

Classification Algorithm for Nocturnal Hypoxemia Using Nocturnal Pulse Oximetry

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Abstract— This paper describes an automatic classification algorithm for nocturnal hypoxemia in patients receiving home oxygen therapy (HOT). Nocturnal hypoxemia is a well-known complication in patients with chronic respiratory disease, and the number of patients receiving HOT has increased in recent years. Many studies have reported that 40% of patients receiving HOT have sleep-related oxygen desaturation. To deal with this situation, a nocturnal pulse oximetry is used to measure oxygen saturation (SpO₂) and control the flow rate of highly concentrated oxygen. However, in some cases, the flow rate is not controlled properly and the same flow rate is adopted both during the day and night. There are several types of nocturnal hypoxemia, and it is difficult to classify these types only according to a subjective assessment of a medical doctor. Furthermore, it is difficult to continuously monitor the measurement results of pulse oximetry, although a flexible treatment depending on the state of hypoxemia is desired. To overcome these difficulties, an automatic classification method for SpO₂ measured by the nocturnal pulse oximetry is proposed in this paper. The proposed method uses the time domain waveform and the frequency characteristics of SpO₂. The classification performance of the method is evaluated by using 48 measured SpO₂ values from patients receiving the HOT. The classification results are validated with decisions of ten chest physicians.

I. INTRODUCTION

Home oxygen therapy (HOT) involves breathing in air that contains more oxygen than normal from a cylinder or machine at one's home. Recently, the number of patients receiving HOT has increased. Particularly, patients who have chronic obstructive pulmonary disease (COPD), aftereffects of tuberculosis, interstitial pneumonia, heart disease, thoracic disease, spinal disease, or neuromuscular disease may receive this treatment. In some cases, such patients experience a nocturnal hypoxemia: a state in which oxygen in arterial blood is desaturated at night during sleep. Nocturnal hypoxemia is a well-known complication in patients with chronic respiratory diseases [1]. The oxygen therapy is often used to treat hypoxemia. In this treatment, the heart rate and oxygen saturation are measured by pulse oximetry through a device attached to the fingertip or earlobe of a patient. Pulse oximetry is a noninvasive measurement method for oxygen saturation. The oxygen saturation is the ratio of saturated hemoglobin to

the total hemoglobin. The measured SpO₂ value is used to decide the flow rate and the density of concentrated oxygen. The patients inspire the oxygen with predefined parameters from an oxygen enricher or an oxygen bottle.

The oxygen flow rate is set in advance by a doctor according to the measured nocturnal pulse oximetry. However, in some cases, the flow rate is not controlled properly in HOT. For example, the same flow rate is adopted both during the day and through the night while sleeping. There are several types of nocturnal hypoxemia, and it is difficult to classify these types only according to a subjective assessment of a specialist doctor. Furthermore, it is difficult to continuously monitor the measurement results of pulse oximetry, although a flexible treatment according to the state of hypoxemia is expected.

A prior work [2] reported that 27–70% of patients with COPD have sleep-related oxygen desaturation, although they do not have oxygen desaturation during the daytime. Another study [3] reported that 40% of patients receiving HOT have sleep-related oxygen desaturation. Therefore, nocturnal hypoxemia should be detected and treated appropriately.

The HOT is a widely adopted treatment for COPD patients. Medical Research Council reported that the prognosis of COPD patients who have about 50-Torr PaO₂ can be improved by using an oxygen inhalation for more than 15 h/day [4]. Nocturnal Oxygen Therapy Trial Group also reported that oxygen inhalation for more than 18 h/day can improve the prognosis compared with oxygen inhalation for 12–15 h/day [5]. A prior work [6] reported that these improvements in prognosis are because of the reduction effect of pulmonary hypertension.

Continuous positive airway pressure (CPAP) is used as a treatment for sleep apnea syndrome (SAS). CPAP applies air pressure continuously to keep the airways open. The efficacy and safety of CPAP are established in a randomized controlled trial [7,8]. Long-term evaluation results obtained in France show that a nine-year survival rate of the treatment group improved to almost the level of normal people [9]. Therefore, CPAP can contribute to improve the prognosis of patients.

Several automatic detection methods for nocturnal hypoxemia use multimodal measured information, which include not only the pulse oximeter but also electroencephalogram (EEG), electromyogram (EMG) electro-oculogram (EOG), and so on. Polysomnography (PSG), which is an inspection method for SAS, combines EEG, EMG, EOG, and a respiration sensor. However, these methods are burdensome to patients and are difficult to apply for daily use. Especially, the PSG requires overnight measurement, and the patient needs to stay at the hospital.

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To improve the SAS diagnosis, several easy-to-use SAS detection methods using only nocturnal pulse oximetry have been proposed. This paper presents an automatic nocturnal hypoxemia classification method based only on oxygen saturation SpO_2 levels from the nocturnal pulse oximetry. The proposed method uses the time domain waveform and the frequency characteristics of SpO_2 .

II. MATERIALS AND METHODS

A. Subjects and Pulse Oximetry Measurements

The current study was conducted with the approval of the Ethics Committees or Institutional Review Board of Kobe University Hospital (170152).

Written, informed consent was obtained from all study participants. Subject enrollment was started in August 2014 and completed in March 2017. The study included patients aged 20 years or older, who underwent home oxygen therapy for chronic respiratory diseases (CRD). The patients whose conditions were stable for 1 month were eligible for enrollment in the study. The exclusion criteria were the positive pressure ventilation in use, complication of cancer, and history of exacerbation of CRD within 1 month.

The study enrolled 48 patients from Kobe University Hospital (Kobe, Hyogo, Japan), Takatsuki Hospital (Takatsuki, Osaka, Japan), Kasai City Hospital (Kasai, Hyogo, Japan), Kakogawa City Hospital (Kakogawa, Hyogo, Japan), Akashi Medical Center (Akashi, Hyogo, Japan), and Kita-harima Medical Center (Ono, Hyogo, Japan). The characteristics of the patients are shown in Table 1.

We collected 48 nocturnal pulse oximetry records from each patients using PULSOX pulse oximeter (Konica Minolta, Inc.). Each record was measured with a 1-Hz sampling rate.

B. Classification of Nocturnal Hypoxemia

The objective of this research was the automatic classification of nocturnal hypoxemia in patients receiving HOT to support optimal treatment. In this work, the nocturnal

TABLE I
SUMMARY OF PATIENT CHARACTERISTICS.

	Mean±Standard Deviation
Gender (F/M)	21/27
Age (years)	74.7±9.5
Body weight (kg)	52.6±10.4
BMI (kg/m ²)	21.2±3.7

hypoxemia is classified into three patterns: sustained pattern, periodic pattern, and intermittent pattern. Fig. 1 shows measured examples of these SpO_2 patterns and simultaneously recorded heart rate.

When the SpO_2 level drops and does not recover for a long time, it is classified as the sustained pattern (see Fig. 1(a)). The time of the drop duration is set as 655 s or more. This threshold is according to the measured results to be discussed in the next section. The assumed treatment for this pattern is the conventional HOT with a constant oxygen flow rate, which is decided according to the clinical condition parameters.

Next, when the drop interval is shorter than that in the sustained pattern, it is classified as the periodic pattern (see Fig. 1(b)). We assume that the clinical condition of this pattern is related to the rapid eye movement (REM) sleep.

Finally, we define the third pattern: intermittent pattern. The drop and recovery of the SpO_2 level are repeated with a cycle of several minutes (see Fig. 1(c)). This is a typical SpO_2 waveform of the patients with SAS. Prior works [10, 11] pointed out the frequency characteristics of this pattern. A commonly used treatment for this condition is CPAP.

Here, our biggest challenge is the treatment for the sustained and periodic patterns. Currently, no treatment other than that for the intermittent pattern is not determined. There

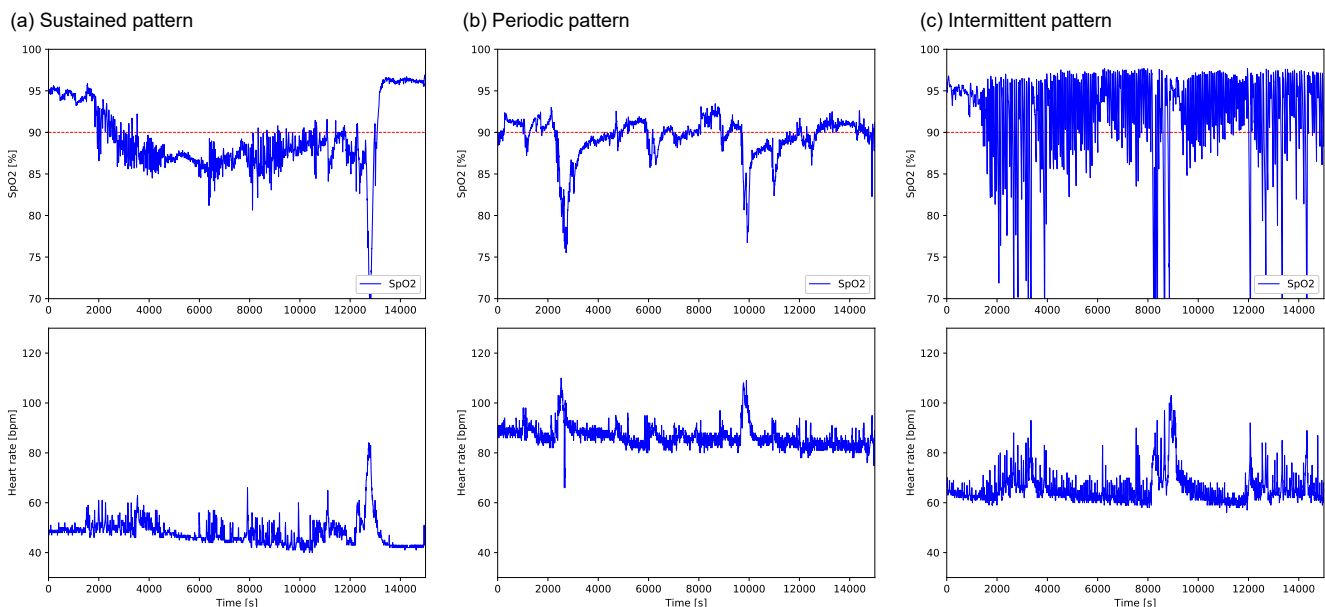


Figure 1. Example waveforms of measured abnormal SpO_2 and simultaneously recorded heart rate.

TABLE II
SUMMARY OF THREE ABNORMAL SpO₂ PATTERNS.

	Sustain pattern	Periodic pattern	Intermittent pattern
Clinical condition	Severe respiration failure	REM-related sleep hypoventilation	SAS
Treatment candidate	Constant Oxygen inhalation	Non-invasive ventilation	CPAP

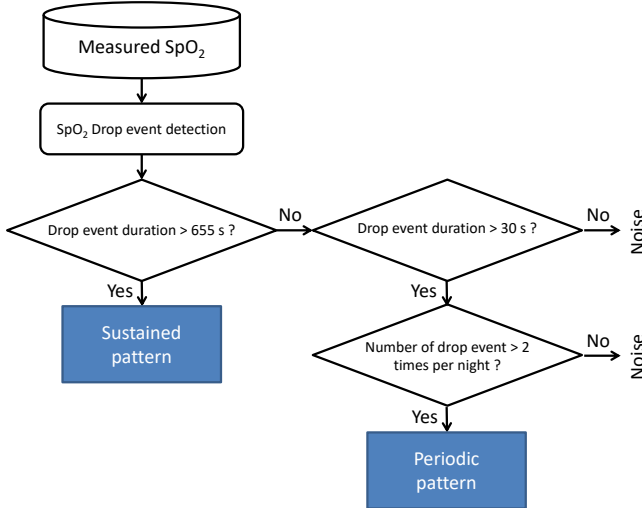


Figure 2. Flowchart of sustained and periodic pattern judgement.

are several cases in which a higher flow oxygen rate is adopted, although it is not necessary. It has a risk for the patient because the unnecessary high flow rate oxygen inhalation may cause ventilatory depression and hypercapnia. Table 2 summarizes three abnormal SpO₂ patterns.

Furthermore, the measurement results show that two or three patterns are mixed in many cases. This indicates that there are several cases requiring a finer oxygen flow rate control. In fact, the mixed pattern of the sustained, periodic, and/or intermittent pattern/s is/are a majority case in our measured results. Because there exist many cases of nocturnal hypoxemia despite the HOT, it is expected that an individually optimized oxygen flow control can improve the prognosis of patients.

To address this situation, a real-time and high-precision algorithm for automatic detection of three abnormal SpO₂ patterns is proposed in this work.

C. Signal Processing for Classification

In this section, the SpO₂ signal processing algorithm is described in detail. As mentioned already, only SpO₂ measured by a pulse oximeter is used to classify three abnormal patterns.

First, the detection process of the sustained pattern is discussed. The left part in Fig. 2 shows a flowchart of this process. When one or more drop events of longer than 655 s occur, the measured data are labeled as the sustained pattern. This threshold value was calculated on the basis of the measured data from 48 patients. All drop events were extracted from the measured data and statistical analysis was performed; Fig. 3 shows its histogram. As shown in Fig. 3, the

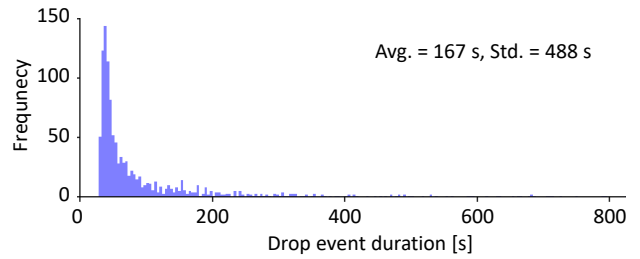


Figure 3. Histogram of drop event duration. Cut-off value of 655 s in sustained judgement is determined by the sum of the average and standard deviation of this histogram.

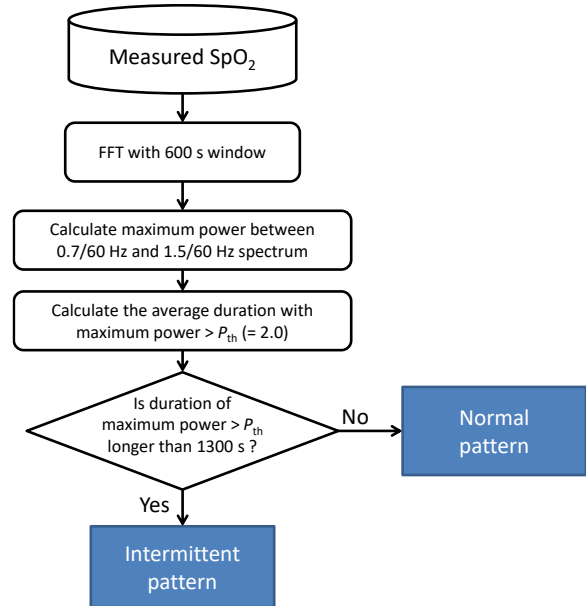


Figure 4. Flowchart of intermittent pattern judgement.

average value and standard deviation σ are 167 s and 488 s, respectively. The sum of the average value and 1σ is used as the cutoff value (655 s) for this decision process.

Here, the detection process of the periodic pattern, which is related to REM sleep, is discussed. The right side in Fig. 2 shows a flowchart of the detection process. The drop event detection process is the same as that for the sustained pattern. Here, the possible drop duration of the periodic pattern is set between 30 s and 655 s. When this drop event occurs more than twice during the measurement period, the pattern is labeled as the intermittent pattern. When the drop event duration is less than 30 s, it is ignored because there is a high possibility of noise.

Finally, the detection process of the intermittent pattern, which is related to SAS, is described. Figs. 4 and 5 show the flowchart and the execution example, respectively, of this process. As discussed in prior works [10, 11], the SpO₂ waveform of SAS patients shows a characteristic frequency pattern. The SpO₂ waveform incessantly shows drop and recovery with several minute intervals for a certain period. Our proposed method is based on this characteristic. The time-frequency analysis using discrete Fourier transform (DFT) is conducted for SpO₂ data. Then, the window length is set to 600 s. Next, the maximum spectral power between (0.7 / 60) Hz and (1.5 / 60) Hz is calculated. The pattern is labeled the intermittent pattern if the maximum spectral power is

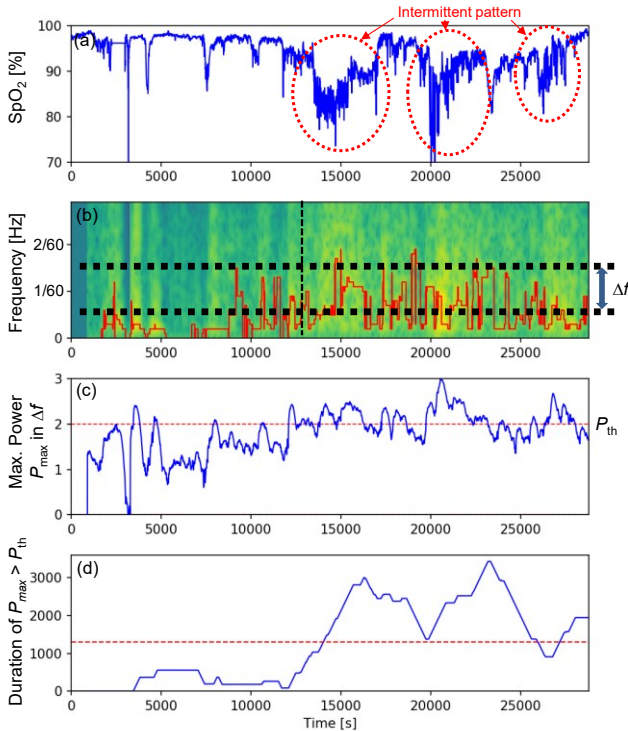


Figure 5. Example of sustained and intermittent pattern judgement.

higher than 2.0 and this state occurs for more than 1,300 s/hr. These thresholds are set based on the suggestions of chest physicians.

III. RESULTS

The measured SpO₂ values obtained through the nocturnal pulse oximetry of 48 patients described in Section II.A are classified using the proposed method. Table 3 shows the summary of the classification results.

First, ten chest physicians evaluated all of the measured data. We explained the classification policy to them in advance, and they classified each reading into three patterns while allowing duplicate decisions. Table 3 shows majority decisions of chest physicians: there are 17 sustained pattern, 30 periodic pattern, and 7 intermittent pattern results.

Next, the classification results obtained from chest physicians were compared with the automatic classification results. We evaluated the sensitivity and positive predictivity, as shown in Table 3. These indices can be calculated from true positive (TP), false positive (FP), and false negative (FN) values. Here, the sensitivity and positive predictivity are calculated as TP/(TP + FN) and TP/(TP + FP), respectively.

The proposed method achieves 100% sensitivity with 81.0% and 73.2% positive predictivities for the sustained and periodic patterns, respectively. In contrast, the sensitivity for the intermittent pattern is 71.4% with 100% positive predictivity.

IV. CONCLUSIONS

In this paper, we proposed an automatic nocturnal hypoxemia classification method using nocturnal pulse oximetry. Three patterns of the abnormal SpO₂ waveform are detected automatically using the proposed signal processing

TABLE III
CLASSIFICATION RESULT OF SpO₂ WAVEFORMS FROM 48 PATIENTS.

		Sustained pattern	Periodic pattern	Intermittent pattern
Classification result by chest physicians (including duplicate decision)		17	30	7
Prop. Method	True positive (TP)	17	30	5
	True negative (TN)	27	7	41
	False positive (FP)	4	11	0
	False negative (FN)	0	0	2
	Sensitivity [%]	100.0	100.0	71.4
Positive predictivity [%]		81.0	73.2	100.0

method. The automatic classification can contribute toward patient-specific home oxygen treatment regimens to treat nocturnal hypoxemia.

The measured SpO₂ waveforms from 48 patients were analyzed using the proposed method and classified into three distinct patterns, namely, sustained, periodic, and intermittent patterns. The same waveform results were also evaluated and classified by ten chest physicians. Both the classification results show that the proposed method achieves 100% sensitivity for the sustained and periodic patterns and the sensitivity of the intermittent pattern is 71.4%.

REFERENCES

- [1] E. C. Fletcher, J. Miller, G. W. Divine, J. G. Fletcher, and T. Miller, "Nocturnal oxyhemoglobin desaturation in COPD patients with arterial oxygen tensions above 60 mm Hg." *Chest*, vol. 92, no. 4, pp. 604–08, Oct 1987.
- [2] R. L. Owens and A. Malhotra, "Sleep-disordered breathing and COPD: the overlap syndrome." *Respir Care*, vol. 55, no. 10, pp. 1333–44; discussion 1344–46, Oct 2010.
- [3] S. Böing and W. J. Randerath, "Chronic hypoventilation syndromes and sleep-related hypoventilation," *J Thorac Dis*, vol. 7, no. 8, pp. 1273–85, Aug 2015.
- [4] Medical Research Council Working Party, "Long term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema," *Lancet*, vol. 317, no. 8222, pp. 681–89, Mar. 1981.
- [5] Nocturnal Oxygen Therapy Trial Group, "Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial," *Ann Intern Med*, vol. 93, no. 3, pp. 391–98, Sept. 1980.
- [6] T. L. Petty and P. L. Bliss, "Ambulatory oxygen therapy, exercise, and survival with advanced chronic obstructive pulmonary disease (the Nocturnal Oxygen Therapy Trial revisited)," *Respir Care*, vol. 45, no. 2, pp. 204–11, Feb. 2000.
- [7] D. I. Loube et al., "Indications for positive airway pressure treatment of adult obstructive sleep apnea patients : a consensus statement," *Chest*, vol. 115, pp. 863–66, 1999.
- [8] American Thoracic Society, "Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes," *Am J Respir Crit Care Med*, vol. 150, no. 6, pp. 1738–45, Dec. 1994.
- [9] D. Veale et al., "Mortality of sleep apnoea patients treated by nasal continuous positive airway pressure registered in the ANTADIR observatory," *Eur Respir J*, vol. 15, no. 2, pp. 326–31, Feb. 2000.
- [10] E. Schmittendorf, B. Schultheiß, and N. Böhring, "Analysis of nocturnal pulse oximetry in sleep medicine" *Biomedical Engineering*, vol. 56, no. 4, pp. 215–22, Aug. 2011, Retrieved Aug. 2018.
- [11] D. Alvarez, R. Hornero, J. Victor Marcos, and F. del Campo, "Multivariate Analysis of Blood Oxygen Saturation Recordings in Obstructive Sleep Apnea Diagnosis," in *IEEE Trans Biomed Engg*, vol. 57, no. 12, pp. 2816–24, Dec. 2010.