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OBJECTIVE ESTIMATION OF PAIN BASED ON THE ANALYSIS OF BIOLOGICAL SIGNALS, ESPECIALLY EEG

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Abstract. *Pain is an unpleasant feeling that is conveyed to the brain by sensory neurons. Doses of medications and anesthesia are determined by pain levels. However, an objective criterion to evaluate pain has not been established yet. Hence, there is risk for administering an inappropriate dose of anesthetics to patients. Therefore, we proposed a method to estimate the patient's pain based on biological signals, mainly electroencephalogram (EEG), using convenient devices. Specifically, we extracted features of pain using the wavelet transform and the ratio between low and high frequency components (LF/HF). Additionally, we proposed a new wavelet analysis focusing on mutual-similarity of biological signals using the mother wavelet of EEG. We monitored EEG, skin conductance, peripheral capillary oxygen saturation (SpO2), and pulse waves as biological signals that were caused by thermal stimulus. The following stimuli were presented alternately to 20 or more healthy subjects: thermal stimulus at a level that caused pain and thermal stimulus equal to the body temperature of the subjects. When the painful stimulus was applied, the feature obtained by the alpha wave band in EEG was attenuated. The reason seems to be that the mutual-similarity was collapsed because the waveform of EEG becomes unstable by pain.*

Keywords: Pain severity, Pain frequency, Wavelet transform, Electroencephalogram, Pulse wave, Heart rate variability

1. **Introduction.** At medical routine, pain relief by anesthesia is often required. However, we cannot define standards because anesthesia effects differ among individuals. These differences are observed owing to the physical condition, sex, and anxiety levels of individuals. Therefore, it is difficult to determine the medication dosage required for anesthesia, in advance. Currently, an objective evaluation criterion for pain has not been defined yet. Anesthetists determine the right dosage amount based on the patient's self-assessment of pain levels. Therefore, patients may be administered inappropriate amounts of anesthetics in some cases. An overdose may result in serious complications or drug dependence. From this viewpoint, the assessment of objective pain to determine the amount of anesthetics needed for each patient can contribute to a healthy living. Visual analog scale (VAS) is a subjective evaluation method useful for the diagnosis of pain [1]. The simplest VAS is a straight horizontal line of fixed length, usually 100 mm. The ends are defined as the extreme limits of the parameter to be measured (symptom, pain, health)

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orientated from the left (worst) to the right (best). The patients mark on the line the point that they feel represents their perception of their current state. There is another evaluation method for measurement of pain intensity that uses an electrical stimulation [2]. However, the subjective declaration of the patient is still necessary. Brain function analysis using magnetic resonance imaging (MRI) is an objective evaluation method [3]. This is an invasiveness method in which a patient is restrained in a closed place for about 30 minutes. It is difficult to use MRI on a daily basis because it requires a large-scale device. Additionally, it requires an engineer who can handle the equipment. In this study, we investigated an objective method to evaluate pain levels. In this method, the patient's pain is detected based on biological signals, mainly from EEG using convenient devices. We also measured the degree of oxygen saturation through SpO2, pulse waves, and skin conductance in addition to monitoring the EEG. In the EEG analysis, we focused on alpha waves. The proposed method focused on mutual-similarity of EEG using wavelet transform. Generally, when evaluating the fractal dimension, almost all biomedical signals have some degree of self-similarities, which allows us to distinguish between the healthy and pained conditions. This experiment was conducted according to the ethics guidelines because the evaluation was done on humans and was invasive.

2. **Biological Signal.**

We measured SpO2, pulse waves, skin conductance, and EEG. This section describes each feature of the biomedical signals.

2.1. **Skin conductance.**

Skin conductance is also known as galvanic skin response (GSR) or electro dermal activity (EDA). The latter refers to electrical changes, which is measured at the surface of the skin, that arise when the skin receives innervating signals from the brain [4]. When we experience emotional activation or increased physical exertion, our brain sends signals to the skin to increase the level of sweating. The electrical conductance of the skin increases to a significantly measurable level because sweat contains water and electrolytes.

2.2. **SpO2.**

Oxygen saturation levels are represented as the levels of hemoglobin contained in erythrocytes combined with oxygen molecules. The pulse oximeter measures the hemoglobin levels, and in turn, mean saturation percentage (SpO2) is calculated; thus, it indirectly measures oxygen saturation levels [5]. This noninvasive process involves inserting a finger into a device where a red light measures the redness of the blood pulsing through the finger.

2.3. **Pulse wave.**

The pulse wave is a waveform that changes according to the volume of the blood vessel being caused by inflow of blood [6]. The arterial system is the direct wave traveling toward the heart, whereas the venous system is the reflective wave. The systolic and diastolic periods can be determined from the pulse wave contour from which we can draw conclusions regarding the interaction of the heart and the arterial system. Pulse waves were measured continuously and noninvasively by a pulse oximeter.

2.4. **Electroencephalogram.**

The EEG is a recording of the electrical activity of the brain from the scalp. An event-related potential (ERP) is the measured brain response that is the direct result of a specific sensory, cognitive, or motor event [7]. We measured ERP that was caused by painful thermal stimuli. Small metal discs covered with a silver chloride coating are placed on the scalp in special positions. Figure 1 shows these positions, which are specified using the international 10/20 system. The essence of this system is the distance in percentages of the 10/20 range between the nasion-inion line and fixed points.

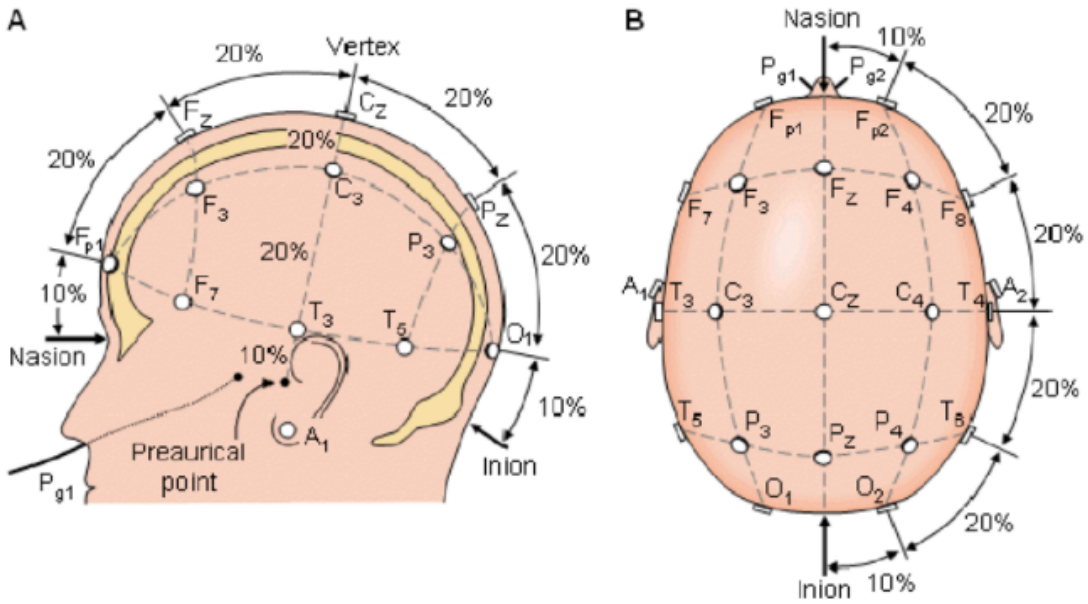

FIGURE 1. Electrodeposition of 10/20 system [7]

3. **Analysis and Feature Extraction.** EEG features were extracted using a time-frequency analysis. Regarding pulse wave features, heart rate variability (HRV) analysis was done to obtain the correlation between pulse wave and heartbeats.

3.1. **LF/HF ratio.** Power spectral analysis of the heart rate variation or the heart period (R-R interval) has become widely used to quantify cardiac autonomic regulation [8]. This method partitions the total variance of a continuous series of beats into its frequency components, identifying two main peaks: low frequency (LF) < 0.15 Hz, and high frequency (HF) between 0.15 and 0.4 Hz. The HF peak reflects cardiac parasympathetic nerve activity. In the same way, the LF peak has a sympathetic component and a parasympathetic component. Based upon these, the ratio of LF to HF (LF/HF) is used to quantify the relationship between sympathetic and parasympathetic nerve activities.

3.2. **Wavelet transform.** The wavelet coefficients of continuous wavelet transform are then given by

$$T(a,b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} x(t)\psi^* \left(-\frac{b-t}{a}\right) dt$$

where $x(t)$ represents the time domain signal of EEG, and a and b are dilation and translation parameters, respectively. The parameter a corresponds to frequency and b corresponds to time. Morley wavelet was used for the mother wavelet $\psi(t)$. This wavelet is then given by the following:

$$\psi(t) = e^{-t^2/2} \cos 5t$$

The parameters a and b affect the translation and extension of the mother wavelet, respectively [9].

3.3. **Proposed wavelet analysis.** The analysis focused on mutual-similarity of biological signals because the mother wavelet is generated from part of the EEG signal. It is possible to reduce artifacts such as movement artifacts due to a fractal feature that becomes prominent using the EEG mother wavelet. Wavelet transformations are performed in a short time, and a mother wavelet is updated every time when an analysis window is transited in time domain. The function $\psi_{EEG}(t)$ defines the extraction signal of EEG. This function must satisfy the following conditions.

1) Wavelets must have finite energy:

$$E = \int_{-\infty}^{\infty} |\psi_{EEG}(t)|^2 dt < \infty$$

The variable E is the integrated square of the amplitude.

2) $\hat{\psi}_{EEG}(f)$ is the Fourier transform $\psi_{EEG}(t)$ that must satisfy the following condition:

$$C_g = \int_0^{\infty} \frac{\hat{\psi}_{EEG}(t)}{f} df < \infty$$

A wavelet whose admissible constant satisfies

$$0 < C_g < \infty$$

is called the admissible wavelet. Traditionally, the constant C_g is called the wavelet admissible constant. An admissible wavelet implies that $\hat{\psi}_{EEG}(t) = 0$, so that it must integrate to zero. In the conventional wavelet, the basis function is used as the analyzing wavelet (AW). In the proposed instantaneous correlation function (ICF) analysis, part of the actual signal is used as the AW.

The ICF analysis is described as:

$$\mathrm{ICF}(t, a) = k_a \int_{-L_a/2}^{L_a/2} s(\tau, a) f(t + \tau) d\tau$$

where $s(\tau, a)$ is the part of the actual signal used as the AW, L_a is the length of the window function, k_a is a normalization parameter, and a and τ are scale and shift parameters, respectively. If part of the observed signal is taken to be $s(\tau, a)$, it is possible to analyze self-similarity between the analyzing wavelet and the observed signal. In the analysis of two signals, it is possible to detect the similarity between $s(\tau, a)$ taken from each signal. The technique can be applied to the analysis of observed signals that have a fundamental frequency and harmonic components. Therefore, when analyzing a signal with harmonic structure, features related to the fundamental frequency and harmonic components are simultaneously detected, being thus anticipated that changes in features with harmonic structure can be identified [10-12].

4. **Experiment.** This section describes the experimental induction of pain by thermal stimulation [13]. We estimated objective pain from various biological signals. Thermal stimuli were applied on the forearms of the subjects to cause pain. We measured changes in vital signs that were caused by this stimulus. Thermal stimuli were presented by a metal probe fixed to the forearm using a band. Painful thermal stimuli and normal thermal stimuli (which are equal to the body temperature of the subjects) were presented alternately while the subjects were in a sitting position. Although a thermal stimulus needs to be high enough to cause pain, there are individual differences in the temperature which subjects feel as painful according to their sensitivity to pain. To solve this problem, subjects declared thresholds for judging the temperature of a thermal stimulus as a pain. We monitored SpO2, pulse wave, skin conductance and EEG.

5. **Experimental Result.** The experiment was conducted with more than 20 subjects, but we will describe only a part of all data in this paper. Figure 2 shows a thermal stimulus pattern and VAS. Thermal stimuli and values of VAS had similar wave shapes.

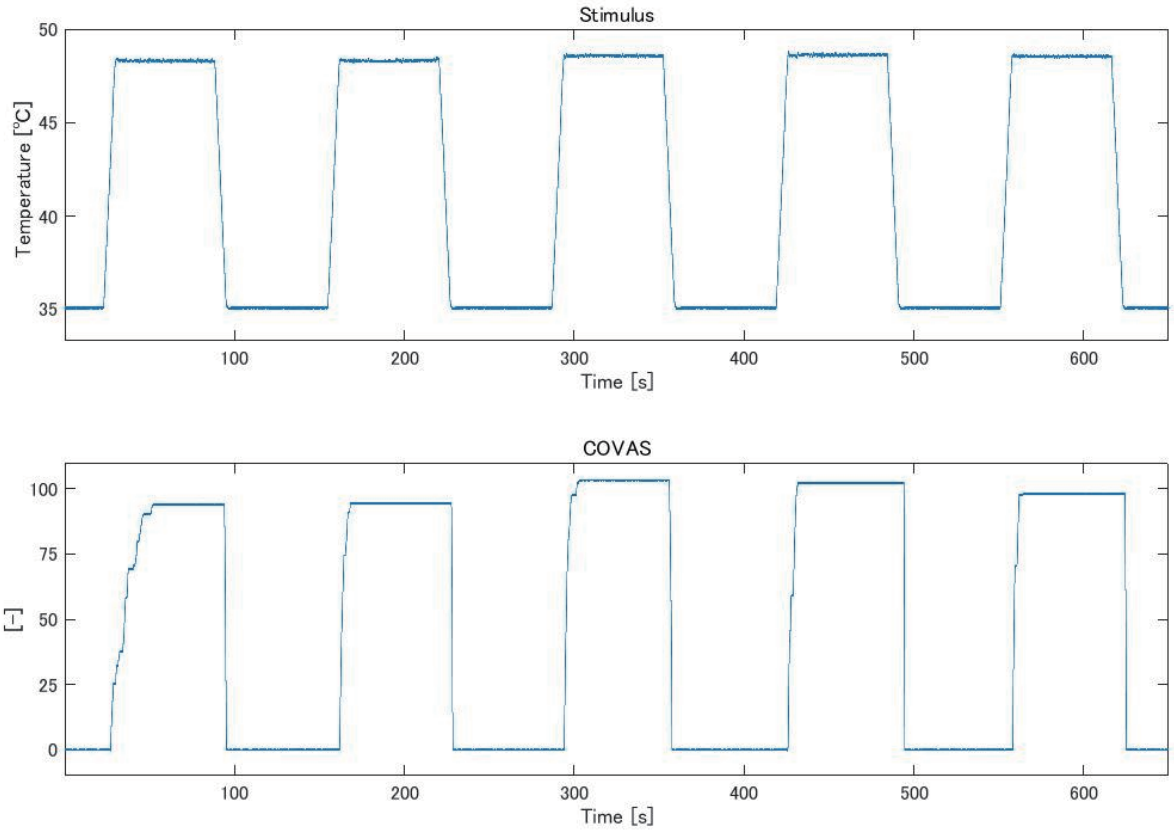

FIGURE 2. Thermal stimulus pattern and VAS

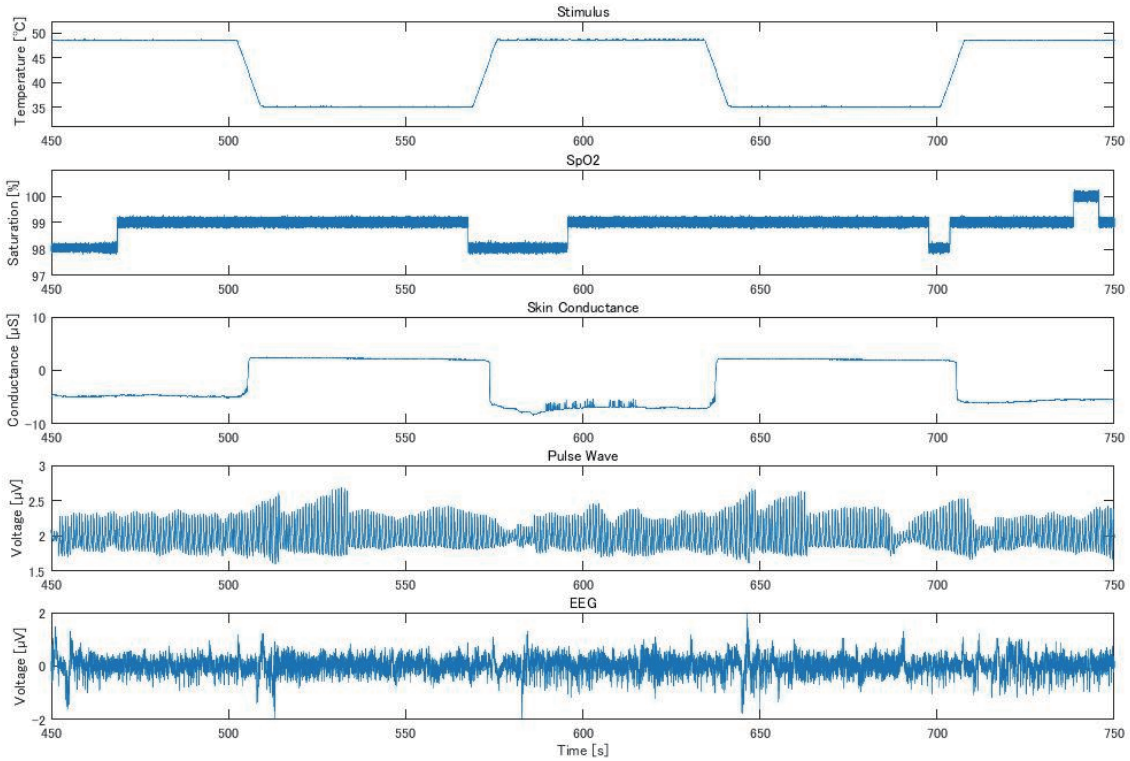

FIGURE 3. All biological signals

5.1. **All biological signals.** Figure 3 shows all biological signals: thermal stimuli, SpO2, skin conductance, pulse wave, and EEG. It is apparent that skin conductance is inversely proportional to a thermal stimulus pattern. Because the sympathetic division of the autonomic nervous system is highly aroused, the sweat gland activity also increases, which in turn increases skin conductance. We elucidated a relationship between pain, EEG, and pulse wave by extracting features from waveform.

5.2. **Result of pulse wave.** Figures 4 and 5 show R-R interval frequencies observed while a subject received a stimulus and that observed while not receiving any stimulus, respectively. The frequencies were obtained from the R-R interval for 60 seconds during the application of the stimulus. HF/LF with pain showed a value of 59, which is large when compared with the painless period. Additionally, the LF component decreased

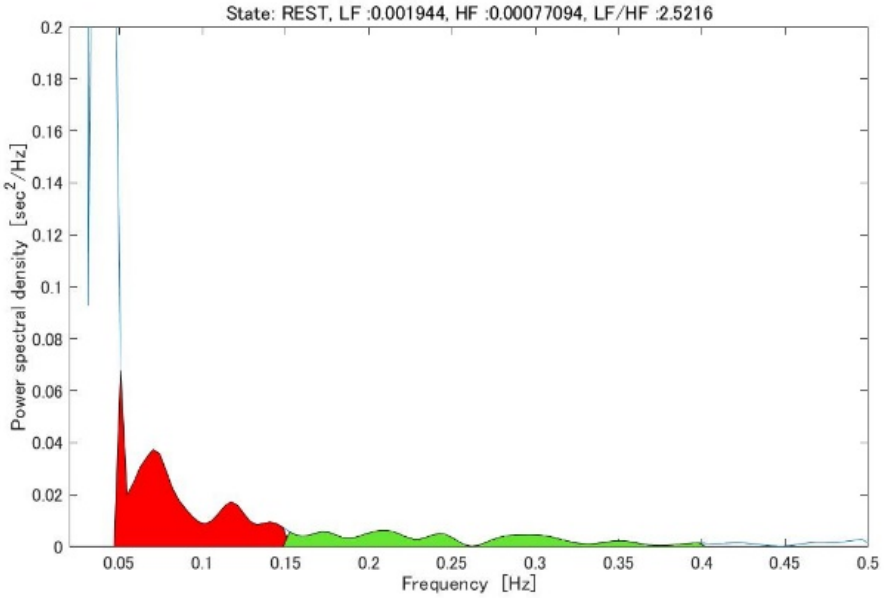

FIGURE 4. LF/HF and R-R interval frequency with stimulus

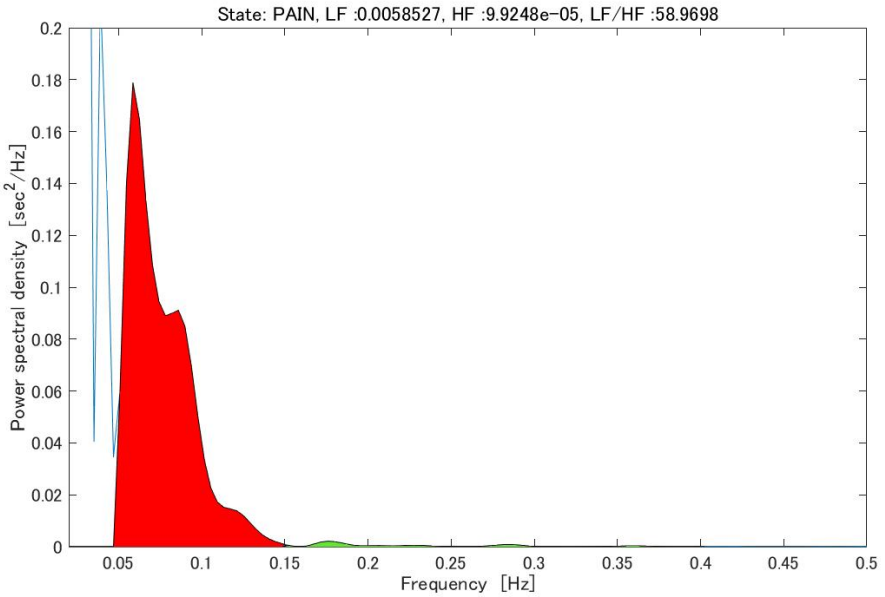

FIGURE 5. LF/HF and R-R interval frequency without stimulus

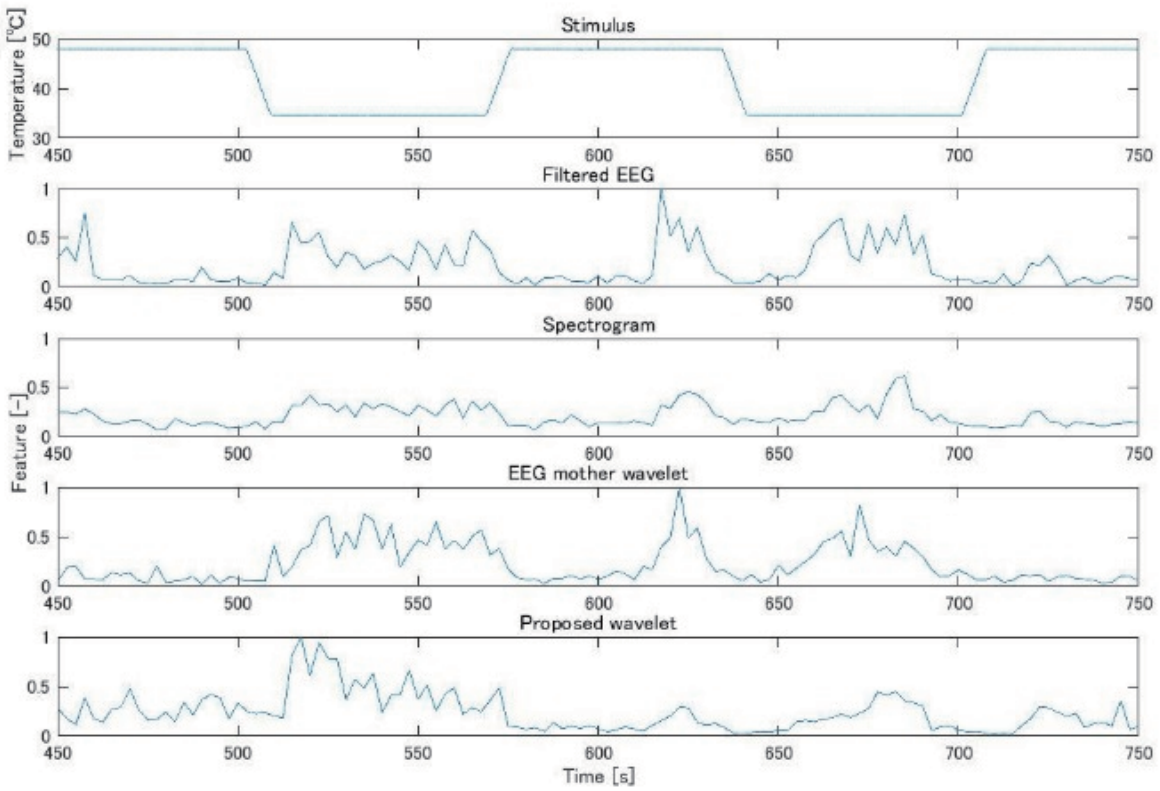

FIGURE 6. Features obtained by EEG

and the HF component increased. Based on these observations, it is inferred that the sympathetic nervous system is activated by thermal stimuli. This result suggests that HF/LF is a pain indicator because it increases with thermal stimuli.

5.3. **Result of electroencephalogram.** The EEG signals were filtered to select the alpha wave band frequencies without introducing extra noises before analysis. Figure 6 shows features that were extracted from EEG signals: thermal stimulus, amplitude (power), Fourier transform, wavelet transform, and the proposed wavelet transform. The features are the sum of numeric values of each scale that were obtained by each transform. All features obtained by EEG tended to increase in painless periods, although in some cases these features increased with pain. The features obtained by the proposed wavelet transform tend to be stronger because they do not increase compared to other features while a subject received a painful stimulus. Noises were reduced with mutual-similarity of EEG. It is inferred that this happens because the proposed wavelet coefficients are involved in waveform rather than amplitude of signals.

6. **Conclusions.** In this paper, we investigated how to extract features and measure various biological signals when subjects receive contact thermal stimuli in order to estimate pain objectively. Although SpO2 was not related to pain, skin conductance decreased with increasing pain. We found that the feature from EEG decreased with increasing pain as well as skin conductance. Especially, the proposed wavelet coefficient has the most prominent feature, as mentioned above. The results suggest that the proposed wavelet coefficient can be a robust feature, as it is not affected by noises such as movement artifacts. However, we were not able to show its effectiveness clearly, because we did not conduct recognition experiments. In a future study, we will evaluate the effectiveness of the proposed wavelet transform on EEG by conducting recognition experiments with other features.

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