) impacts the viability

| Flow  | Canonical Correlation $\tilde{R}_{1,1}^{\text{CCA}}$ | Alternating Diffusion $\tilde{R}_{2,1}^{\text{AD}}$ | Dynamic Laplacian $\tilde{R}_{1}^{\text{DL}}$ | Two-channel ensemble |
|-------|--------------------------------|--------------------------------|--------------------------------|---------------------|
| 2 minutes | $4.80 \pm 2.06$ | $4.77 \pm 2.13$ | $4.79 \pm 2.11$ | $4.72 \pm 2.13$ |
| 5 minutes  | $4.83 \pm 2.04$ | $4.87 \pm 2.18$ | $4.78 \pm 2.14$ | $4.69 \pm 2.07$ |
| 15 minutes | $4.80 \pm 2.03$ | $4.79 \pm 2.08$ | $4.71 \pm 2.02$ | $4.75 \pm 2.11$ |
| 30 minutes | $4.81 \pm 1.88$ | $4.80 \pm 2.14$ | $4.79 \pm 1.97$ | $4.67 \pm 2.09$ |

| Flow  | Canonical Correlation $\tilde{R}_{1,1}^{\text{CCA}}$ | Alternating Diffusion $\tilde{R}_{2,1}^{\text{AD}}$ | Dynamic Laplacian $\tilde{R}_{1}^{\text{DL}}$ | Two-channel ensemble |
|-------|--------------------------------|--------------------------------|--------------------------------|---------------------|
| 2 minutes | $0.77 \pm 0.40$ | $0.70 \pm 0.30$ | $0.64 \pm 0.27$ | $0.58 \pm 0.22$ |
| 5 minutes  | $0.75 \pm 0.40$ | $0.66 \pm 0.30$ | $0.65 \pm 0.29$ | $0.59 \pm 0.24$ |
| 15 minutes | $0.77 \pm 0.43$ | $0.67 \pm 0.32$ | $0.67 \pm 0.31$ | $0.60 \pm 0.26$ |
| 30 minutes | $0.77 \pm 0.42$ | $0.75 \pm 0.34$ | $0.72 \pm 0.32$ | $0.67 \pm 0.29$ |

| Flow  | Canonical Correlation $\tilde{R}_{1,1}^{\text{CCA}}$ | Alternating Diffusion $\tilde{R}_{2,1}^{\text{AD}}$ | Dynamic Laplacian $\tilde{R}_{1}^{\text{DL}}$ | Two-channel ensemble |
|-------|--------------------------------|--------------------------------|--------------------------------|---------------------|
| 2 minutes | $1.32 \pm 0.86$ | $1.04 \pm 0.62$ | $1.00 \pm 0.61$ | $0.93 \pm 0.54$ |
| 5 minutes  | $1.28 \pm 0.86$ | $1.07 \pm 0.67$ | $1.21 \pm 0.73$ | $0.96 \pm 0.59$ |
| 15 minutes | $1.31 \pm 0.85$ | $1.29 \pm 0.75$ | $1.27 \pm 0.79$ | $1.02 \pm 0.56$ |
| 30 minutes | $1.31 \pm 0.85$ | $1.26 \pm 0.71$ | $1.20 \pm 0.71$ | $1.12 \pm 0.65$ |

| Flow  | Canonical Correlation $\tilde{R}_{1,1}^{\text{CCA}}$ | Alternating Diffusion $\tilde{R}_{2,1}^{\text{AD}}$ | Dynamic Laplacian $\tilde{R}_{1}^{\text{DL}}$ | Two-channel ensemble |
|-------|--------------------------------|--------------------------------|--------------------------------|---------------------|
| 2 minutes | $0.85 \pm 0.44$ | $0.87 \pm 0.38$ | $0.83 \pm 0.36$ | $0.78 \pm 0.29$ |
| 5 minutes  | $0.91 \pm 0.45$ | $0.86 \pm 0.36$ | $0.83 \pm 0.35$ | $0.74 \pm 0.32$ |
| 15 minutes | $0.94 \pm 0.43$ | $0.87 \pm 0.37$ | $0.88 \pm 0.36$ | $0.78 \pm 0.32$ |
| 30 minutes | $0.98 \pm 0.50$ | $0.90 \pm 0.37$ | $0.90 \pm 0.38$ | $0.79 \pm 0.29$ |

Table 4. Performance of the proposed two-channel ensembled ECG-derived respiratory (EDR) signals evaluated by the OT distance, the $\eta$ index. Entries in the table are the median \pm median absolute deviation of all $\eta$ indices. A statistically significant improvement by the two-channel ensembled EDR (as evaluated by a one-sided Wilcoxon signed rank test with significance level $p < 0.05$) is indicated by the marker $\dagger$. recover this manifold, but we can guarantee that somewhere in these chosen eigenvectors lies the respiratory information. We furthermore note that this distortion is preferable to allowing additive noise near the manifold to contaminate our embedding $[11]$. One issue that we do not address in this work is the linearity of the interpolation step. In principle, the interpolation should be done along the surface of the manifold. Algorithms for accomplishing this step will be explored in future work.
TABLE 5. Examining the effects of signal length on the performance of the two-channel ensembled EDR signal. When Friedman’s test indicates the presence of signal length effects, these effects are investigated using Tukey’s honestly significant difference criteria. The notation $a \gg b$ means that using signals of length $a$ minutes was significantly better than using signals of length $b$ minutes. “Null” means that Friedman’s test did not allow a rejection of the null hypothesis.

|      | $\gamma$   | $\eta$   |
|------|-------------|-----------|
| FLOW | $2, 5 \gg 15, 30$ | Null $2, 5 \gg 30$ |
| CFLOW| Null        | $2, 5 \gg 30$ |
| THO  | $5 \gg 30$  | Null      |
| ABD  | $5 \gg 30$  | Null      |

FIGURE 2. An unsupervised ensembling of EDR signals produces one which accurately measures the respiratory cycle. From top to bottom, we show: the ensembled EDR signal; the FLOW signal; the CFLOW signal; the THO signal; and the ABD signal.

of the wave-shape oscillatory model for modeling dynamics in the ECG signal has not yet been explored [22].

In our algorithm, all parameters were chosen ad hoc and without any explicit optimization or search. In particular, there is freedom to experiment with different bandwidths for the Gaussian kernel used in our algorithm, or to use the previously proposed selection criteria [39]. An optimization approach may yield stronger results but also may lead to
over-fitting at the database level. As is illustrated in Figure 1, different EDR signals might be out of phase. Such out-of-phase behavior might downgrade the SVD performance. It is possible to consider the synchronization idea like graph connection Laplacian [35] to synchronize the global phase before applying SVD. However, due to the time-varying nature of the respiratory rate, and probably other physiological interactions among ECG and respiratory dynamics, a direct application of this global phase synchronization idea does not work well. A systematic study of this issue is of an independent interest, and will be explored in the future work.

For validating our ensembled EDR signal, we propose the use of four different signals (FLOW, CFLOW, THO, ABD) because of the indirect way all of these signals are able to monitor breathing activity and we do not have access to ground truth breathing information. While physiologically these channels all capture the same breathing activity, by examining the $\gamma$ values between each of the four respiratory signals (see Table 6), we can quantitatively confirm that they contain common information. Moreover, the $\gamma$ values between the different respiratory signals give a standard for what we could hope to achieve using the ECG signal. The evaluation metric $\gamma$ has been inherited from a previous work.
which introduced the use of kernel PCA for obtaining an EDR signal [39]. One other interesting observation in Tables 1 and 5 is that in the single-channel case, the respiratory signal that is most highly correlated with our new EDR signal is the ABD signal.

Further studies to explore the practical value of sensor fusion EDR is warranted, in particular the application in remote monitoring or mobile healthcare via smartphone app. Nowadays, as the advance of sensor technologies, there are more and more easy-to-use, mobile capable, or less-invasive sensors. While their qualities are tended to be questioned, the ensemble idea considered in this paper might be helpful to improve the overall quality of the collected signal. For example, it is well known that the photoplethysmogram not only reflects hemodynamic status but also the breathing activity [1]. Thus, we may consider combining respiratory information extracted from the ECG or photoplethysmogram [5], or even surveillance video, to further improve the quality of the obtained respiratory signal. On the other hand, the proposed ensemble EDR may contain richer respiratory information that could be better extracted by the advanced signal processing tools; for example, we may apply the time-frequency analysis [40] to more accurately extract the momentary respiratory rate, or other respiratory quantities.

We mention that there exists other approach that units a pool of estimates for the breathing activity made on a one- or two-channel ECG signal. Specifically, time-frequency analysis has been proposed for the task of sensor fusion [2]: the spectrograms of different EDR estimates are averaged to obtain a robust estimate for the respiratory rate. This method has merit for respiratory rate estimation, but its performance of recovering respiratory signal is not clear due to its lossy nature of spectrogram fusion.

This work has several limitations. Since the kernel methods we employ (such as the diffusion maps algorithm) involve computing the top eigenvectors of $N \times N$ matrices (where $N$ is the number of heartbeats), the computational time required by our algorithm is high and increases as the length of the signal increases. For very long ECG signals where additionally non-stationarity will come into play, we suggest estimating the respiratory signal over short windows of 5 minutes. The recently proposed algorithm, Roseland (Robust and Scalable Embedding via LANmark Diffusion) [32], could be considered to speed up those diffusion-based algorithms. A second limitation of our study is that we do not explicitly handle premature ventricular contractions, a significant obstacle when estimating the amplitude modulation of the ECG signal. These morphologically distinct beats should be removed by an algorithm such as [26] before running any EDR algorithm. We do not detect and remove motion artifacts from the ECG signals considered in this study, but our novel normalization procedure is designed to minimize their effect. Furthermore, we do not assess the signal quality of the accompanying FLOW, CFLOW, THO, and ABD signals before using them to assess the various EDR signals considered in this work. As far as we
know, suitable signal quality indices for such signals have not yet been developed. Finally, we only consider sleeping subjects without sleep apnea in this work, and we cannot confirm the effectiveness of our algorithm on awake subjects or on sleeping subjects with sleep apnea. Our future work will include validating the proposed algorithm in a more general population.

In summary, we proposed and verified an ensembling approach to unite the information in different EDR algorithms. The resulting ensembled EDR signal was demonstrated to be of superior quality. We envision its clinical value and its application in clinical medicine and healthcare.

REFERENCES

1. Aymen A Alian and Kirk H Shelley, Photoplethysmography, Best Practice & Research Clinical Anaesthesiology 28 (2014), no. 4, 395–406.
2. Iman Alikhani, Kai Noponen, Arto J Hautala, Rahel Ammann, and Tapio Seppänen, Spectral data fusion for robust ecg-derived respiration with experiments in different physical activity levels., HEALTHINF, 2017, pp. 88–95.
3. Gila Benchetrit, Breathing pattern in humans: diversity and individuality, Respiration physiology 122 (2000), no. 2-3, 123–129.
4. Maou-Ying Bien, You Shui Lin, Chung-Hung Shih, You-Lan Yang, Hui-Wen Lin, Kuan-Jen Bai, Jia-Horng Wang, and Yu Ru Kou, Comparisons of predictive performance of breathing pattern variability measured during t-piece, automatic tube compensation, and pressure support ventilation for weaning intensive care unit patients from mechanical ventilation, Critical care medicine 39 (2011), no. 10, 2253–2262.
5. Peter H Charlton, Timothy Bonnici, Lionel Tarassenko, Jordi Alastruey, David A Clifton, Richard Beale, and Peter J Watkinson, Extraction of respiratory signals from the electrocardiogram and photoplethysmogram: technical and physiological determinants, Physiological measurement 38 (2017), no. 5, 669.
6. Gari D Clifford, Francisco Azuaje, Patrick McSharry, et al., Advanced methods and tools for ecg data analysis, Artech house Boston, 2006.
7. Ronald R Coifman and Stéphane Lafon, Diffusion maps, Applied and computational harmonic analysis 21 (2006), no. 1, 5–30.
8. Ingrid Daubechies, Yi Wang, and Hau-tieng Wu, Conceft: Concentration of frequency and time via a multitapered synchrosqueezed transform, Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 374 (2016), no. 2065, 20150193.
9. D. Dunson, H.-T. Wu, and N. Wu, Spectral convergence of graph laplacian and heat kernel reconstruction in $l^\infty$ from random samples, submitted (2019).
10. AAMI/ANSI EC57:2012, Testing and reporting performance results of cardiac rhythm and st-segment measurement algorithms, American National Standard (2012).
11. Noureddine El Karoui, Hau-Tieng Wu, et al., Graph connection laplacian methods can be made robust to noise, The Annals of Statistics 44 (2016), no. 1, 346–372.
12. Mia Folke, L Čemerud, M Ekström, and Bertil Hök, Critical review of non-invasive respiratory monitoring in medical care, Medical and Biological Engineering and Computing 41 (2003), no. 4, 377–383.
13. Mia Folke, Fredrik Granstedt, Bertil Hök, and Håkan Scheer, Comparative provocation test of respiratory monitoring methods, Journal of clinical monitoring and computing 17 (2002), no. 2, 97–103.
14. Gary Froyland, Dynamic isoperimetry and the geometry of lagrangian coherent structures, Nonlinearity 28 (2015), no. 10, 3587.
15. Thomas J Gal, Nunn applied respiratory physiology, Anesthesia & Analgesia 90 (2000), no. 4, 1010.
16. Yue Gao, Hong Yan, Zhi Xu, Meng Xiao, and Jinzhong Song, A principal component analysis based data fusion method for ecg-derived respiration from single-lead ecg, Australasian physical & engineering sciences in medicine 41 (2018), no. 1, 59–67.
17. Eric Helfenbein, Reza Firoozabadi, Simon Chien, Eric Carlson, and Saeed Babaeizadeh, Development of three methods for extracting respiration from the surface ecg: a review, Journal of electrocardiology 47 (2014), no. 6, 819–825.
18. Harold Hotelling, Relations between two sets of variates, Breakthroughs in statistics, Springer, 1992, pp. 162–190.
19. Philip Langley, Emma J Bowers, and Alan Murray, Principal component analysis as a tool for analysing beat-to-beat changes in electrocardiogram features: Application to electrocardiogram derived respiration, IEEE Trans. Biomed. Eng 7 (2010), 7.
20. Roy R Lederman and Ronen Talmon, *Learning the geometry of common latent variables using alternating-diffusion*, Applied and Computational Harmonic Analysis 44 (2018), no. 3, 509–536.

21. Chen-Yun Lin, Li Su, and Hau-Tieng Wu, *Wave-shape function analysis*, Journal of Fourier Analysis and Applications 24 (2018), no. 2, 451–505.

22. Yu-Ting Lin, John Malik, and Hau-Tieng Wu, *Wave-shape oscillatory model for biomedical time series with applications*, 2019.

23. Haipeng Liu, John Allen, Dingchang Zheng, and Fei Chen, *Recent development of respiratory rate measurement technologies*, Physiological measurement 40 (2019), no. 7, 07TR01.

24. John Malik, Elsayed Z. Soliman, and Hau-Tieng Wu, *An adaptive qrs detection algorithm for ultra-long-term ecg recordings*, Journal of Electrocardiology (2020).

25. George B Moody, Roger G Mark, Andrea Zoccola, and Sara Mantero, *Derivation of respiratory signals from multi-lead ecgs*, Computers in cardiology 12 (1985), no. 1985, 113–116.

26. Julien Oster, Joachim Behar, Omid Sayadi, Shamim Nemati, Alistair EW Johnson, and Gari D Clifford, *Semisupervised ecg ventricular beat classification with novelty detection based on switching kalman filters*, IEEE Transactions on Biomedical Engineering 62 (2015), no. 9, 2125–2134.

27. Jacobus W Portegies, *Embeddings of riemannian manifolds with heat kernels and eigenfunctions*, Communications on Pure and Applied Mathematics 69 (2016), no. 3, 478–518.

28. Nadi Sadr and Philip de Chazal, *A fast principal component analysis method for calculating the ecg derived respiration*, 2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), IEEE, 2018, pp. 5294–5297.

29. Omer Sagi and Lior Rokach, *Ensemble learning: A survey*, Wiley Interdisciplinary Reviews: Data Mining and Knowledge Discovery 8 (2018), no. 4, e1249.

30. Benedict J Semmes, Martin J Tobin, James V Snyder, and Ake Grenvik, *Subjective and objective measurement of tidal volume in critically ill patients*, Chest 87 (1985), no. 5, 577–579.

31. Tal Shnitzer, Mirela Ben-Chen, Leonidas Guibas, Ronen Talmon, and Hau-Tieng Wu, *Recovering hidden components in multimodal data with composite diffusion operators*, SIAM Journal on Mathematics of Data Science 1 (2019), no. 3, 588–616.

32. EA Simoes, R Roark, S Berman, LL Esler, and J Murphy, *Respiratory rate: measurement of variability over time and accuracy at different counting periods*, Archives of disease in childhood 66 (1991), no. 10, 1199–1203.

33. Amit Singer and H-T Wu, *Vector diffusion maps and the connection laplacian*, Communications on pure and applied mathematics 65 (2012), no. 8, 1067–1144.

34. Ronen Talmon and Hau-Tieng Wu, *Latent common manifold learning with alternating diffusion: analysis and applications*, Applied and Computational Harmonic Analysis 47 (2019), no. 3, 848–892.

35. Devy Widjaja, Carolina Varon, Alexander Dorado, Johan AK Suykens, and Sabine Van Huffel, *Ecg-derived respiration: Comparison and new measures for respiratory variability*, 2010 Computing in Cardiology, 2010, pp. 149–152.

36. D. Widjaja, J. Taelman, S. Vandeput, M. A. Braeken, R. A. Otte, B. R. Van den Bergh, and S. Van Huffel, *Ecg-derived respiration: Comparison and new measures for respiratory variability*, 2010 Computing in Cardiology, 2010, pp. 149–152.

37. Hau-Tieng Wu, Yi-Hsin Chan, Yu-Ting Lin, and Yung-Hsin Yeh, *Using synchrosqueezing transform to discover breathing dynamics from ecg signals*, Applied and Computational Harmonic Analysis 36 (2014), no. 2, 354–359.
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