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Automatic Sleep Stage Determination by Conditional Probability Based on Expert Knowledge

BY

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Abstract

Sleep is now known to be a dynamic process, and our brains are active during sleep. Sleep affects human physical and mental health, and is essential for the normal functioning of all the systems of human body. In sleep itself, there are 2 distinct states that alternate in cycles and reflect differing levels of neuronal activity. Sleep consists of non-rapid eye movement (NREM) and rapid eye movement (REM) states. NREM is further subdivided into the following 4 stages: Stage I, II, III and IV. The most well-known criteria for sleep stage scoring were published by Rechtschaffen and Kales in 1968. Each state is characterized by a different type of brain wave activity. Sleep stage scoring is an important task for inspecting neurophysiological diseases of subjects. Currently, sleep stage scoring has been widely used for evaluating the condition of sleep and diagnosing the sleep related disorders in hospitals and institutions.

Automatic sleep stage determination can free the clinicians from the heavy task of visual inspection on sleep stages. Rule-based waveform detection methods, according to Rechtschaffen and Kales criteria, have been developed in many studies. However, Rechtschaffen and Kales criteria include typical waveforms of healthy persons under ideal recording condition for sleep stage scoring. It would be insufficient to cover the variable sleep data of patients under usual recording condition in hospitals and institutions. The conventional rule-base methods have the similar limitations for clinical practice.

An expert knowledge-based probabilistic method is developed in order to overcome the limitation of conventional rule-based methods. Sleep stage scoring is considered as a multi-valued decision making problem in the filed of clinics. The visual inspection of sleep stage scoring by a qualified clinician is adopted as the expert knowledge. According to the visual inspection on a set of training data, an expert knowledge database is established in terms of probability density functions of parameters for various sleep stages. The sleep stage decision making algorithm is repeated with conditional probability and predicted probability among the consecutive sleep data segments. Sleep stages is determined automatically by the maximum value of conditional probabilities based on the joint probability of parameters. Since the visual inspection and the training data are obtained from real clinics, the expert knowledge database of probability density functions reflected the actual distribution of parameters for sleep stages. The developed expert knowledge database is desirable for automatic sleep stage determination to deal with the sleep data from real clinics.

In the expert knowledge-based method, the probability density function influences the performance of automatic sleep stage decision making by conditional probability. During the learning process of expert knowledge database construction, the probability density functions of parameters for various sleep stages are developed by using Cauchy distribution to approximately estimate the parameter distribution on histogram. Due to the infinite variance of Cauchy distribution, it had heavier tails to abate the effect of the mis-determination caused by artifacts. Comparing with Gaussian distribution, the performance of expert knowledge-based automatic sleep stage determination was improved to deal with the sleep data contaminated by artifacts.

The requirement of sleep stage scoring for patients with sleep diseases may differ from hospitals and institutions. Individual differences are also commonly existed, even under the same recording condition. An automatic parameter selection process is developed in order to establish an adaptive expert knowledge database. A set of characteristic parameters are defined as candidates. The parameter which is effective for sleep stage discrimination is selected automatically. The adaptive expert knowledge database is consisting of those selected parameters. Automatic sleep stage determination is carried out based on the adaptive expert knowledge database. After learning from clinicians' visual inspection, adaptive expert knowledge database can be constructed automatically. The developed expert knowledge-based automatic sleep stage determination system has flexible performance to meet the customized requirements of sleep diseases in hospitals and institutions.

In real clinics, clinician adopts additional rules to smooth the sleep stage scoring result especially for the continuity of stage II and onset/offset of stage REM. The corresponding sleep data may have few or no characteristics of the sleep stages which have been smoothed by the clinician. The automatic determination algorithm would be difficult to detect the sleep change and continuity only according to the characteristics of sleep data. An amendment function is developed to modify the decision making of sleep stage by the expert knowledge-based method. It is designed according to the additional rules by clinician for the continuity of stage II and onset/offset of stage REM. The cyclic rhythm of stage change and continuity by automatic sleep stage determination integrated with amendment function presented well comparing with visual inspection. The amendment function enhanced the performance of our expert knowledge-based method on stage change and continuity detection.

Approval

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Ph.D DISSERTATION

This is to certify that the Ph.D Dissertation of
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Dedication

To my dear husband, and to my lovely daughter,
they contribute me great encouragement and support
in all my endeavours for success.

and

To all my loving teachers, who taught and
equipped me with discipline and knowledge.

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Chapter 1

Introduction

1.1 Overview of Human Sleep

1.1.1 Historical perspective

Since the dawn of civilization, the mysteries of sleep have intrigued poets, artists, philosophers, and mythologists. The fascination with sleep is reflected in literature, folklore, religion, and medicine. Upanishad, the ancient Indian textbook of philosophy, sought to divide human existence to four states: the waking, the dreaming, the deep dreamless sleep, and the superconscious [1] [2]. One finds the description of pathologic sleepiness in the mythologic character Kumbhakarna in the great Indian epic Ramayana [3] [4]. Kumbhakarna would sleep for months at a time, then get up to eat and drink voraciously before falling asleep again.

The definition of sleep and a description of its functions have always baffled scientists. Mornzzi, while describing the historical development of the deafterentation hypothesis of sleep, quoted the concept Lucretius articulated 2,000 years ago--that sleep is the absence of wakefulness [5]. A variation of the same concept was expressed by Hartley in 1794, and again in 1830 by Macnish [6] [7]. Macnish defined sleep as suspension of sensorial power, in which the voluntary functions are in abeyance, but the involuntary powers, such as circulation or respiration, remain intact. The modern sleep scientist defines sleep on the basis of both behavioral and physiologic criteria [8] [9]. The behavioral criteria include (1) lack of mobility or slight mobility, (2) closed eyes, (3) reduced response to external stimulation (i.e., increased arousal threshold), (4) characteristic sleeping posture, and (5) reversibly unconscious state. The physiologic criteria (see Sleep Architecture and Sleep Profile) are based on the findings from electroencephalography (EEG), electroculography (EOG), and electromyography (EMG).

Historically, sleep was thought to be a passive state. Throughout literature, a close relationship between sleep and death has been perceived, but the rapid reversibility of sleep episodes differentiates sleep from coma and death. Sleep and wakefulness, the two basic processes of life, are like two different worlds, with independent controls and functions. Hippocrates, the father of medicine, postulated a humoral mechanism for sleep and asserted that sleep was caused by the retreat of blood and warmth into the inner regions of the body, whereas the Greek philosopher Aristotle thought sleep was related to food, which generates heat and causes sleepiness. Paracelsus, a sixteenth-century physician, wrote that "natural" sleep lasted 6 hours, eliminating tiredness and refreshing the sleeper. He also suggested that people not sleep too much or too little, but awake when the sun rises and go to bed at sunset. This advice from Paracelsus is strikingly similar to modem thinking about sleep. Views about sleep in the seventeenth and eighteenth centuries were expressed by Alexander Stuart, the British physician and physiologist, and by the Swiss physician, Albrecht yon Haller. According to Stuart, sleep was due to a deficit of the "animal spirits"; von Haller wrote that the flow of the "spirits" to the nerves was cut off by the thickened blood in the heart, resulting in sleep. Nineteenth century scientists used principles of physiology and chemistry to explain sleep. Both Humboldt and Pfluger thought that sleep resulted from a reduction or lack of oxygen in the brain.

Ideas about sleep were not based on solid scientific experiments until the twentieth century. Ishimori, in 1909, and Legendre and Pieron, in 1913, observed sleep promoting substances in the cerebrospinal fluid of animals during prolonged wakefulness [10] [11]. The discovery of the EEG waves in dogs by the English physician Caton in 1875 and of the alpha waves from the surface of the human brain by the German physician Hans Berger in 1929 provided the framework for contemporary sleep research [12][13]. It is interesting to note that Kohlschutter, a nineteenth-century German physiologist, thought sleep was deepest in the first few hours and became lighter as time went on. Modern sleep laboratory studies have generally confirmed these observations.

The golden age of sleep research began in l937 with the discovery by American physiologist Loomis and colleagues of different stages of sleep reflected in EEG changes [14]. Aserinsky and Kleitinan's discovery of rapid eye movement (REM) sleep in the l950s at the University of Chicago elect1ified the scientific community and propelled sleep research to the forefront [15]. This was followed by Rechtschaffen and Kale, technique of sleep scoring based on results of the EEG, EMG. and EOG, which has become the gold standard for sleep scoring throughout the world [16]. The other significant milestone in the history of sleep medicine was the discovery in 1965 (independently) by Gastaut and colleagues in France and Jung and Kuhlo in Germany of upper airway obstruction during sleep in patients with sleep apnea syndrome [17] [18].

1.1.2 Importance of sleep

Sleep is not a waste of time. It is now known to be a dynamic process, and our brains are active during sleep. Sleep is defined as a state of unconsciousness from which a person can be aroused [19]-[21]. In this state, the brain is relatively more responsive to internal stimuli than external stimuli. Sleep should be distinguished from coma. Coma is an unconscious state from which a person cannot be aroused [23] [24].

Sleep is essential for the normal, healthy functioning of the human body. It is a complicated physiological phenomenon that scientists do not fully understand. Although researchers are not exactly sure why we need sleep, there are two basic theories. Sleep enables the body and mind to rejuvenate, reenergize, and restore. As a person sleeps, it is thought that the brain performs vital housekeeping tasks, such as organizing long-term memory, integrating new information, and repairing and renewing tissue, nerve cells and other biochemicals. Sleep allows the body to rest and the mind to sort out past, present, and future activities and feelings. Sleep may have evolved as a protective adaptation-finding food in the daytime and hiding at night is easier. Nearly every animal sleeps to some degree. Thus, it only makes sense that predators sleep more than animals that are prey. For humans, the amount and quality of sleep achieved is directly proportional to the amount and quality of the next day's productivity

Sleep is a necessary and vital biological function. It is essential to a person's physical and emotional well being. Studies have shown that without enough sleep, a person's ability to perform even simple tasks declines dramatically. The average sleep-deprived individual may experience impaired performance, irritability, lack of concentration, and daytime drowsiness. They are less alert, attentive, and unable to concentrate effectively. Additionally, because sleep is linked to restorative processes in the immune system, sleep deprivation in a normal adult causes a biological response similar to the body fighting off an infection. Persistent sleep deprivation can cause significant mood swings, erratic behavior, hallucinations, and in the most extreme, yet rare cases, death. The jury is still out on the long-term effects of sleep deprivation on health. Current research in this area is examining the effects of sleep deprivation on the immune system.

A pioneer in sleep research, Dr. William Dement, noted that most undergraduates enter college with some knowledge of personal health, but little to no knowledge of the value of sleep. He suggests that all students should not only learn the importance of physical fitness and good nutrition, but healthy sleep, calling all three the "fundamental triumvirate of health."

At least 40 million Americans each year suffer from chronic, long-term sleep disorders each year, and an additional 20 million experience occasional sleeping

problems. These disorders and the resulting sleep deprivation interfere with work, driving, and social activities. The most common sleep disorders include insomnia, sleep apnea, restless legs syndrome, and narcolepsy.

Almost everyone occasionally suffers from short-term insomnia. This problem can result from stress, jet lag, diet, or many other factors. Insomnia almost always affects job performance and well-being the next day. Sleep apnea is a disorder of interrupted breathing during sleep. It usually occurs in association with fat buildup or loss of muscle tone with aging. These changes allow the windpipe to collapse during breathing when muscles relax during sleep.

1.2 Sleep Stage Scoring

1.2.1 Definition of sleep stages

As mentioned earlier, sleep is a dynamic process. There are 2 distinct states that alternate in cycles and reflect differing levels of neuronal activity. Each state is characterized by a different type of brain wave (electrical activity that is recorded with the help of electrodes placed on the skull) activity [25] [26]. Sleep consists of non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. NREM is further subdivided into the following 4 stages:

- Stage I (light sleep)
- Stage II
- Stage III & IV (deep sleep)

The stages of NREM sleep and REM sleep cycle over and over again during a night's sleep. Stages I, II, III, and IV are followed by REM sleep. A complete sleep cycle, from the beginning of stage I to the end of REM sleep, usually takes about one and a half hours.

For the purpose of analysis, a night’s sleep is divided into 3 equal time periods: sleep in the first third of the night, which comprises the highest percentage of NREM; sleep in the middle third of the night; and sleep in the last third of the night, the majority of which is REM. Awakening after a full night’s sleep is usually from REM sleep.

NREM sleep

Stage I is a stage of light sleep and is considered a transition between wakefulness and sleep. During this stage, the muscles begin to relax. It occurs upon falling asleep and during brief arousal periods within sleep, and usually accounts for 5-10% of total sleep time. An individual can be easily awakened during this stage.

Stage II occurs throughout the sleep period and represents 40-50% of the total sleep time. During stage II, brain waves slow down with occasional bursts of rapid waves. Eye movement stops during this stage.

In stage III, extremely slow brain waves called delta waves begin to appear. They are interspersed with smaller, faster waves. In stage IV, delta waves are the primary waves recorded from the brain. These 2 stages are distinguished from each other only by the percentage of delta activity. Together they represent up to 20% of total sleep time. Stages III and IV are called deep sleep, during which all eye and muscle movement ceases. It is difficult to wake up someone during these 2 stages. If someone is awakened during deep sleep, he does not adjust immediately and often feels groggy and disoriented for several minutes after waking up. Some children experience bedwetting, night terrors, or sleepwalking during deep sleep.

REM sleep

REM sleep represents 20-25% of the total sleep time. REM sleep follows NREM sleep and occurs 4-5 times during a normal 8- to 9-hour sleep period. The first REM period of the night may be less than 10 minutes in duration, while the last may exceed 60 minutes. In a normal night's sleep, bouts of REM occur every 90 minutes.

When the person is extremely sleepy, the duration of each bout of REM sleep is very short or it may even be absent. REM sleep is usually associated with dreaming. During REM sleep, the eyeballs move rapidly, the heart rate and breathing become rapid and irregular, and the blood pressure rises. The muscles of the body are virtually paralyzed. The brain is highly active during REM sleep, and the overall brain metabolism may be increased by as much as 20%. The electrical activity recorded in the brain during REM sleep is similar to that which is recorded during wakefulness.

1.2.2 Importance of sleep stage scoring

Sleep has been regarded as a testing situation for the autonomic nervous system, because its activity is modulated by sleep stages. Sleep stage scoring is an important task for inspecting neurophysiological diseases of subjects.

Sleep related breathing disorders also influences the autonomic nervous system and can cause heart rate changes known as cyclical variation. Sleep apnea is a cardio-respiratory disorder characterized by brief interruption of breathing during sleep, and is often more generically described as sleep disordered breathing. Typical sleep patterns of a sufferer can involve heavy snoring interspersed with both partial or complete waking and grasping for breath. The primary health implications of sleep apnea are its impact on the cardiovascular system, increased accident levels due to sleepiness, and quality of life issues. Moreover, obstructive sleep apnea is not a rare condition. It occurs in 2%-4% of middle-aged adults and in 1%-3% of preschool

children. However, there is a surprisingly low public and medical awareness of the illness despite the fact that apnea has such health and quality of life implications, For example, of the 10-20 million sufferers in the U.S. with moderate-to-severe sleep apnea, it is estimated that only 10%-15% have been diagnosed.

A contributing factor to the low level of awareness of this disease is the relatively limited access to diagnostic tests in the general population. In most countries, the gold standard for diagnosis of sleep apnea is overnight sleep by polysonomography, which is carried out in a specialized hospital or sleep laboratory. Currently, sleep stage scoring has been widely used for evaluating the condition of sleep and diagnosing the sleep related disorders in hospitals and institutions.

1.2.3 Computerized sleep staging techniques

Finding a way to study sleep data and getting valuable information from the data is a challenging task. Classifying this data can help medical professionals to diagnose sleep related disorders efficiently and accurately.

Recent advances in the computing power and storage devices have made computer-based recording of polysomnograms very attractive. Digital polysomnograms offer the possibility of automating many tedious and time-consuming tasks of identifying sleep related events.

Making visual inspection on sleep stages is a rather heavy task for clinicians. To make visual inspection of one's overnight sleep requires skillful knowledge about the sleep EEGs and stage-scoring criteria. Additionally, it is a rather laborious task, because sleep recording always contains large amount of data (about 7-8 hours). The computerized sleep stage determination technique can free the clinician from the heavy tasks of visual inspection. Automation also introduces a measure of objectivity in the scoring of various discrete events. Many researches were investigated on developing the computerized sleep stage scoring system [27] [28].

Waveform detection

The waveform detection methods were firstly used for sleep analyzing by Smith et al. They started their research works on sleep stage analyzing in 1970’s [29]. In their study, the characteristic waveforms and phasic events detection methods were developed in order to realize automatic sleep stage determination. Smith et al. described the method used for spindle detection in 1975 [30]. They developed and applied slow wave amplitude and period analysis for sleep analyzing in 1978 [31]. The digital filters used in their analyzing system were described in 1972 and 1973 [32]. In their later papers, they described many applications of their system of EEG analysis [33]. The systematic description of their method can be found in the

handbook of EEG and Clinical Neurophysiology in 1986 [34] [35].

Many studies have been conducted concerning methods for characteristic waveforms detection for automatic sleep stage interpretation. Ben et al. investigated on detection of K complex and sleep spindle. They developed an object-oriented approach and tried to test Artificial Neural Nets method for sleep EEG interpretation by waveform detection [36] [37]. Another study on sleep spindle detection was by Akgul et al. Their work characterized the dynamics of sleep spindle, observed in EEG recorded from human sleep, using both time and frequency domain methods which depend on higher order statistics and spectra [38]. Rapid eye movement is the indicator for REM sleep. In Agarwal et al. works, they presented a detection scheme that combines many of the intrinsic properties of rapid eye movements [39]. Discrete wavelet transform was adopted by Tsuji et al. for automatic detection of rapid eye movements [40].

A practical computer system for real-time analysis of sleep EEG was described by Lim et al. [41]. Their method was based on a two-component model of the signal in which waves are detected by a combination zero-crossing and peak detection algorithm. Principle et al. developed an automated sleep staging method by combining signal information, human heuristic knowledge in the form of rules, and a mathematical framework [42]. The EEG/EOG/EMG events related for sleep staging were detected in real time by an existing front-end system. An automatic sleep stager as close as possible to Rechtschaffen and Kales criteria was designed by Oxford Medical [43] [44]. An automated method for sleep stage scoring by using hybrid rule-based and case-based reasoning method was proposed by Park el al. [45]. Their rule-based reasoning was based on waveform or phasic event detection method. Their case-based reasoning method was in the field of artificial intelligence as a revision to rule-based result. An expert system for automatic identification of sleep stages based on characteristic waveforms and background EEG activity by using a decision tree was described by Anderer et al. [46] [47]. Another similar work was done by Sušmáková et al., which also going through the basic knowledge about classification of sleep stages from polysomnographic recordings [48] A huge number of characteristics, including relevant simple measures in time domain, characteristics of distribution, linear spectral measures, measures of complexity and interdependency measures were computed for sleep recordings. A multi-channel and temporal coincidences approach was proposed by Saccomandi et al. to detect transient EEG events in sleep stages [49].

Autoregressive model (AR model)

For decades, linear parametric model have proved very useful in various applications. Autoregressive model are of particular interest because (1) AR model coefficients can be easily estimated by solving a set of linear equations or recursively computed using the Levinson-Durbin recursion formula, and (2) When new data

became available, AR coefficients can be efficiently updated with Kalman filter equations.

AR model have been employed in characterizing the EEG of various sleep stages as well as detecting the occurrence of transients of epileptic origin by Jansen et al. [50]. The application of AR model with bispectual analysis was developed by Ning et al [51]. In their study, they reviewed the basic properties of AR modeling and bispectural analysis and provided their application in EEG research of sleep stage scoring. Spectral estimation of EEG signals by Autoregressive modeling was developed by Estrade et al. [52]. They proposed Itakura Distance for AR model to measure the degree of similarity between EEG and EOG signals.

Neural Network model

Neural networks have been applied to various kinds of problems in many fields due to their ability to analyze complicated systems without accurate modeling in advance. Neural network was compared with several classification methods to select the most efficient classifier for rat sleep staging in Robert et al. [53] [54]. NN technique was developed for modeling the dynamic-transition during human sleep by Nakao et al. [55]. Sleep stage scoring using the neural network model was investigated by Schaltenbrand et al. for comparison between visual and automatic analysis in normal subjects and patients [56]. Similar work was done in Caffarel et al. study of neural network system evaluation for automatic sleep stage scoring [57].

Based on the conventional neural network method, Shimada et al. proposed a new type of neural network (NN) model referred to as a sleep EEG recognition neural net work (SRNN) which enables to detect several kinds of important characteristic waves in sleep EEG which are necessary for diagnosing sleep stages [58].

Artificial neural network (ANN) and wavelet based method was developed by Sinha [59]. In his study, EOG and EMG signals were used for manual identification of sleep states before training and testing of ANN. The percentages power of the 2 s epochs of the digitized EEG signals were calculated and analyzed to select the manually confirmed sleep-wake states for each epoch. Second order Daubechies mother wavelet has been used to get the wavelet coefficients for the selected EEG epochs.

Fuzzy model

Neurofuzzy systems find their applications in many areas, medical diagnosis being one of many areas. Classification of sleep stages for infants has been analyzed by using fuzzy models. A neuro-fuzzy classifier (NFC) of sleep-wake states and stages has been developed for healthy infants of ages 6 mo and onward by Held et al. [60] [61]. Their sleep classification process is divided into three steps: data acquisition, pattern identification, and sleep-waking state-stage classification.

Another study was done by Pinero et al. [62]. Their system is divided into four

modules: the first processes the electrophysiological signals and determines its most relevant parameters; the second module establishes fuzzy rules that will be used during the classification process; the third module is an inference module, it implements a fuzzy model. They applied their system to classify patients with different sleep disorders.

Non-linear model

Application of non-linear dynamics methods to the physiological sciences demonstrated that non-linear models are useful for understanding complex physiological phenomena such as abrupt transitions and chaotic behavior. Sleep stages and sustained fluctuations of autonomic functions such as temperature, blood pressure, EEG, etc., can be described as a chaotic process. The EEG signals are highly subjective and the information about the various states may appear at random in the time scale.

Sleep data analysis is carried out using non-linear parameters by Acharya UR [63]. The parameters consisted of correlation dimension, fractal dimension, largest Lyapunov entropy, approximate entropy, Hurst exponent, phase space plot and recurrence plots. Spectral and nonlinear EEG measures were compared by Fell et al. for sleep stages discrimination [64]. Hidden Markov model was utilized by Doroshenkov et al. for sleep stage classification based on calculation of characteristics of the main sleep rhythms [65]. Grube et al. reported an automatic sleep staging system with a fully automatic, probabilistic sleep-analyzer using Hidden Markov Models (HMMs) based on data from a single EEG channel [66].

Other techniques

Several signal processing techniques have been applied to realize the automatic sleep staging. Data mining was investigated by Laxminarayan et al. [67]. They introduced a specialized association rule mining technique that can extract patterns from complex sleep data comprising polysomnographic recordings, clinical summaries, and sleep questionnaire responses. Blind signal separation was investigated by [68]. They developed a staging system in ambulatory conditions. The sleep EEG, EMG and EOG were separated using the Independent Component Analysis approach. A novel approach was developed by Schwaibold et al. for automated sleep stage recognition, which mimics the behaviour of a human expert visually scoring sleep stages [69]. A nonparametric statistical approach for EEG segmentation was utilized by Kaplan et al. to detect the change-points between quasi-stationary EEG segments based on the EEG characteristics within four fundamental frequency bands (delta, theta, alpha and beta) [70]. An expert system was developed by Ray et al. for computer sleep stage scoring in [71].

A computer-assistant staging system for clinical application was proposed by Gotman et al. [72]. Their method used the principle of segmentation and

self-organization technique based on primitive sleep-related features to find the pseudonatural stages present in the sleep record. Sample epochs of these natural stages were presented to the user, who can classify them according to the Rechtschaffen and Kales or any other standard. The method then learned from these samples to complete the classification. Their method allowed the active participation of the operator in order to customize the staging to their preferences.

A noncontact method for sleep stage estimation was proposed by Watanabe et al. [73] [74]. They described a novel method to estimate the sleep stage through noninvasive and unrestrained means. A mathematical model was created which was consisting of a sleep stage classifier and observer. The sleep state transition equation was the basis for the design of observer, which the observed relationships were the basis for designing classifier.

Other signals

The sleep-related diseases may be related to cardiogram, respiration. The measurement for sleep data recording may include other signals besides sleep EEG, such as respiration, leg movements, ECG, EOG, EMG etc. There are several studies challenged on small amount of EEG data [75] and other signals for automatic sleep staging.

A particular application of the FFT (Fast Fourier Transformation) on heart rate was described by Lisenby et al. [76]. In their method, the beat-by-beat intervals were represented as the magnitude of a periodically sampled function. When FFT is applied to these data, pseudofrequency information from Beatquency Domain was obtained for sleep cycle detection. The effect of sleep stages and sleep apnea on autonomic activity by analyzing heart rate variability was investigated by Penzel et al. [77]. A cardiorespiratory-based sleep staging in subjects with obstructive sleep apnea was described in the study by Redmond et al. [78]. The reliability of classification performance based on heart rate variability was investigated by Lewick et al. [79]. They considered rejecting the unreliable segments before applying classification methods.

Another signal utilized for sleep staging was Electro-oculography (EOG). Virkkala et al. investigated on EOG signal for sleep analysis. In their study, EOG was adopted for automatic slow wave sleep detection [80] [81]. An amplitude criterion was used for detecting slow waves. They developed EOG analysis for automatic detection of unintentional sleep onset [82]. An automatic estimation of slow eye movements was developed and used as the main criterion to separate sleep stage I from wakefulness by Magosso et al. [83]. Additionally, synchronous EEG activity was used to determine wakefulness. Their method was developed for the classification of wakefulness, stage REM, Stage I, II and slow wave sleep using two-channel electro-oculography.

Choi et al. introduces a method of bed actigraphy (BACT) for user-friendly sleep-wake monitoring [84]. BACT provides a non-intrusive acquisition of activity

data, and in particular does not require that sensors be attached to the subject's body. The system consists of four load-sensing cells supporting the bed, an A/D converter, and a microcontroller with appropriate software.

1.3 Research Motivation

The guidelines of Rechtschaffen and Kales are meant as a reference method. It becomes a gold standard for sleep stage scoring. Today, this technique seems not be sufficient enough to support the description of sleep process demanded for clinical practice [85]. Rechtschaffen and Kales criteria include rules of typical waveforms from healthy persons. However, sleep stage scoring is used for evaluating the condition of sleep and diagnosing the sleep related disorders in hospitals. The subjects are patients suffered by sleep disorders. Additionally, the typical waveforms shown in Rechtschaffen and Kales criteria are under ideal recording condition. The sleep data under usual recording condition at hospitals are inevitably contaminated by various artifacts. The surrounding circumstances may be variable in different hospitals. In practical, rules are often difficult or impossible to follow and deviations are common.

Similar insufficiency can be found in the conventional rule-based computerized sleep stage scoring techniques. Those techniques are designed according to the rules for sleep staging in Rechtschaffen and Kales criteria. Artifacts and surrounding circumstance in clinical practice are not considered in those techniques as well as the patients with sleep disorders. Using Rechtschaffen and Kales criteria only, those rule-based methods may be successful for the sleep data under ideal recording condition of healthy persons, but not for the sleep data under usual recording condition of patients at hospitals.

For clinical practice, effective technique is still needed. In the field of clinics, commercial systems are not efficiently usable. The reason may be that the commercial systems utilized rule-base method which is insufficient to deal with the sleep data under usual condition at hospitals and institutions. Clinicians have not been free from the heavy and qualified task of sleep stage scoring. It is necessity to develop usable computerized sleep stage scoring technique for clinical practice.

1.4 Research Objective

The aim of this research work is to establish an effective and reliable automatic sleep stage determination system which can be utilized for clinical practice. Most elaborate descriptions are itemized as follows:

1. The sleep data recorded under the usual condition at the hospital is investigated in order to testify effectiveness of our developed technique for clinics.
2. The visual inspection on sleep stages by a qualified clinician is investigated in order to develop the knowledge-based methodology for automatic sleep stage determination.
3. The modeling of probability density function of parameters for sleep stages is investigated by considering the artifacts contamination problem.
4. Automatic parameter selection algorithm is investigated in order to make the automatic sleep stage determination system flexible for variable cases of sleep disorders.
5. Amendment function for automatic sleep stage determination is investigated by considering the additional rules by clinicians after visual scoring of sleep stages.

1.5 Thesis Structure

The structure of the thesis is shown in Figure 1.1. Background, research motivation and objective are explained in Chapter 1. Main probabilistic method of automatic sleep stage determination is explained in Chapter 2. The following Chapter 3, 4 and 5 are developed based on the main method in Chapter 2. The conclusions and contributions of current study are explained, and future study is discussed in Chapter 6.

In **Chapter 1**, the overview of human sleep was introduced through the historical stories on human sleep and the importance of sleep. The general knowledge of sleep stage scoring was introduced by illustrating the definition of sleep stages and the clinical importance of sleep stage scoring. The automatic sleep stage determination techniques were investigated. The motivation, objective of this research was explained. The structure of the thesis was explained briefly.

In **Chapter 2**, an expert knowledge-based automatic sleep stage determination system is introduced. The sleep stage scoring is considered as a multi-valued decision making problem in the field of clinics. Visual inspection by a qualified clinician on sleep stage scoring is utilized to obtain the probability density functions of parameters

for various sleep stages during the learning process of knowledge database construction. Sleep stage is determined automatically based on conditional probability.

In **Chapter 3**, the expert knowledge database for sleep stage determination is developed. Cauchy distribution is adopted to model the probability density function of parameters to the histogram. Comparing with Gaussian distribution, Cauchy distribution has heavier tails which can abate the affect of artifacts during sleep stage determination process.

In **Chapter 4**, the expert knowledge-based automatic sleep stage determination is developed with a process of automatic parameter selection. Optimal parameters are selected for variable sleep disorder cases. The selected parameters were utilized for automatic sleep stage determination.

In **Chapter 5**, the expert knowledge-based automatic sleep stage determination is developed integrated with an amendment function. The amendment is carried out to modify the decision making of sleep stages by the expert knowledge-based method. The amendment algorithm is designed according to the humanized visual inspection by qualified clinician for continuity of stage II and onset/offset of stage REM detection.

In **Chapter 6**, the research works of current study are explained. The contributions of research works explained in Chapter 2, 3, 4 and 5 are indicated to show the effectiveness. Finally, the future study is discussed by several research topics facing to the application in hospital.

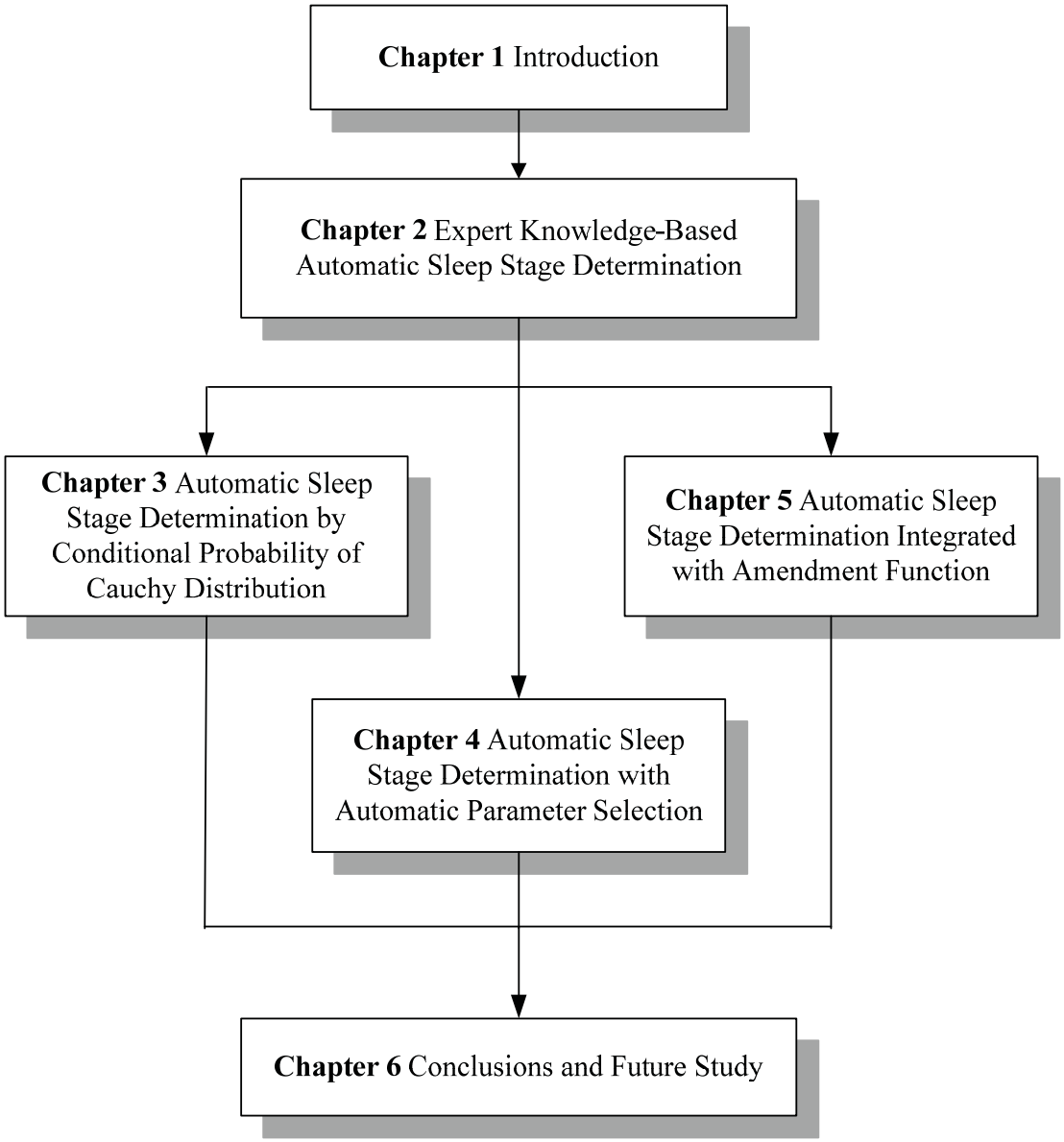


Figure 1.1: Thesis structure.

Chapter 2

Expert Knowledge-based Automatic Sleep Stage Determination

2.1 Introduction

Human sleep contains several stages. They are stage awake, REM (Rapid Eye Movement) and NREM (non-Rapid Eye Movement). NREM sleep is consisting of stage I, II, III and IV. For normal and healthy persons, those types of stages corresponding to certain frequency bands and amplitudes follow a fairly well-behaved cyclic pattern of sleep EEG (electroencephalograph) throughout the night. Sleep stage scoring is an important task for inspecting neurophysiological diseases of subjects. The most well-know criteria for sleep stage scoring is Rechtschaffen and Kales criteria [16]. Currently, sleep stage scoring has been widely used for evaluating the condition of sleep or diagnosing the sleep related disorders in the sleep laboratories and hospitals. To make visual inspection of one's overnight sleep requires skillful knowledge about the sleep EEGs and stage-scoring criteria. Additionally, it is a rather laborious task, because sleep recording always contains large amount of data (about 7-8 hours).

Many researchers investigated on developing the computerized sleep stage scoring system in order to free the clinicians from the heavy task of visual inspection. Waveform detection method was firstly applied by Smith et al. in human sleep analyzing [31] [35]. Their sleep analyzing system consists of several characteristic EEG waveform detectors. They presented an agreement of 83% comparing with visual inspection for nine subjects (5-79 years of age). Their sleep stage I and REM sleep were mixed. An automatic sleep stager as close as possible to Rechtschaffen and Kales criteria was designed by Oxford Medical [44]. The comparison with the visual inspection by two experienced clinicians for ten male subjects (20-40 years of age) was evaluated. The agreement was 74.1%. The limitation of it was not scoring sufficient stage wake, REM and II, but too many stages I, II and IV. Automatic sleep stage scoring by using a neural network model was investigated by Schaltenbrand et

al. [56]. They compared and analyzed on a sleep recording set of 60-subjects, consisting of 20 normal subjects, 20 depressed patients and 20 insomniac patients. For each group, the agreements were 84.5%, 81.5% and 81.0% respectively. The main differences between their automatic analyze and visual inspection were observed in stage I and the confusion between stage III and IV. An automated method for sleep stage scoring by using hybrid rule-based and case-based reasoning method was proposed by Park el al. [45]. Their rule-based reasoning was based on waveform or phasic event detection method. Their case-based reasoning method was in the field of artificial intelligence as a revision to rule-based result. The accuracy evaluation with three expert manual scoring was 87.5% in normal recordings and 85.3% in abnormal recordings. Their method had limitation in differentiating stage I from stage II and stage REM. A computer-assisted sleep staging method was presented by Agarwal and Gotman [72]. By using their segmentation and self-organization technique, sleep EEGs could be subsequently classified according to Rechtschaffen and Kales criteria or other sleep stage methodologies. They evaluated their method for 12 subjects, 4 subjects with different pathologies and 8 normal subjects. The overall agreement between their computer scoring and one expert visual inspection was 76.8%. Their stage I has the poorest agreement with almost misclassified into stage REM and stage wake. An expert system for automatic identification of sleep stages based on characteristic waveforms and background EEG activity by using a decision tree was described by Anderer et al. [46]. They utilized 590 polysomnographies (PSGs) recordings. All the recordings were visual inspected by thirty sleep experts from 8 different sleep labs. Their final validation revealed an overall agreement of 80% with the human expert visual inspection. Their disagreement was specifically concerning misclassifications of the stage wake, stage I, stage II and stage REM.

The above techniques had their advantages in the automatic recognition of sleep stages. However, there is still no powerful sleep stage determination methodology being developed for real clinics. Almost all the methodologies were designed as close as Rechtschaffen and Kales criteria. Rechtschaffen and Kales criteria are worthy for sleep stage scoring. However, the typical waveforms for normal and healthy persons in Rechtschaffen and Kales criteria are insufficient to cover the variable cases in real clinics. The conventional rule-based techniques, only according to Rechtschaffen and Kales criteria, have the similar limitations to deal with the sleep data in hospitals. For clinical application, effective and reliable automatic determination technique is still required.

In this study, we developed a sleep stage determination system based on expert knowledge of visual inspection. The developed sleep stage determination system is according to a multi-valued decision making method. The knowledge base for sleep stage determination is developed in terms of probability density functions (*pdf*) of parameters with interest according to the visual inspection by a qualified clinician. The clinician made visual inspection on stage awakes, stage REM, stage I, II, III and

IV for the sleep data recorded in real clinics. Stage awake is classified to open eyes and close eyes states so as to have a well fit between the parameters and the stages. Sleep stage is determined automatically by the values of conditional probabilities.

2.2 Method

2.2.1 Subjects and sleep data

Eight subjects had been analyzed in this study across the patients having an average age about 50 years old. They had breathing disorders during sleep (Sleep Apnea Syndrome). Their overnight sleeping data were recorded after the treatment of Continuous Positive Airway Pressure (CPAP) based on the polysomnographic (PSG) measurement from the department of Clinical Physiology, Toranomon Hospital in Tokyo, Japan. Detail explanation was done for all the patients before PSG recordings and informed consent was obtained. The subjects information is shown in Table 2.1. For each subject, age, sex and disease were notified. "○" indicated that the sleep data of the subject had been visually inspection by clinician including open eyes and close eyes states during awake.

Table 2.1: Subjects information

Subject ID	Age, Sex	Visual inspection
A	52, Male	--
B	60, Male	○
C	58, Male	--
D	54, Male	○
E	44, Male	--
F	50, Male	○
G	50, Male	--
H	36, Male	○

The sleep data recording in Toranomon hospital is illustrated in Figure 2.1. Figure 2.1 (A) showed the pictures of actual recording circumstance. Subject was in a quiet room. Some electrodes were pasted on the head. In another room, the recorded sleep data can be reviewed on digital computers. Clinician make visual inspection for those recording sleep data. Figure 2.1 (B) showed the raw sleep data recorded under PSG measurement used in Toranomon Hospital. It includes four EEG recordings, two EOG recordings and one EMG recording. EEGs were recorded on central lobes and occipital lobes with reference to opposite earlobe electrode (C3/A2, C4/A1, O1/A2 and O2/A1) according to the International 10-20 system [88]. EOGs were derived on Right Outer Canthus and Left Outer Canthus with reference to earlobe electrode A1 (LOC/A1 and ROC/A1). EMG was obtained from muscle areas on and beneath chin (chin-EMG). Initially, EEGs and EOGs were recorded under a sampling rate of 100 Hz, with a high frequency cutoff of 35Hz and a time constant of 0.3s. Chin-EMG was recorded under a sampling rate of 200Hz, with a high-frequency cutoff of 70Hz and a low frequency cutoff of 10Hz. The sleep data were divided into consecutive 30-second data for sleep stage scoring in Toranomon hospital.

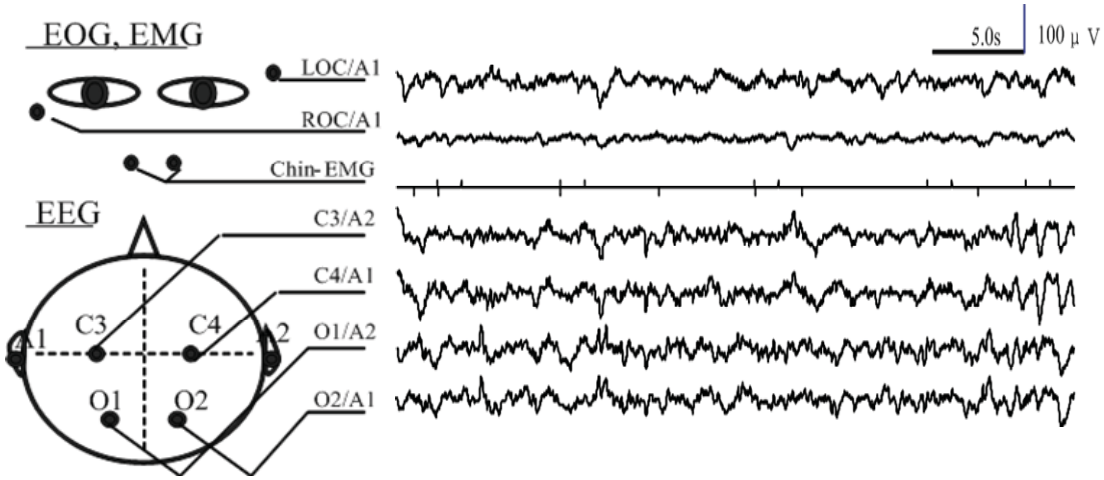
2.2.2 Visual inspection

The sleep stage definition with typical characteristics in Rechtschaffen and Kales criteria is summarized in Table 2.2. Visual inspection by a qualified clinician which covers the staging criteria was adopted for expert knowledge database construction. “Expert” indicated to the qualified clinician who is the specialist.

In this study, the data of visual inspection was obtained by an experienced clinician who is one of the co-author (F.K.) in Toranomon Hospital. The clinician made visual inspection based on her knowledge and experience though an epoch-by-epoch approach. The PSG recording of subject was divided into consecutive 30-second recordings, which are called epochs. Then, each epoch was assigned a single sleep stage by the clinician. When more than one stage was presented in an epoch, the one which took up the greatest portion of the epoch was scored as the stage of that epoch.

Seven types of stages were inspected. In the stage of the awake or the wakefulness, EEGs (O1/A2, O2/A1) show predominant rhythmic alpha activity when the subject is relaxed with the eyes closed [89] [90]. This rhythmic EEG pattern significantly attenuates with attention, as well as when the eyes are open. The waking EOG consists of rapid eye movements and eye blinks when the eyes are open and few or no eye movements with the eyes closed. The EMG shows a relatively high level of tonic activity. In this study, the clinician classified stage awake into two sleep stages though her visual inspection. They were open eyes awake (O(W)) and close eyes awake (C(W)) according to the alpha activity on O1/A2 and O2/A1 channels and the existence of eye movements on EOGs.

(A) Sleep stage recording in hospital



(B) The recorded sleep data

Figure 2.1: Sleep data recording. (A) Sleep data recording and monitoring in the hospital; (B) The recorded sleep EEGs, EOGs and EMG.

In sleep stage itself, the clinician made visual inspection on REM (rapid eye movement) sleep and NREM (non rapid eye movement) sleep of stage I, II, III and IV. The stage REM was characterized by activated EEG, bursts of rapid eye movements and suppression of the EMG activity. The stage I was evaluated as low-voltage, mixed frequency EEG pattern. The stage II sleep was distinguished from stage I sleep on the basis of two specific EEG patterns: the sleep spindle and the K-complex. The stage III and the stage IV were discriminated by the presence of the high-voltage slow wave activity as deep sleep, with very low levels of EMG and without eye movements. Usually stage III was scored when 20% to 50% of slow wave activities appeared in an epoch and stage IV was scored when more than 50% of slow wave activities occupied in an epoch according to Rechtschaffen and Kales criteria. For old persons, stage III and IV of deep sleep could not be obviously discriminated based on Rechtschaffen and Kales criteria. In this study, the clinician inspected stage III and stage IV based on a relatively different presence of slow wave activity in an epoch.

Table 2.2: Sleep stage scoring criteria

Stage	Characteristics
Awake	Dominant alpha activity 8-13Hz, low voltage fast wave
REM	Episodic REMs, low voltage EMG
I	Low voltage slow wave of 2-7Hz
II	Slow wave (less than 20%), Sleep spindle, k-complex
III	High voltage slow wave of 0.5-2Hz (20%-50%)
IV	High voltage slow wave of 0.5-2Hz (more than 50%)

2.2.3 Parameter definition

In order to carry out the automatic sleep stage determination, a set of parameters for sleep stage discrimination is defined in this section. The definitions of three types of parameters are given in Table 2.3. The following items are the meaning of each type.

- ***Ratio***
  The duration of EEG components are calculated by the maximum value of the ratios of the summation of periodogram with certain frequency bands ω to the total frequency band T in EEG channels (C3/A2, C4/A1 and O1/A2, O2/A1) between two hemispheres.

- ***Amplitude***
  The amplitude of EEG components are calculated by the maximum value of the square root of the summation of periodogram [91] with certain frequency bands ω in EEG channels (C3/A2, C4/A1 and O1/A2, O2/A1) between two hemispheres.

- ***Amount***
  The amount of EOG components are calculated by the summation of periodogram with certain frequency band in EOG channels (LOC/ROC, LOC/A1, ROC/A1). The amount of EMG components is calculated by the summation of periodogram with certain frequency band in EMG channel (chin-EMG).

In Table 2.3, the certain frequency bands ω were defined according to the consisting components of EEGs (delta, alpha, theta, beta) . The total frequency band T of EEGs was 0.5-25 Hz. For sleep EOGs, the certain frequency bands corresponded to the eye movements (2-10 Hz). For sleep EMG, the certain frequency bands corresponded to the high frequency activity of muscles (25-100 Hz).

According to the definition of sleep stages, each state reflected the different neural actvity and was characterized by brain waveforms. In clinical practice, clinicians also paid attention to the frequency characteristics of the sleep data duirng the visual inspection on sleep stages. Therefore, the parameters utilized in this study were extracted from the frequecny domain of sleep EEGs, EOGs and EMG.

Table 2.3: Parameters for sleep stage discrimination

	Meaning	Parameter
EEG	Ratio [%]	$R_\omega = \max\left\{\frac{S_\varpi(C3)}{S_T(C3)}\times 100\%, \frac{S_\omega(C4)}{S_T(C4)}\times 100\%\right\}$
		$R_\omega = \max\left\{\frac{S_\omega(O1)}{S_T(O1)}\times 100\%, \frac{S_\omega(O2)}{S_T(O2)}\times 100\%\right\}$
	Amplitude [μV]	$A_\omega = \max\left\{6\times\sqrt{S_\omega(C3)}, 6\times\sqrt{S_\omega(C4)}\right\}$
		$A_\omega = \max\left\{6\times\sqrt{S_\omega(O1)}, 6\times\sqrt{S_\omega(O2)}\right\}$
EOG	Amount [μV^2]	$S(LOC-ROC)$, $S(LOC)$, $S(ROC)$
Chin-EMG	Amount [μV^2]	$S(Chin-EMG)$

2.2.4 Expert knowledge database construction

A set of training data is required for knowledge base construction. In this study, the knowledge base is constructed based on the overnight sleep recording data of subjects and the visual inspection by clinician.

The whole sleep recording data are divided into epochs. Each epoch is subdivided into still smaller segments of 5-second. In order to yield the parameter values, the periodogram is derived by taking 512-point FFT (Fast Fourier Transform) for EEG's and EOG's, whereas 1024-point FFT for EMG. The parameter values are calculated based on the definition of Table 2.3. The parameter values of consisting segments are taken average to derive the parameter value of one epoch for training purpose.

The epochs are classified into sleep stage groups according to the visual inspection. Finally, each epoch is assigned to a single sleep stage based on the visual inspection of clinician and described by a set of parameter values. For each sleep stage, the values of parameters are counted to make the histograms.

In Figure 2.2, the expert knowledge database is the *pdf*s of parameters corresponding to stages. Stage awake was classified into open and close eyes awake. $f(y|\zeta)$ corresponds to the *pdf* of parameter y in stage ζ, m indicated number of parameters, n indicated number of sleep stages.

According to the training data set and the visual inspection, a transitional probability matrix of sleep stage change is calculated. As the visual inspection is made for each epoch, the consisted segments of one epoch are considered having the same scoring result within one epoch. The transitional probability between sleep stages can be calculated and designates the probabilities of sleep stage transition between two conjoint segments.

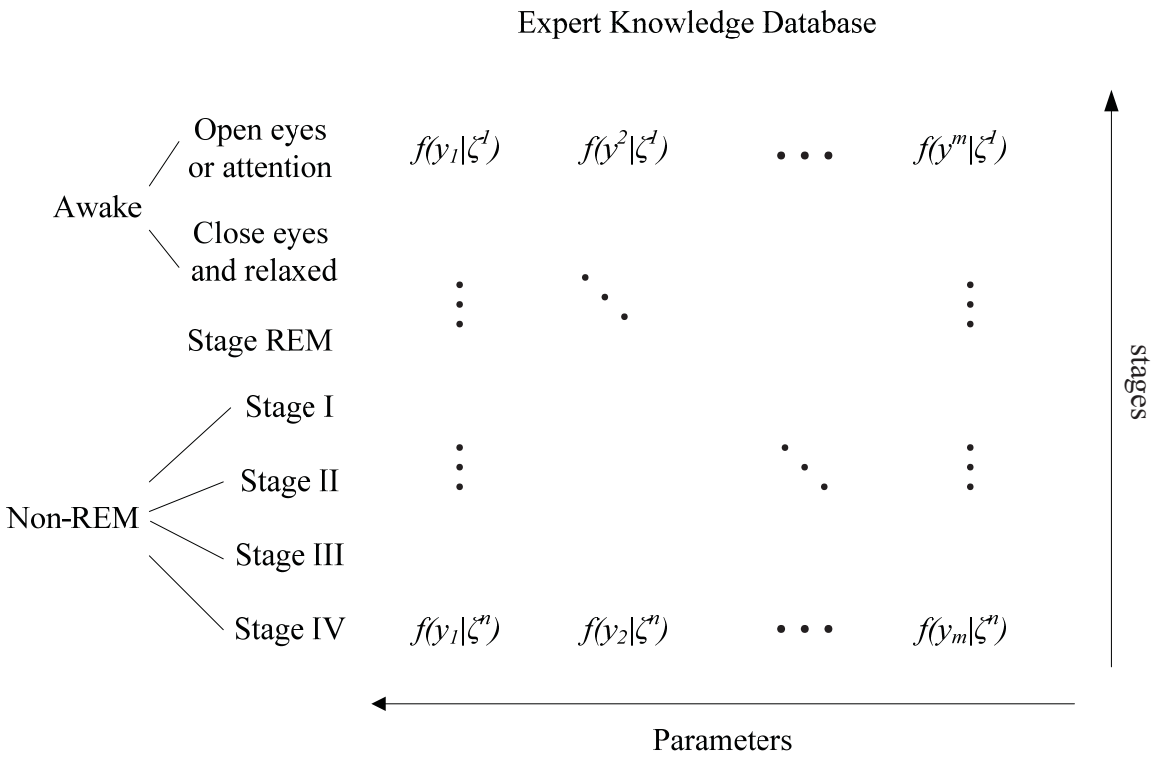


Figure 2.2: The probability density functions of parameter distributions for each sleep stage, where $f(y|\zeta)$ corresponds to the *pdf* of parameter y in stage ζ and m is the index number of parameters, n is the index number of sleep stages.

2.2.5 Automatic sleep stage determination

The test recording of one's sleep is divided into epochs and segments as same as the training data. The automatic sleep stage determination is processed on those consecutive segments, following the algorithm in Figure 2.3.

- **Initialization**

The initialization includes a supposition of predicted probability $P_{1|0}=1/n$. At the beginning of the processing, the predicted probability of first segment for various sleep stages shared the probability equally with a value of $1/n$, where n is the number of the types of sleep stages.

- **Conditional probability**

The joint *pdf* of the parameters for current segment k is calculated as

$$f(y_k \mid \zeta^i) = \prod_{l=1}^{m} f(y_k^l \mid \zeta^i) \tag{2.1}$$

where $y_k=\{y_k^1, y_k^2, ..., y_k^m\}$ is a parameter vector which denotes the parameters calculated for the current segment k, and ζ^i denotes the sleep stage. In Eq.2, each parameter y_k^l in y_k is assumed to be independent with each other.

The conditional probability of segment k is calculated based on the Bayesian rule,

$$P_{k|k}(\zeta^i) = \frac{f(y_k \mid \zeta^i) P_{k|k-1}(\zeta^i)}{\sum_{j=1}^{n} f(y_k \mid \zeta^j) P_{k|k-1}(\zeta_j)} \tag{2.2}$$

where $P_{k|k-1}(\zeta^i)$ is the predicted probability of current segment k. The conditional probability indicates the possibility of the occurrence of the sleep stage ζ^i in the current segment k.

- **Decision making**

The sleep stage ζ^* is determined by choosing the maximum value among the conditional probabilities corresponding to various sleep stages as

$$\zeta^* : \max(P_{k|k}(\zeta^i)). \tag{2.3}$$

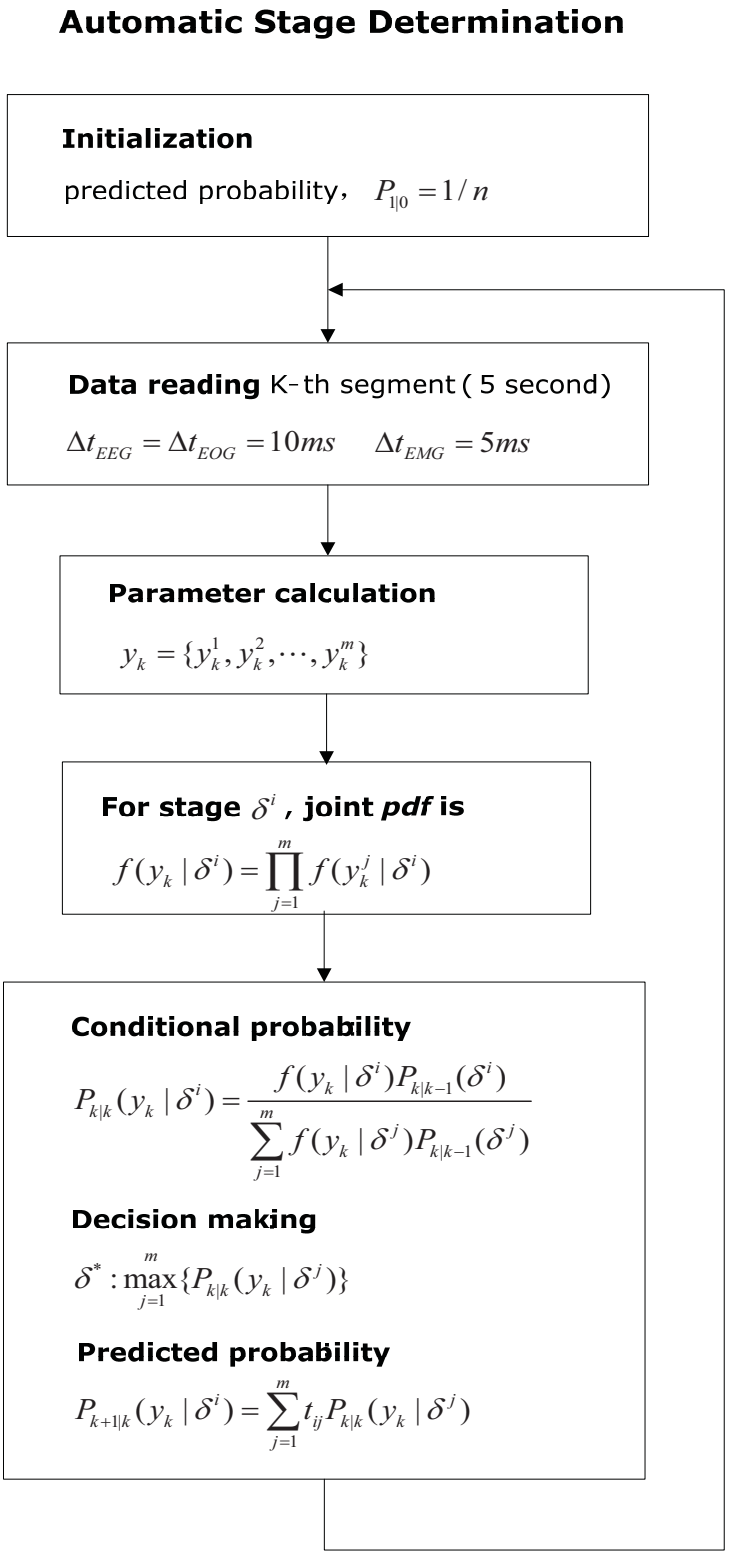


Figure 2.3: Algorithm of automatic stage determination.

- **Predicted probability**

The predicted probability $P_{k+1|k}(\zeta^i)$ of next segment k+1 is given by

$$P_{k+1|k}(\zeta^i) = \sum_{j=1}^{n} t_{ij} P_{k|k}(\zeta^j) \tag{2.4}$$

where t_{ij} denotes the probability of transition from stage i to stage j and $P_{k|k}(\zeta^j)$ the conditional probability of current segment.

The automatic sleep stage determination is iterated though the calculation of conditional probability (Equation 2.2) and predicted probability (Equation 2.4) among the consecutive segments. The decision (Equation 2.3) is made based on the value of conditional probabilities. Then the sleep stage for each epoch is determined by choosing the stage which takes up the greatest portion in one epoch. The derivation of each equation can be found in the previous work by some of the authors.

2.3 Results

2.3.1 Expert knowledge database

The continuous sleep recordings of two subjects were utilized as the training data to obtain the knowledge base of *pdfs* of parameters and the transitional probability matrix of sleep stage change.

The transitional probability matrix T was derived from the same training subjects. According to the visual inspection of the training recordings by the clinician, the elements in the matrix T were obtained as Equation 2.5,

$$T = \begin{array}{c} \begin{array}{ccccccc} \text{O(W)} & \text{C(W)} & \text{R} & \text{I} & \text{II} & \text{III} & \text{IV} \end{array} \\ \left\{ \begin{array}{ccccccc} 0.996 & 0.003 & 0.000 & 0.001 & 0.000 & 0.000 & 0.000 \\ 0.008 & 0.932 & 0.000 & 0.058 & 0.002 & 0.000 & 0.000 \\ 0.000 & 0.002 & 0.996 & 0.002 & 0.000 & 0.000 & 0.000 \\ 0.000 & 0.014 & 0.002 & 0.942 & 0.042 & 0.000 & 0.000 \\ 0.000 & 0.002 & 0.001 & 0.008 & 0.986 & 0.003 & 0.000 \\ 0.000 & 0.001 & 0.000 & 0.000 & 0.015 & 0.973 & 0.012 \\ 0.000 & 0.000 & 0.000 & 0.000 & 0.005 & 0.008 & 0.987 \end{array} \right\} \end{array} \begin{array}{c} \text{O(W)} \\ \text{C(W)} \\ \text{R} \\ \text{I} \\ \text{II} \\ \text{III} \\ \text{IV} \end{array} \tag{2.5}$$

The stages from left to right and top to bottom were open eyes awake, close eyes awake, REM, stage I, II, III and IV. The row denoted the present sleep stage while the column denoted the next sleep stage. The values on the diagonal indicated the probabilities of continuing stages. In Equation 2.5, the sleep stages were continued with high probability and with a relatively low probability of transition during one's continuous overnight sleep recording.

2.3.2 Stage determination by conditional probability

Another two subjects were tested by automatic sleep stage determination. Following the algorithm of multi-valued decision making, their overnight sleep recordings (about 8-hour) were analyzed.

In Figure 2.4, the expert knowledge-based automatic sleep stage determination was illustrated step by step. (A) is the recorded raw sleep data of 5-second segment. For each segment, a set of parameter values were shown in (B). According to the probability density function of expert knowledge database, the probability of paramters for various sleep stages were obtained. Thus, joint probability of a parameter for various sleep stages can be calculated. The values of joint proabability were shown in (C). Conditional probability were obtained for sleep stages based on the joint probability and predicted probability of previous segment in (D). The decision making of sleep stage was carried our by choosing the sleep stage which had maximum value of the conditional probability. This segment containing blinks in EOG channels and high voltage high frequency components in EMG channel, which are the indicators for open eyes awake. The final decision making for this segment was stage awake with eyes opened in (E). The conditional probability was utilized to calculate the predicted probability of next segment in (F).

In Figure 2.5, the automatic sleep stage determination process was illustrated. Figure 2.5 (A) showed the raw sleep data of 30-second epoch, which included the sleep data in Figure 2.4 at the second segment. Figure 2.5 (B) is the calculation process repeated by predicted probability and conditional probability among the consecutive segments. The maximum value of conditional probabilities for segments were marked by grey color. According to the maximum value, a certain sleep stage was decided for each segment. Automatic sleep stage determination was done by choosing the sleep stage which occupied major portion in the epoch. The sleep data showed similar characterisitcs as in Figure 2.4. The decision for total 6 segments were stage awake with eyes opened. The final determination result for this epoch was stage awake with eyes opened, which was consistent with visual inspection.

Similar process for detemination of stage awake with eyes closed, stage REM, stage I, stage II, stage III and stage IV were illustrated in Figure 2.6, 2.7, 2.8, 2.9, 2.10 and 2.11 respectively. In Figure 2.6, alpha activity (8-13 Hz) can be observed in EEG channels of O1/A2 and O2/A1. Alpha activity is the idicator for stage awake with eyes closed. The decision of sleep stage for the five segments were stage awake with eyes closed and last segment was stage I. The final determination result for this epoch was stage awake with eyes closed. In Figure 2.7, rapid eye movements can be observed in EOG channels and EMG level were rather low. Those are indicators for stage REM. The decision making result showed all segments were stage REM. The final determination result for this epoch was stage REM. In Figure 2.8, sleep data showed mixed frequency. Compare with stage awake, the EMG lever were lower. The decision making result for the first five segments were stage I, last segment was stage II. Since stage I occipied major portion of this epoch, stage I was determined as the sleep stage for this epoch. In Figure 2.9, sleep spindle can be observed which is the indicator of stage II. The decision making result showed all segments were stage II. The final determination result for this epoch was stage II. In Figure 2.10, slow wave activity can be observed. For deep sleep, the amount of slow wave activity was the indicator. The decision making result showed almost al the semgnes were stage III exept the third segment. Since stage III occipied major portion of this epoch, stage III was determined as the sleep stage for this epoch. In Figure 2.11, the amount of slow wave activity were larger than in Figure 2.10. The decision making result showed the latter five segments were stage IV, the first segment was stage III. Since stage IV occipied major portion of this epoch, stage IV was determined as the sleep stage for this epoch.

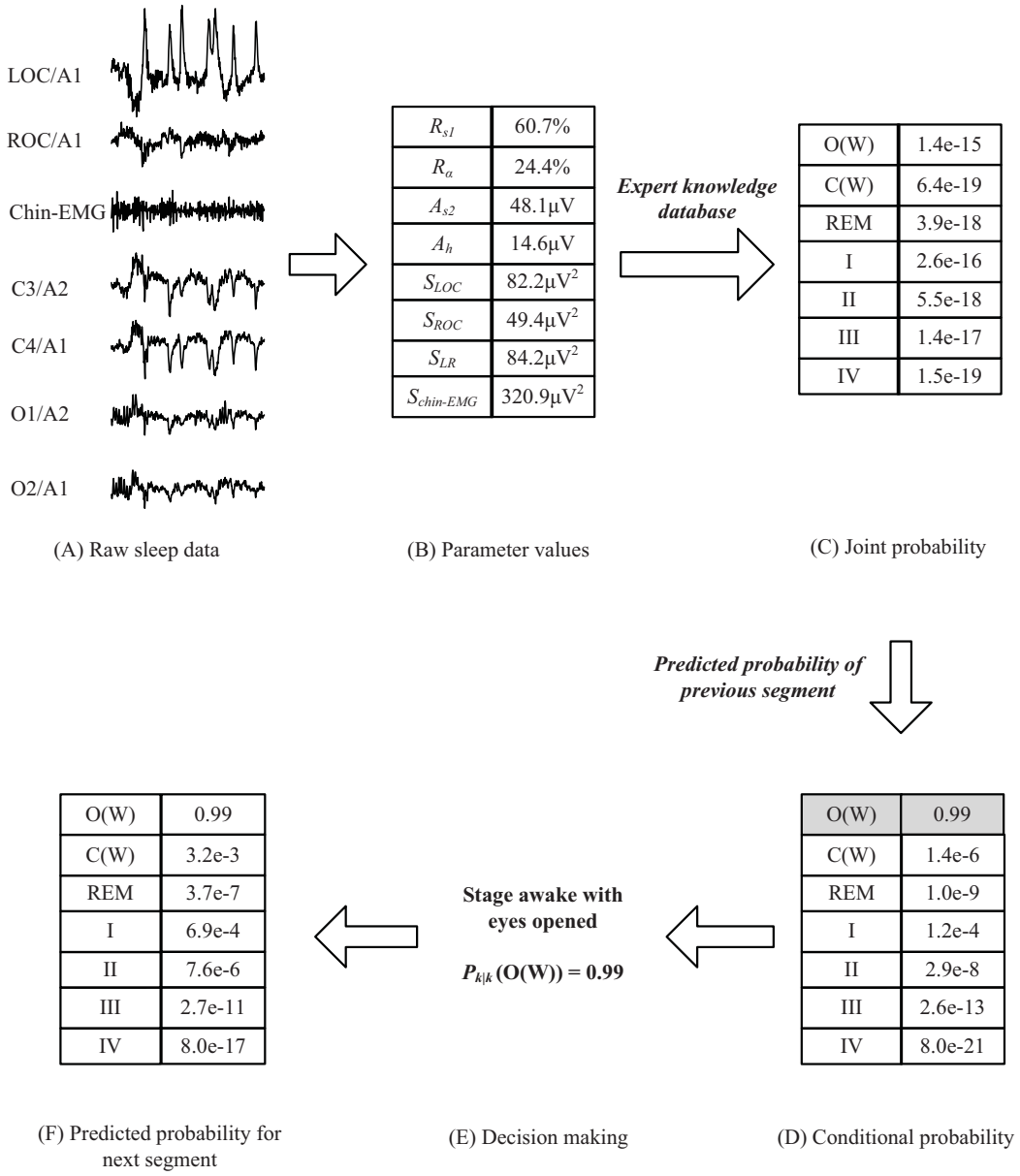
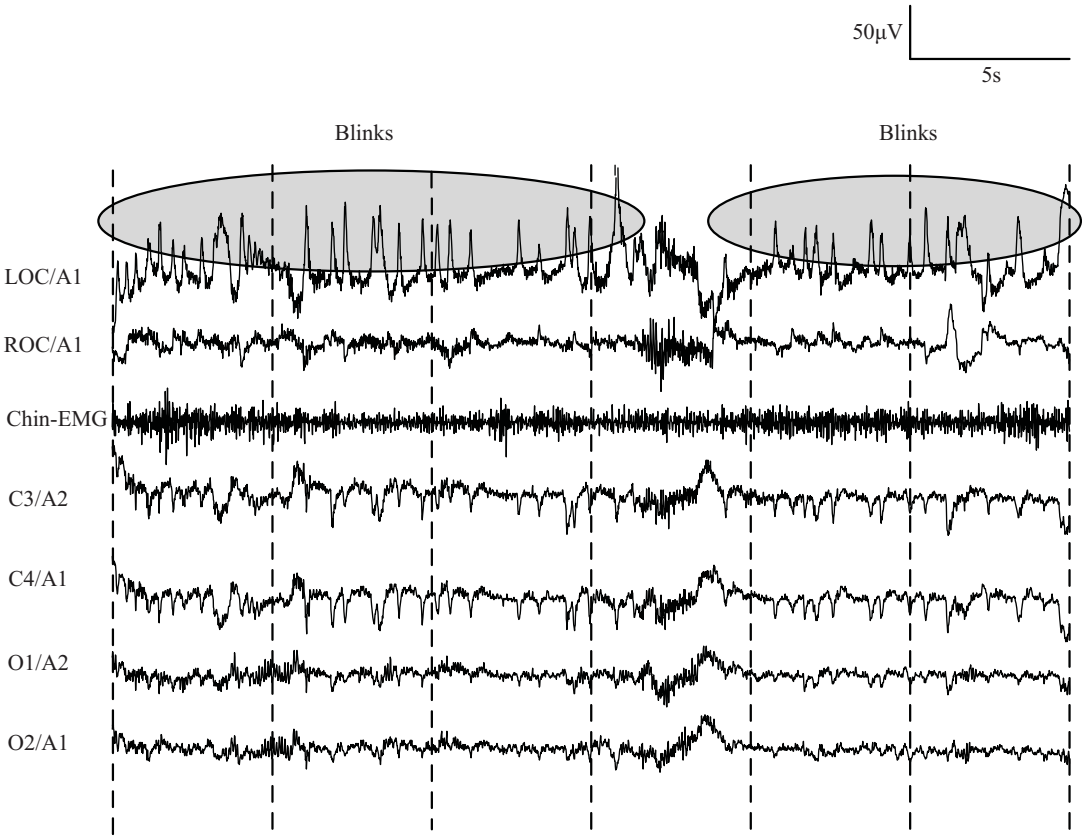


Figure 2.4: Expert knowledge-based automatic sleep stage determination algorithm. (A) Raw sleep data of 5-second segment. (B) Parameter values for current segment. (C) Joint probability of parameters for various sleep stages obtained from the expert knowledge database of probability density functions. (D) Conditional probability based on joint probability and predicted probability of previous segment. (E) Decision making of sleep stage based on the maximum valued of conditional probability. (F) Predicted probability for next segment based on Conditional probability.

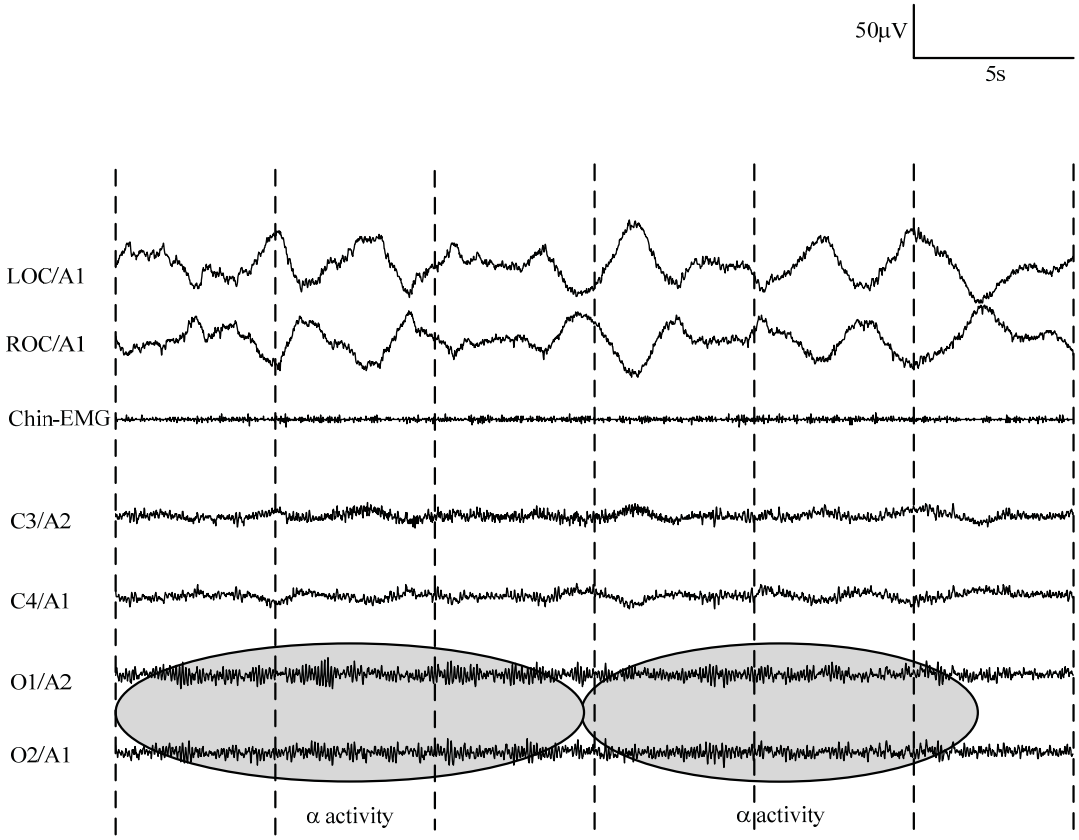


(A) Raw sleep data

	K		K+1		K+2		K+3		K+4		K+5	
Stage	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.71	0.71	0.99
C(W)	3.2e-3	1.3e-5	3.2e-3	1.4e-6	3,1e-3	8.0e-7	3.1e-3	1.1e-3	4.1e-3	9.8e-6	6.4e-3	5.1e-4
REM	2.3e-8	1.6e-10	3.7e-7	1.0e-6	2.5e-7	1.4e-7	1.7e-6	5.2e-10	1.4e-9	8.3e-8	6.0e-4	3.8e-6
I	5.3e-4	2.8e-4	6.9e-4	1.2e-4	6.4e-4	7.5e-4	1.2e-3	4.3e-7	5.9e-4	0.28	0.27	2.0e-3
II	4.1e-7	8.1e-9	7.6e-6	2.9e-8	5.2e-6	2.1e-6	3.4e-5	1.8e-11	1.8e-6	3.0e-4	0.01	3.4e-6
III	1.0e-12	6.6e-15	2.7e-11	2.6e-13	9.4e-11	7.7e-14	7.0e-9	5.3e-13	5.8e-13	1.8e-14	9.9e-7	6.6e-8
IV	6.6e-15	1.1e-18	8.0e-17	8.0e-21	3.1e-15	3.4e-20	9.2e-16	1.1e-19	6.4e-15	1.2e-19	2.1e-16	9.9e-17
Result	O(W)		O(W)		O(W)		O(W)		O(W)		O(W)	
Automatic determination:	Stage Awake with eyes opened											
Visual inspection:	Stage Awake with eyes opened											

(B) Calculation process

Figure 2.5: Automatic sleep stage determination – stage awake with eyes opened. (A) Raw sleep data of two EOG recordings, one EMG recording and four EEG recording. (B) Calculation process repeated by predicted probability and conditional probability among consecutive segments. The final determination result is stage awake with eyes opened which is consistent with visual inspection by clinician.

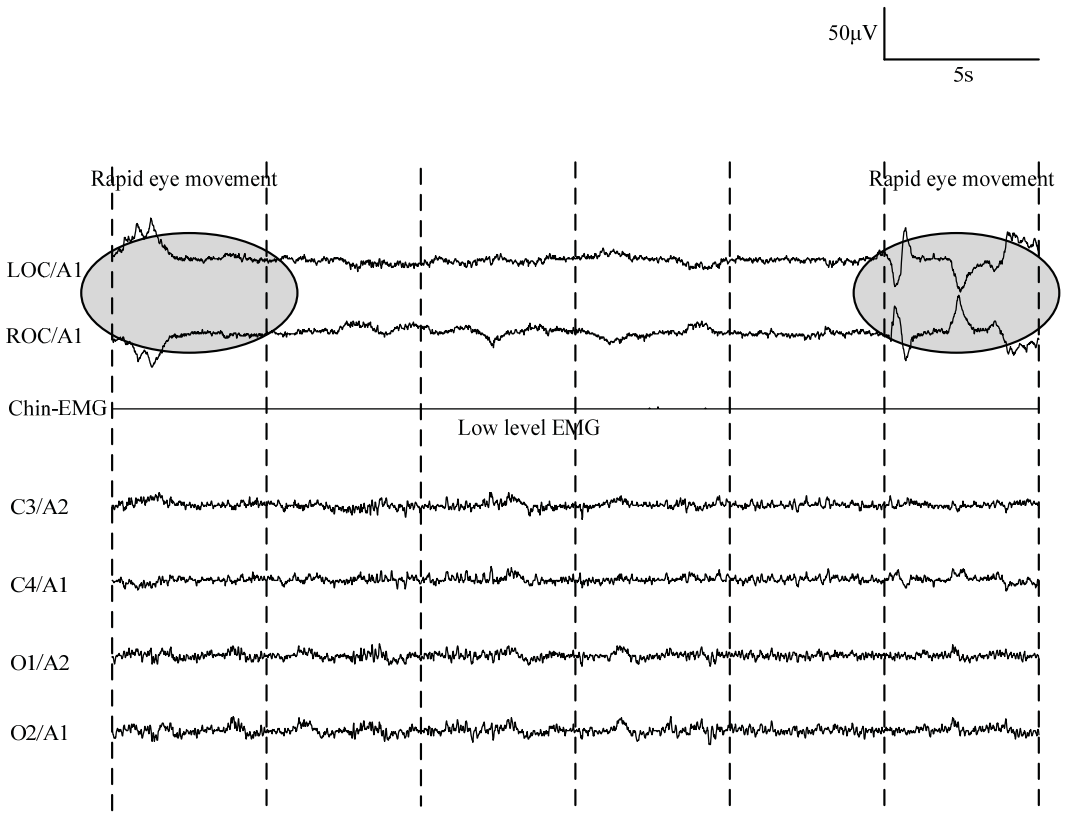


(A) Raw sleep data

	K		K+1		K+2		K+3		K+4		K+5	
Stage	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	0.03	3.0e-5	7.7e-3	5.3e-6	7.7e-3	5.7e-7	7.7e-3	7.7e-7	7.7e-3	2.0e-5	7.7e-3	7.5e-3
C(W)	0.81	0.99	0.93	0.99	0.93	0.99	0.93	0.99	0.93	0.99	0.93	0.28
REM	2.3e-4	7.6e-9	2.5e-8	4.4e-14	1.1e-9	1.4e-15	2.6e-10	9.8e-16	1.6e-9	4.5e-13	1.9e-7	7.1e-9
I	0.15	8.3e-6	0.06	5.4e-7	0.06	1.2e-7	0.06	7.5e-7	0.06	9.3e-5	0.06	0.71
II	5.9e-3	1.1e-10	1.5e-3	9.3e-11	1.5e-3	3.9e-12	1.5e-3	9.7e-12	1.5e-3	7.1e-10	1.5e-3	2.2e-5
III	6.0e-9	9.4e-16	3.8e-13	1.3e-20	3.0e-13	4.0e-21	1.2e-14	3.6e-22	3.2e-14	3.3e-20	2.3e-12	3.8e-15
IV	1.9e-19	1.7e-25	1.1e-17	1.7e-25	1.6e-22	1.7e-30	4.8e-23	5.0e-30	4.3e-24	8.8e-30	4.0e-22	8.2e-27
Result	C(W)		C(W)		C(W)		C(W)		C(W)		I	
Automatic determination:	Stage Awake with eyes closed											
Visual inspection:	Stage Awake with eyes closed											

(B) Calculation process

Figure 2.6: Automatic sleep stage determination – stage awake with eyes closed. (A) Raw sleep data of two EOG recordings, one EMG recording and four EEG recording. (B) Calculation process repeated by predicted probability and conditional probability among consecutive segments. The final determination result is stage awake with eyes closed which is consistent with visual inspection by clinician.

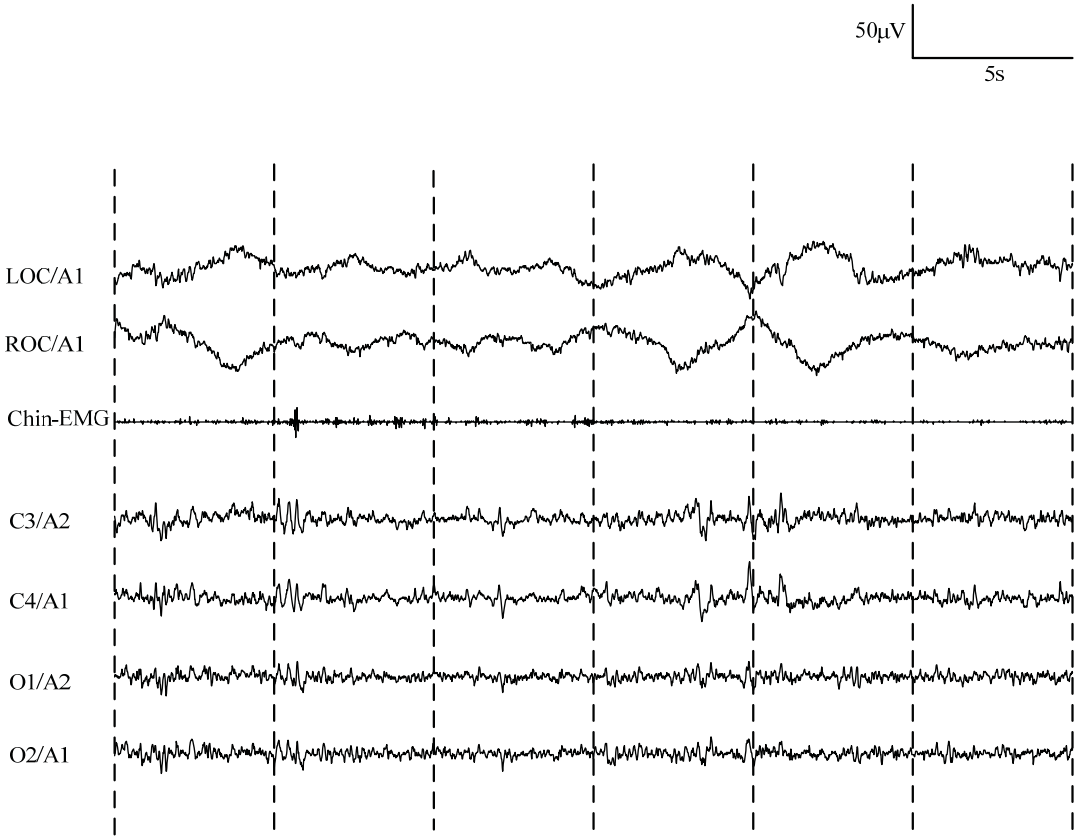


(A) Raw sleep data

	K		K+1		K+2		K+3		K+4		K+5	
Stage	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	1.7e-5	6.4e-6	1.1e-5	6.0e-7	8.9e-7	6.7e-8	3.1e-7	2.0e-8	3.4e-7	1.2e-9	6.2e-7	6.2e-7
C(W)	2.4e-3	4.7e-6	2.2e-3	1.5e-6	2.2e-3	7.1e-8	2.2e-3	5.7e-7	2.2e-3	1.9e-7	2.2e-3	2.3e-4
REM	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
I	0.02	6.5e-3	8.2e-3	4.0e-4	2.5e-3	3.5e-4	2.5e-3	4.6e-4	2.6e-3	9.0e-4	3.0e-3	7.9e-4
II	8.4e-4	4.7e-6	2.8e-4	1.4e-8	1.7e-5	9.2e-9	1.5e-5	2.2e-6	2.2e-5	1.3e-5	5.0e-5	2.3e-7
III	6.2e-8	3.6e-12	1.5e-8	9.0e-13	4.5e-11	3.4e-16	3.0e-11	1.8e-15	7.1e-9	3.5e-13	4.1e-8	1.1e-10
IV	3.4e-13	1.1e-19	4.3e-14	4.6e-21	1.1e-14	3.0e-22	4.1e-18	1.1e-24	2.1e-17	4.1e-25	4.2e-15	3.6e-18
Result	REM		REM		REM		REM		REM		REM	
Automatic determination:	Stage REM											
Visual inspection:	Stage REM											

(B) Calculation process

Figure 2.7: Automatic sleep stage determination – stage REM. (A) Raw sleep data of two EOG recordings, one EMG recording and four EEG recording. (B) Calculation process repeated by predicted probability and conditional probability among consecutive segments. The final determination result is stage REM which is consistent with visual inspection by clinician.

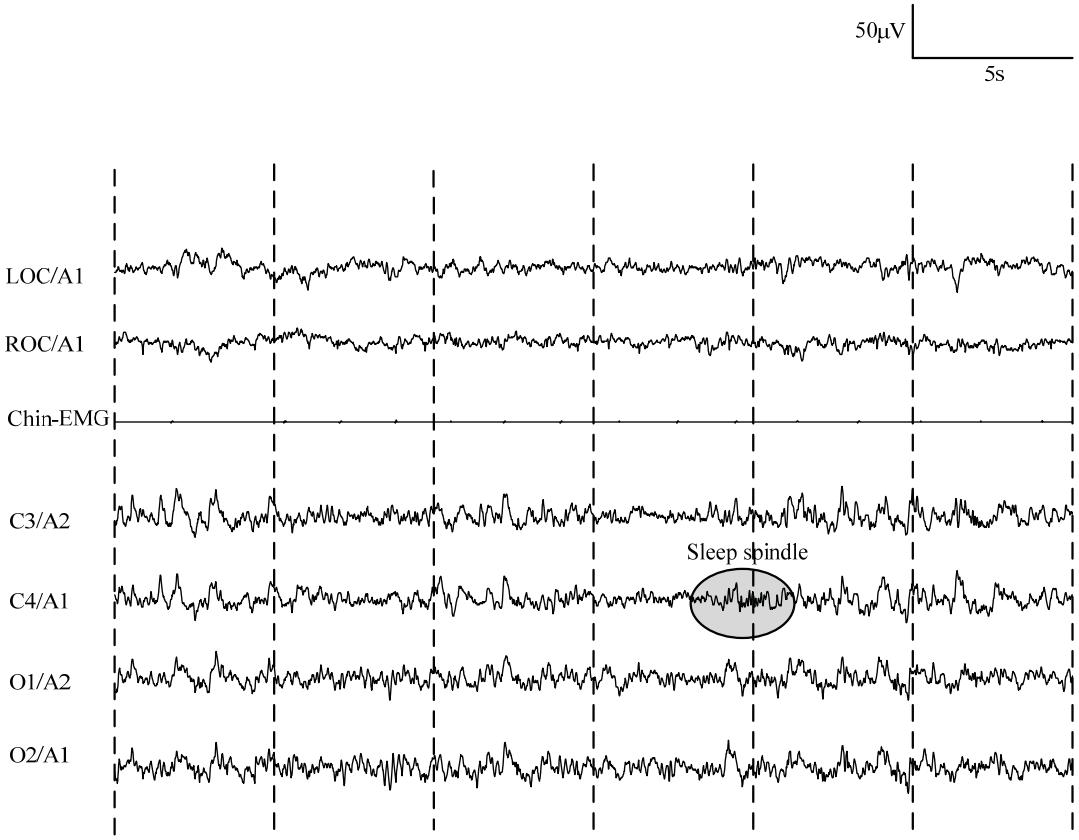


(A) Raw sleep data

	K		K+1		K+2		K+3		K+4		K+5	
Stage	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	0.12	1.4e-3	2.1e-3	3.5e-6	6.8e-4	4.9e-4	1.2e-3	6.5e-7	6.0e-4	5.1e-7	4.4e-4	9.2e-7
C(W)	0.01	2.5e-7	0.01	5.9e-8	0.01	1.5e-5	0.01	6.3e-8	0.01	2.9e-9	8.5e-3	7.6e-8
REM	0.02	1.9e-3	3.9e-3	5.0e-5	2.1e-3	5.2e-3	7.3e-3	7.0e-5	1.9e-3	5.0e-5	1.5e-3	3.0e-5
I	0.81	0.99	0.94	0.97	0.91	0.99	0.94	0.82	0.78	0.52	0.49	0.14
II	0.03	7.5e-4	0.04	0.02	0.07	2.9e-5	0.04	0.17	0.20	0.47	0.49	0.85
III	6.8e-7	1.7e-4	2.5e-6	2.0e-9	9.4e-5	1.7e-8	1.1e-7	3.2e-11	5.6e-4	2.1e-8	1.6e-3	5.4e-8
IV	1.3e-11	5.0e-18	2.1e-13	8.1e-20	2.4e-11	4.6e-16	2.0e-10	3.9e-17	3.8e-13	1.1e-21	2.5e-10	1.4e-16
Result	I		I		I		I		I		II	
Automatic determination:	Stage I											
Visual inspection:	Stage I											

(B) Calculation process

Figure 2.8: Automatic sleep stage determination – stage I. (A) Raw sleep data of two EOG recordings, one EMG recording and four EEG recording. (B) Calculation process repeated by predicted probability and conditional probability among consecutive segments. The final determination result is stage I which is consistent with visual inspection by clinician.

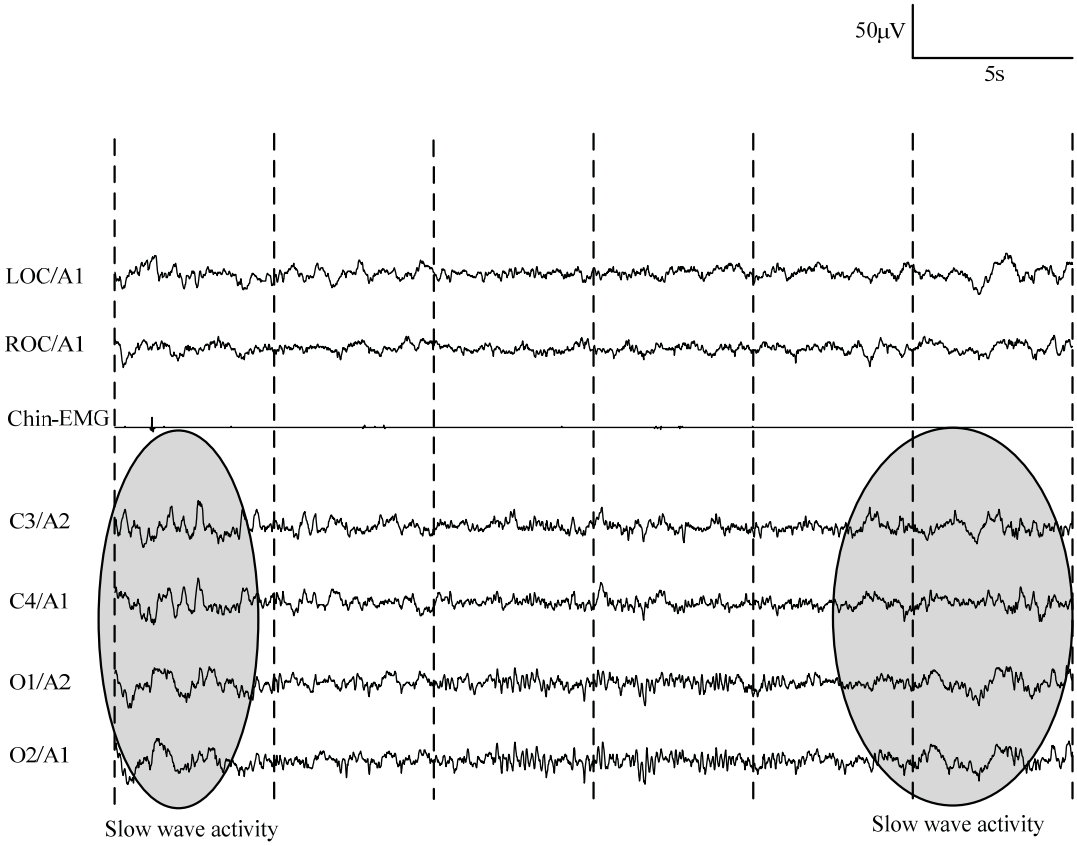


(A) Raw sleep data

	K		K+1		K+2		K+3		K+4		K+5	
Stage	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	1.7e-4	6.8e-9	1.7e-4	2.2e-10	1.7e-4	8.4e-10	1.7e-4	3.6e-4	1.7e-4	1.9e-9	1.7e-4	2.0e-8
C(W)	2.1e-3	3.2e-11	2.1e-3	6.1e-13	2.1e-3	8.1e-12	2.1e-3	2.4e-12	2.1e-3	7.1e-12	2.1e-2	4.0e-11
REM	8.6e-4	1.7e-6	8.6e-4	5.8e-7	8.6e-4	1.3e-6	8.6e-4	7.1e-8	8.6e-4	2/7e-6	8.6e-4	1.9e-6
I	7.4e-3	7.0e-5	7.4e-3	5.9e-6	7.4e-3	8.3e-6	7.4e-3	3.6e-6	7.4e-3	3.2e-5	7.4e-3	7.4e-5
II	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
III	3.3e-3	2.3e-3	5.5e-3	3.8e-7	3.3e-3	5.5e-5	3.3e-3	2.3e-7	3.3e-3	1.7e-4	3.4e-3	1.4e-3
IV	3.0e-8	3.9e-12	2.8e-5	5.4e-14	4.6e-9	2.6e-12	6.6e-7	1.3e-15	2.7e-9	9.9e-16	2.1e-6	5.7e-12
Result	II		II		II		II		II		II	
Automatic determination:	Stage II											
Visual inspection:	Stage II											

(B) Calculation process

Figure 2.9: Automatic sleep stage determination – stage II. (A) Raw sleep data of two EOG recordings, one EMG recording and four EEG recording. (B) Calculation process repeated by predicted probability and conditional probability among consecutive segments. The final determination result is stage II which is consistent with visual inspection by clinician.

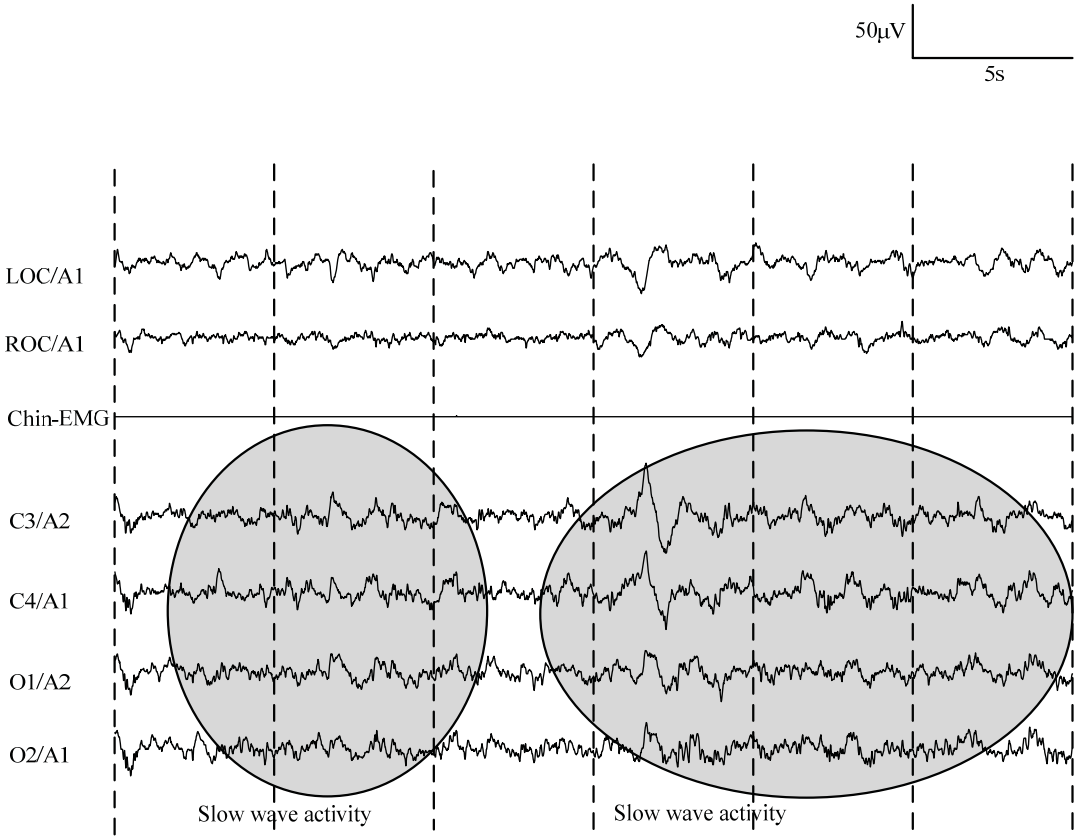


(A) Raw sleep data

	K		K+1		K+2		K+3		K+4		K+5	
Stage	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	6.7e-12	1.1e-12	3.0e-6	1.3e-9	2.0e-8	6.5e-12	1.7e-4	3.2e-4	3.5e-4	1.2e-6	1.2e-6	6.0e-11
C(W)	3.4e-5	1.5e-9	9.4e-4	1.2e-7	1.1e-3	8.4e-11	2.1e-3	4.3e-6	1.4e-3	3.9e-7	1.1e-3	1.6e-9
REM	3.1e-11	9.1e-12	1.5e-5	2.3e-8	1.1e-7	2.6e-9	8.6e-4	3.0e-3	3.1e-3	9.6e-7	1.1e-6	1.3e-9
I	2.7e-10	4.7e-10	1.3e-4	3.2e-7	1.0e-6	1.1e-7	7.4e-3	9.0e-3	9.6e-3	3.2e-5	3.0e-5	1.0e-7
II	5.1e-3	0.02	0.03	1.0e-5	0.01	0.99	0.99	0.15	0.16	4.8e-5	0.02	5.4e-5
III	0.04	0.82	0.80	0.98	0.96	1.8e-4	3.4e-3	0.83	0.82	0.99	0.96	0.99
IV	0.95	0.15	0.16	0.01	0.02	6.3e-10	2.2e-6	1.8e-7	0.01	2.4e-3	0.01	5.5e-3
Result	III		III		II		III		III		III	
Automatic determination:	Stage III											
Visual inspection:	Stage III											

(B) Calculation process

Figure 2.10: Automatic sleep stage determination – stage III. (A) Raw sleep data of two EOG recordings, one EMG recording and four EEG recording. (B) Calculation process repeated by predicted probability and conditional probability among consecutive segments. The final determination result is stage III which is consistent with visual inspection by clinician.



(A) Raw sleep data

	K		K+1		K+2		K+3		K+4		K+5	
Stage	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	9.9e-11	4.8e-15	2.3e-11	1.4e-14	6.0e-10	6.7e-13	4.5e-10	2.1e-14	3.5e-11	5.7e-14	4.8e-10	1.0e-11
C(W)	3.4e-5	2.5e-11	8.2e-4	7.3e-8	5.0e-4	4.7e-8	2.3e-4	4.1e-9	1.5e-5	4.7e-8	3.6e-6	6.0e-10
REM	3.0e-11	8.8e-16	1.1e-10	4.2e-14	2.2e-10	8.0e-14	4.0e-10	7.2e-15	1.5e-11	7.5e-14	6.1e-10	9.6e-12
I	9.6e-10	1.5e-13	9.8e-10	1.5e-13	6.1e-9	6.8e-12	6.3e-9	1.3e-13	3.7e-10	4.0e-13	8.0e-9	3.0e-10
II	5.0e-3	1.3e-7	0.01	2.5e-7	9.6e-3	4.7e-7	7.0e-3	1.8e-8	4.9e-3	7.1e-7	4.8e-3	2.5e-5
III	0.04	0.84	0.82	0.45	0.45	0.20	0.21	0.01	0.02	3.3e-3	0.01	0.47
IV	0.95	0.15	0.16	0.54	0.54	0.79	0.78	0.98	0.97	0.99	0.98	0.52
Result	III		IV		IV		IV		IV		IV	
Automatic determination:	Stage IV											
Visual inspection:	Stage IV											

(B) Calculation process

Figure 2.11: Automatic sleep stage determination – stage IV. (A) Raw sleep data of two EOG recordings, one EMG recording and four EEG recording. (B) Calculation process repeated by predicted probability and conditional probability among consecutive segments. The final determination result is stage IV which is consistent with visual inspection by clinician.

2.4 Discussion

2.4.1 Visual inspection

In recent studies, guideline of stage scoring published by Rechetsffenn and Kales is frequently used either in medical or scientific field. In some sense, Rechetsffenn and Kales criteria supply kinds of exact rules for sleep stage discrimination. Waveform or phasic events detection methods, which have designed according to Rechetsffenn and Kales criteria, can be found in many computerized sleep stage recognition studies.

In Rechtschaffen and Kales criteria, sleep stages were defined by typical waveforms under ideal recording condition for normal and healthy adults. In the field of real clinics, Rechtschaffen and Kales criteria were insufficient. Firstly, the subjects at hospital were patients. The patients suffered by special disease may have particular characteristics, where Rechtschaffen and Kales criteria did not mention. Secondly, sleep data were long-term recording which was inevitably contaminated by various artifacts. The occurrence of artifacts increased the difficulty of sleep stage recognition either by visual inspection or by computerized algorithm. Third, difference between hospitals was existed in real clinics. The recording circumstances were different from hospitals and institutions. Each clinician usually made visual inspection based on their experience and knowledge by considering special circumstances. Therefore, rules in Rechtschaffen and Kales criteria can not cover all the cases in real clinics. Those rule-based sleep stage recognition techniques, designed according to Rechtschaffen and Kales criteria, also can not be successful to deal with the sleep data from real clinics.

In this study, we are investigating the automatic sleep stage determination technique which can be applied for real clinics. Unlike the rule-based method, our method was knowledge based. In the learning process of expert knowledge base construction, sleep data from real clinics and visual inspection by a qualified clinician was adopted. The obtained probability density functions can reflect the actual distribution of parameters corresponding to each sleep stage. In the automatic determination process, sleep stage was automatically determined by conditional probability. The conditional probability indicated the most possible stage for present sleep data, which mimic the humanized work of visual inspection by clinician.

2.4.2 Conditional probability

We determined sleep stage according to the conditional probability. A joint probability of all the selected parameters is calculated and utilized to obtain the value of conditional probability corresponding to each sleep stage. The conditional probability indicates the possibility of the occurrence of the stage under current parameters values. For current segment of sleep data, the maximum value of condition probability was searched and the related stage was determined from O(W), C(W), REM, I, II, III and IV by one step.

The decision of sleep stage was made for every 5-second segment of the continuous sleep recording. The stage, which occupied major portion of the consisting segments in a 30-second epoch, was chosen. Previous epoch would be referred when it was difficult to judge. Our automatic sleep stage determination algorithm mimicked the humanized visual inspection work by clinician. In another hand, our algorithm was sensitive to the sleep stage change between the consecutive 5-seond segments. The sleep stage transition can be estimated.

2.5 Conclusion

In this study, we utilized a method of multi-valued decision making operated on expert knowledge base for automatic sleep stage determination. The expert knowledge base was created on the visual inspections made by a qualified clinician. The visual inspection covered staging criteria and considered surrounding circumstance in real clinics. The developed expert knowledge databased of visual inspection was reliable for automatic sleep stage determination for clinical practice. The automatic sleep stage determination based on conditional probability can utilized to mimic the humanized visual inspection by clinician for clinical practice.

Chapter 3

Automatic Sleep Stage Determination by Conditional Probability of Cauchy Distribution

3.1 Introduction

Human sleep is a dynamic behavior. It is consisted of several types of stages which can be interpreted by the characteristics of bio-neurological signals, sleep EEG (electroencephalogram), EOG (electrooculogram) and EMG (electromyogram). Sleep stage scoring is an important task for inspecting neurophysiological diseases of subjects. One's overnight sleep always contains large amount of data. During the long term recording, sleep data are inevitable to be contaminated by various kinds of artifacts. To make visual inspection on sleep stages requires skillful knowledge on both of the stage-scoring criteria and sleep data under usual recording conditions.

Techniques of automatic sleep stage determination not only can reduce the clinicians' laborious work of visual inspection on sleep stages, but also can provide quantitative and objective evaluation on human sleep. Waveform detection technique (first applied by Smith et al.) could be found in many studies on automatic sleep stage determination [31] [35]. The rule-based methods had also been developed in recent years. However the conventional rule-based methods containing waveform detection or phasic event detection techniques may have advantages in automatic sleep stages recognition under ideal recording condition without artifacts. When sleep recording was contaminated by artifacts, the detection methods had limitations in discriminating the actual waveforms from artifacts.

In our previous studies, multi-valued decision making can be applied to realize automatic sleep stage determination. However, the cortical EEG signals are inevitably contaminated with electrical activities arising from sources of human body other than the brain. We found that artifacts can affect the recognition of sleep stages during the automatic analysis [92]. Various artifacts can be found in sleep EEG. For different types of artifacts, increasing efforts had been made to minimize and identify the artifacts in sleep analysis (for a review, see [93]). Muscle artifacts are the most

common artifacts which can be characterized by surges in high frequency to the local background activity [94]. Although it caused problems in sleep stage recognition, but it also contained valuable information related to body movement or arousal which would facilitate the determination of sleep stages.

In this study, we developed a sleep stage determination system to deal with the sleep data contaminated by artifacts. The main method of automatic sleep stage determination is by using the knowledge-based multi-valued decision making method, which has explained in Chapter 2. The knowledge base for sleep stage determination is consisted of probability density functions (*pdfs*) of parameters according to the visual inspection by a qualified clinician. In order to abate the effect of artifacts, we used Cauchy distribution instead of Gauss distribution to construct the knowledge base of characteristic parameter distributions.

3.2 Method

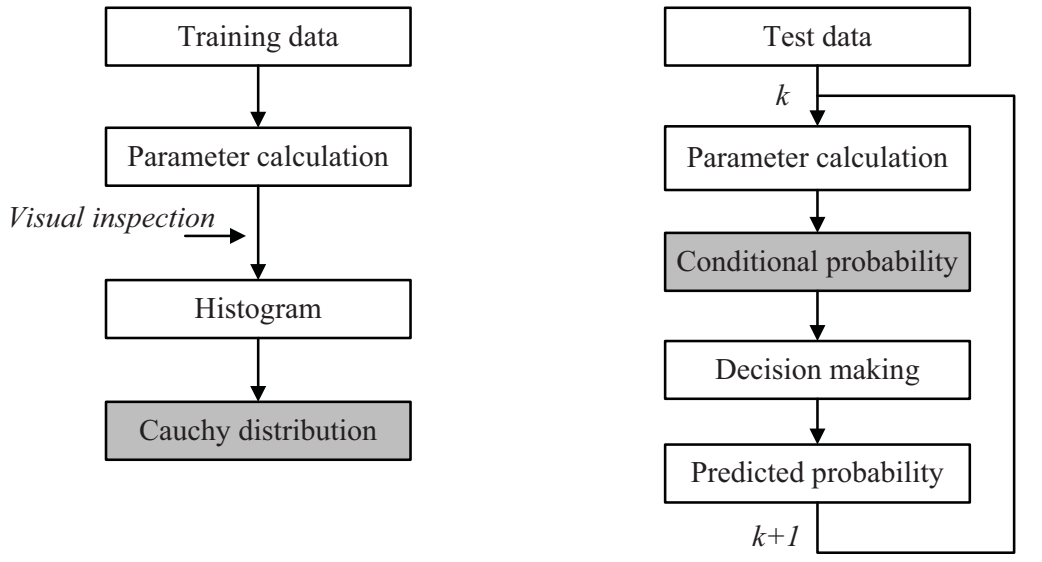
3.2.1 Data acquisition

All the sleep data were recorded at the department of Clinical Physiology, Toranomon Hospital in Tokyo, Japan. Totally eight subjects were participated, having an average age about 50 years old. They were suffered by breathing disorders during sleep (Sleep Apnea Syndrome). Their overnight sleeping data were recorded after the treatment of Continuous Positive Airway Pressure (CPAP) based on the polysomnographic (PSG) measurement. The PSG measurement at Toranomon Hospital includes four EEG recordings, two EOG recordings and one EMG recording.

The subjects were same with Table 2.1 in Chapter 2. The recording condition have been described in detail in Chapter 2, subsection 2.2.1 Subjects and sleep data.

3.2.2 Expert knowledge database construction

The block diagram of multi-valued decision making method in Chapter 2 is summarized in Figure 3.1. It consists of two modules. Figure 3.1 (A) is a learning process of expert knowledge database construction. Visual inspection is adopted. Figure 3.1 (B) shows the algorithm of automatic sleep stage determination iterating through the consecutive segments. The probability density function of parameters is estimated approximately by using Cauchy distribution. The decision making of sleep stages is carried out based on the conditional probability of Cauchy distribution.



(A) Expert knowledge database construction (B) Automatic sleep stage determination

Figure 3.1: Black diagram of processing. (A) Expert knowledge database of probability density functions approximated by Cauchy distribution. (B) Automatic sleep stage determination based on conditional probability of Cauchy distribution.

3.2.2.1 Parameter calculation

The overnight sleep recording data is divided into 30-second epochs. Each epoch was subdivided into still smaller segments of 5-second. In order to calculate the parameter values, the periodogram was derived by taking 512-point FFT (Fast Fourier Transform) for EEGs and EOGs, whereas 1024-point FFT for EMG. The parameters included the ratio of EEG components in C3/A2, C4/A1 and O1/A2, O2/A1 channels, the amplitude of EEG components in C3/A2 and C4/A1 channels, the amount of EOG components in LOC/ROC, LOC/A1 and ROC/A1 channels, and the amount of EMG components in chin-EMG channel. The detail description of parameter definition was in Chapter 2, subsection 2.2.3 Expert Knowledge Database Construction.

3.2.2.2 Probability density function of Cauchy distribution

The epochs are classified into sleep stage groups according to the visual inspection by a qualified clinician (F. K.) in Toranomon Hospital. Each epoch is assigned to a single sleep stage and described by a set of parameters values. For each sleep stage, the values of parameters are counted to make the histograms.

The *pdf* of parameter of each stage is approximately evaluated using histograms with Cauchy distribution. Based on the definition of Cauchy distribution, the *pdf* of parameter y in stage ζ can be mathematically expressed by,

$$f(y \mid \zeta) = \frac{b}{\pi((y-a)^2 + b^2)} \quad , \tag{3.1}$$

where a is the location parameter and b is the scale parameter. The values of a is determined by media and b is determined by quartile [95][96].

In addition, a transitional probability matrix of sleep stage change is calculated by using the same method in Chapter 2, subsection 2.2.3 Expert knowledge database construction.

3.2.3 Sleep stage determination by conditional probability

Following the algorithm described in Chapter 2, subsection 2.2.4 Automatic sleep stage determination, the predicted probability of first segment $P_{1|0}$ for various sleep stages shared the probability equally with a value of *1/n*, where *n* is the number of the types of sleep stages. The automatic sleep stage determination is repeated by calculating the conditional probability and predicted probability among the consecutive segments. The decision is made based on the maximum value of conditional probabilities. The sleep stage for each epoch is determined by choosing the stage which takes up the greatest portion in one epoch.

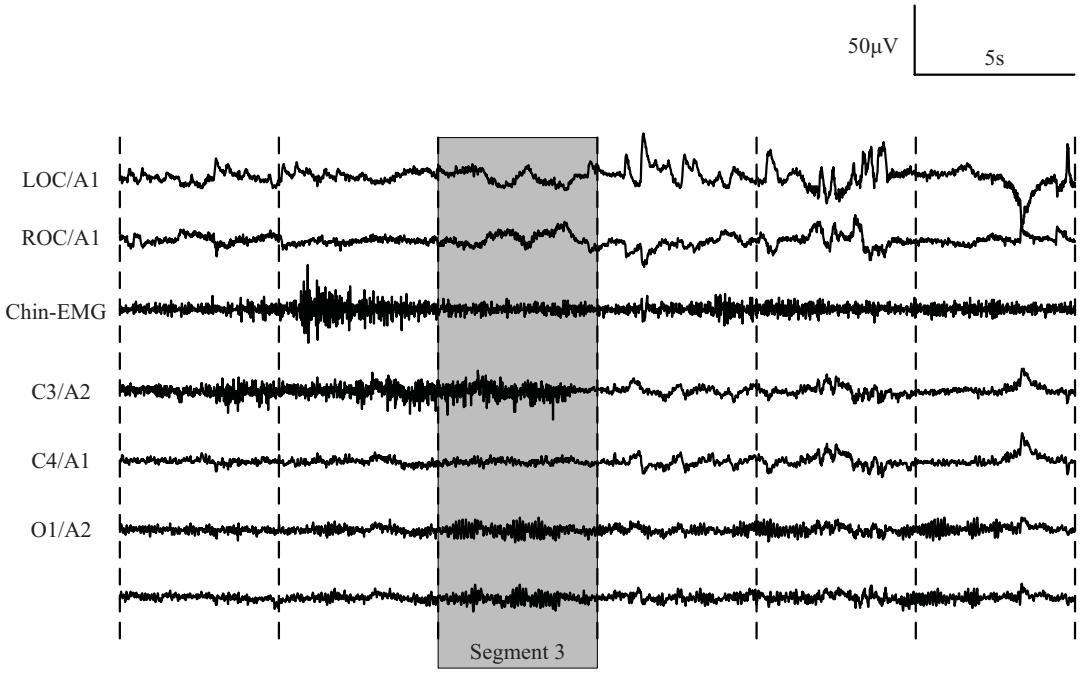
In this study, the probability density function was modeled by Cauchy distribution. According to the particular feature of infinite variance, the probability density functions of parameters were obtained by approximate methods [97]. A joint probability of parameters was obtained approximate to the Cauchy distribution. Therefore, conditional probability may indicate the possibility of sleep stage occurrence for certain segment of sleep data under Cauchy distribution.

3.3 Results

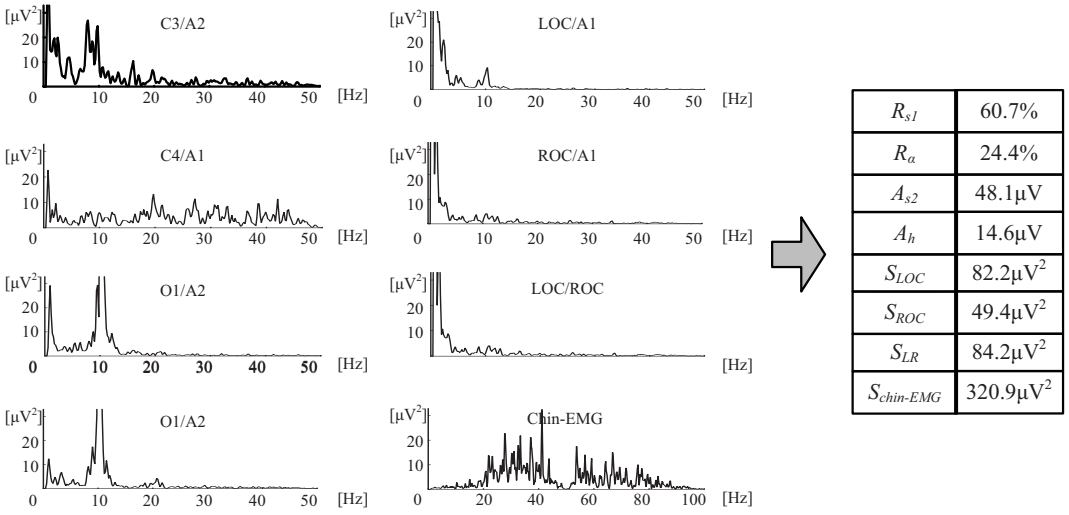
3.3.1 Probability density function of Cauchy distribution

The continuous sleep recordings of two subjects (Subject D and H) were utilized as the training data to obtain the knowledge base of *pdfs* of parameters for sleep stages. Figure 3.2 showed the parameter calculation process. The continuous sleep data was divided into 30-second epochs. Each epoch was sub-divided into 5-second segments. Figure 3.2 (A) illustrated a 30-second epoch sleep raw data consisting 6 segments. For each segment, a set of parameters were calculated. Figure 3.2 (B) showed the parameter for the third segment in Figure 3.2 (A). The periodogram was obtained for sleep EEGs, EOGs and EMG. A set parameter was calculated based on the periodograms. The obtained parameter values were shown in a table. According to the visual inspection, the parameter values were grouped for various sleep stage to make the histograms.

In this study, Cauchy distribution was adopted to approximate the histogram instead of Gaussian distribution. The histogram, Gaussian distribution and Cauchy distribution of the ratio of alpha (R_α, α: 0.5-2 Hz) for stage awake with eyes closed were illustrated in Figure 3.3. The vertical bars corresponded to the histogram, the solid line was Cauchy distribution and the dotted line was Gaussian distribution. Cauchy distribution had similar shape as Gaussian distribution but the infinite variance allowed much heavier tails comparing with Gaussian distribution.



(A) Raw sleep data



R_{s1}	60.7%
R_{α}	24.4%
A_{s2}	48.1μV
A_h	14.6μV
S_{LOC}	82.2μV^2
S_{ROC}	49.4μV^2
S_{LR}	84.2μV^2
$S_{chin\text{-}EMG}$	320.9μV^2

(B) Periodograms and parameters

Figure 3.2: Parameter calculation process.

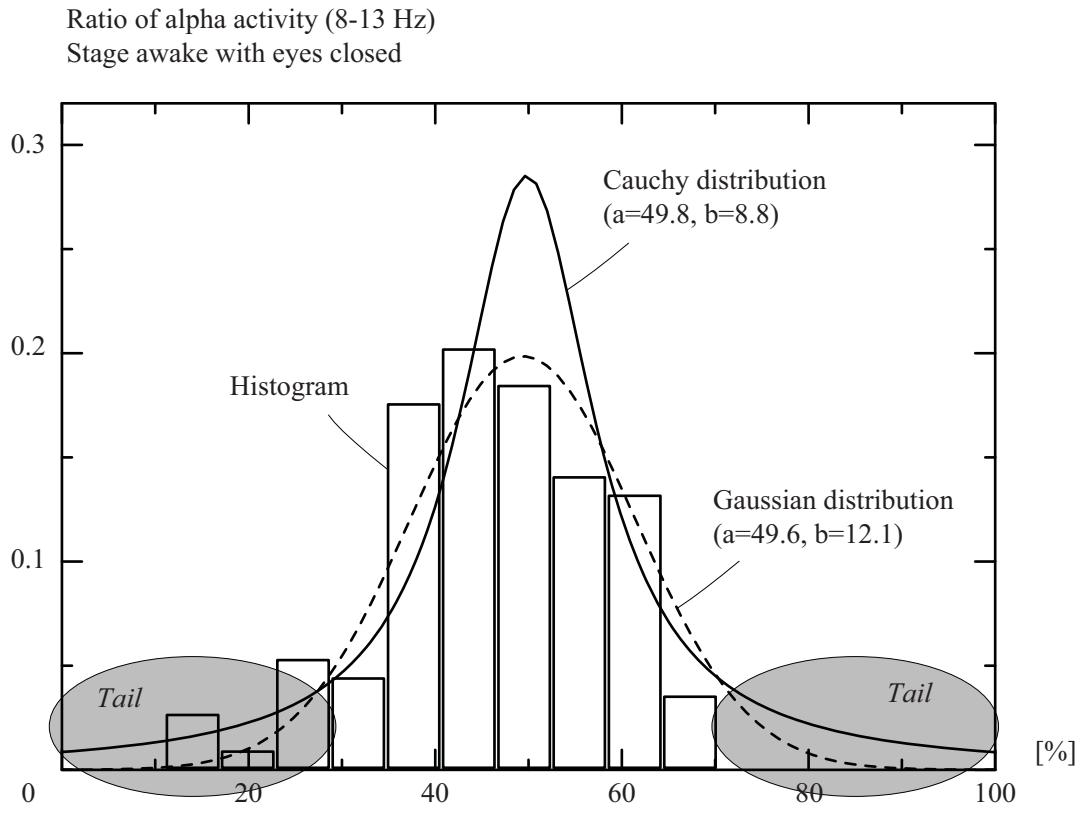


Figure 3.3: Histogram, Gaussian distribution and Cauchy distribution of R_α (8-13 Hz) of the stage awake with eyes closed. The tails of Cauchy distribution were much heavier than Gaussian distribution.

3.3.2 Automatic sleep stage determination

The algorithm of automatic determination was applied on another two subjects. Following the algorithm of multi-valued decision making, their overnight sleep recordings (about 8-hour) were analyzed. Among the recording data, one epoch was selected and the calculation processing was illustrated with the time series of PSG measurement in Figure 3.4 and Figure 3.5. The result by conditional probability of Cauchy distribution was in Figure 3.4. The result by conditional probability of Gaussian distribution was in Figure 3.5.

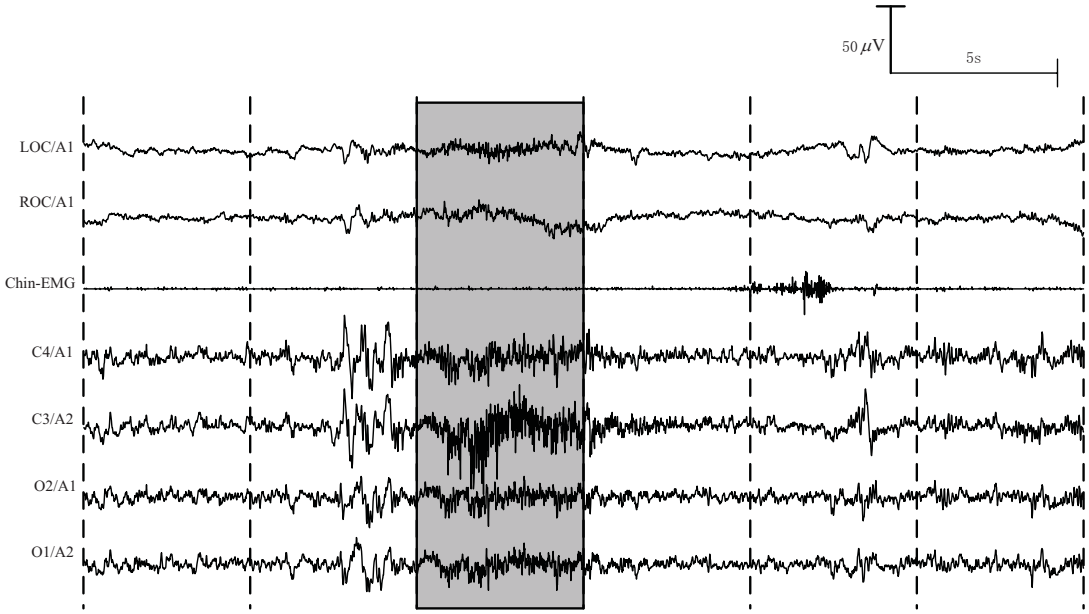
In Figure 3.4 (A), the third segment k+2 of the raw sleep data was contaminated with electrode artifact. Figure 3.4 (B) illustrated the derivation of conditional probability of Cauchy distribution for this segment. A set of parameters were calculated for this segment. Those values were utilized to obtain the joint probability for each sleep stage. Based on the joint probability of parameters and predicted probability, the conditional probability of Cauchy distribution was obtained. For this segment, the artifact did not affect the decision making with Cauchy distribution. The result is stage I. In Figure 3.4 (C), the decision making result for all the segments were stage I and final determination result for the epoch was stage I which is consistent with the visual inspection by clinician.

In Figure 3.5, the calculation process for the same time series in Figure 3.4 was showed by using conditional probability of Gaussian distribution. In Figure 3.5 (B), the value of joint probability included rather small value close to 0 for stage III and IV. The decision making for the segment contaminated by electrode artifacts was affected and judged to stage awake. In Figure 3.5 (C), the decision of sleep stage for the following segments were also affected which were judged to stage awake. The final determination result was inconsistent with the visual inspection. The main reason caused the mis-determination by Gaussian distribution was related to the exponentially decrease tail.

3.3.3 Accuracy evaluation

The automatic sleep stage determination result of subject B was compared with visual inspection in Figure 3.6. Figure 3.6 (A) was the visual inspection by the clinician. Figure 3.6 (B) was the result of automatic sleep stage determination by using Gaussian distribution. Figure 3.6 (C) was the result of automatic sleep stage determination by using Cauchy distribution. The automatic sleep stage determination results of subject F by using Gaussian distribution and Cauchy distribution were compared with visual inspection in Figure 3.7. The hypnogram of automatic determination presented well comparing with visual inspection on sleep cycles and changes during the overnight recording by using Cauchy distribution.

The results of automatic sleep stage determination on two test subjects were evaluated. The epochs which have the consistent determination result with visual inspection were counted. The amount of the epochs was divided by the total amount of sleep stage scored by clinician to calculate the accuracy. For subject B, the determination result by Gaussian distribution was in Table 3.1 and Cauchy distribution in Table 3.2. For subject F, the determination result by Gaussian distribution was in Table 3.3 and Cauchy distribution in Table 3.4.The total accuracy was improved by Cauchy distribution comparing with Gaussian distribution.



(A) Raw sleep data including EEGs, EOGs and EMG of an 30-second epoch

Parameter	
R_{δ}	15.03
R_{α}	28.51
A_{θ}	39.63
A_h	48.84
S_{LOC}	76.01
S_{ROC}	71.70
S_{LR}	75.32
$S_{Chin-EMG}$	311.41

Probability density function	
O(W)	5.34e-9
C(W)	1.07e-17
REM	7.15e-20
I	1.59e-17
II	1.71e-20
III	2.21e-21
IV	5.52e-23

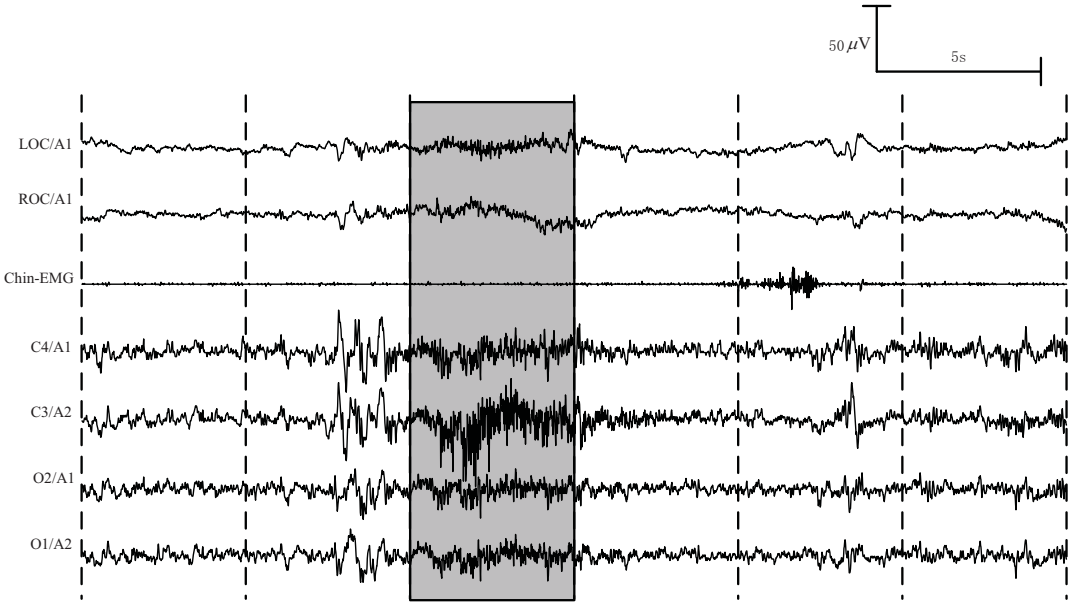
Conditional probability	
O(W)	5.0e-4
C(W)	8.7e-3
REM	1.6e-5
I	0.99
II	3.1e-4
III	1.1e-7
IV	1.3e-15

(B) Derivation of conditional probability of Cauchy distribution for segment k+2.

	K		K+1		K+2		K+3		K+4		K+5	
Stage	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	8.2e-4	4.0e-5	7.2e-4	6.2e-7	5.9e-4	5.0e-4	1.2e-3	0.02	0.02	0.06	0.06	2.3e-3
C(W)	0.01	1.6e-5	0.01	7.4e-9	0.01	8.7e-3	0.02	5.0e-4	0.01	1.8e-6	0.01	1.0e-5
REM	2.3e-3	7.9e-3	9.9e-3	9.6e-4	2.8e-3	1.6e-5	2.1e-3	5.3e-4	2.6e-3	1.2e-3	3.2e-3	3.6e-3
I	0.93	**0.99**	0.93	**0.81**	0.76	**0.99**	0.93	**0.98**	0.92	**0.94**	0.88	**0.99**
II	0.05	3.2e-3	0.04	0.18	0.22	3.1e-4	0.04	2.1e-4	0.04	2.3e-3	0.04	1.0e-5
III	3.1e-5	2.2e-7	1.1e-5	2.5e-8	6.3e-4	1.1e-7	1.1e-6	1.5e-10	6.7e-7	1.1e-8	7.6e-6	3.0e-8
IV	2.4e-8	1.4e-12	2.7e-9	6.7e-11	2.9e-10	1.3e-15	1.4e-9	4.9e-14	1.8e-12	2.0e-17	1.3e-10	1.8e-16
Result	I		I		I		I		I		I	
Automatic determination	I											

(C) Calculation process of sleep stage determination by using Cauchy distribution

Figure 3.4: Calculation process of automatic sleep stage determination by conditional probability of Cauchy distribution. (A showed the raw sleep data of an epoch; (B) showed the procedures to obtain the conditional probability of Cauchy distribution of segment k+2; (C) was the calculation repeated among the consecutive segments for one epoch.



(A) Raw sleep data including EEGs, EOGs and EMG of an 30-second epoch

Parameter	
R_{δ}	15.03
R_{α}	28.51
A_{θ}	39.63
A_h	48.84
S_{LOC}	76.01
S_{ROC}	71.70
S_{LR}	75.32
$S_{Chin\text{-}EMG}$	311.41

Probability density function	
O(W)	3.07e-52
C(W)	5.10e-23
REM	1.60e-80
I	2.37e-35
II	1.02e-239
III	0.00
IV	0.00

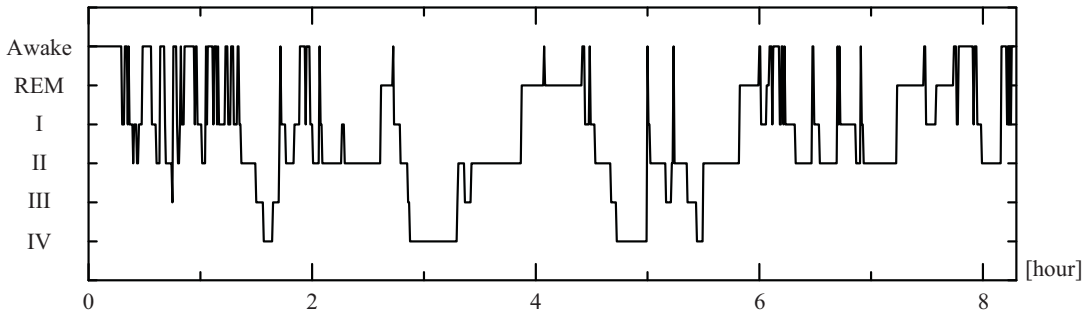
Conditional probability	
O(W)	5.34e-9
C(W)	1.07e-17
REM	7.15e-20
I	1.59e-17
II	1.71e-20
III	2.21e-21
IV	5.52e-23

(B) Derivation of conditional probability of Gaussian distribution for segment k+2.

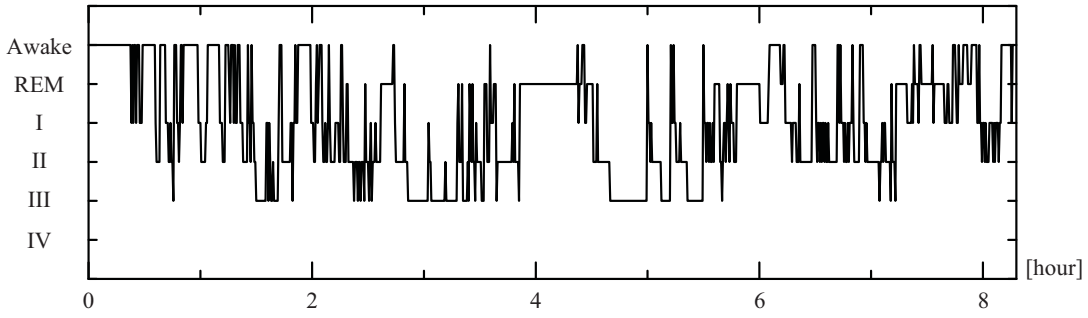
	K		K+1		K+2		K+3		K+4		K+5	
Stage	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	6.8e-4	1.7e-10	6.7e-4	7.8e-14	6.4e-4	0.16	0.17	**0.99**	0.99	**0.99**	0.99	**0.99**
C(W)	0.01	1.0e-27	0.01	3.7e-35	0.01	**0.83**	0.77	1.2e-12	3.1e-3	7.8e-48	3.1e-3	7.4e-9
REM	2.1e-3	0.01	0.02	3.3e-3	1.9e-3	9.8e-58	1.3e-12	6.5e-27	1.2e-6	1.9e-7	5.9e-7	3.0e-3
S1	0.91	**0.98**	0.92	**0.89**	0.83	6.3e-10	0.05	5.6e-4	1.0e-3	1.9e-4	7.0e-4	3.0e-3
S2	0.07	7.7e-9	0.04	0.10	0.14	4.5e-215	1.2e-3	1.0e-81	2.3e-5	7.3e-15	8.1e-6	2.8e-32
S3	8.9e-5	6.1e-37	2.5e-11	6.5e-43	3.3e-4	0.00	1.5e-217	0.00	3.4e-83	2.7e-143	2.4e-17	4.4e-188
S4	2.8e-26	1.7e-166	7.3e-39	1.5e-206	7.8e-45	0.00	0.00	0.00	0.00	0.00	3.2e-145	0.00
Result	I		I		C(W)		O(W)		O(W)		O(W)	
Automatic determination	O(W)											

(C) Calculation process of sleep stage determination by using Gaussian distribution

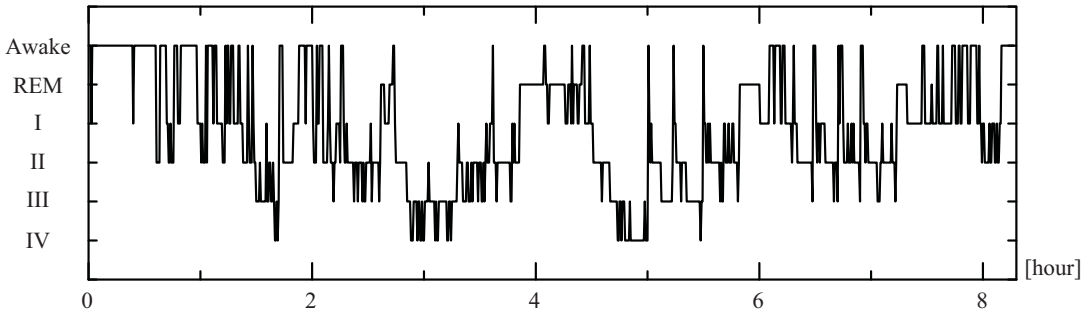
Figure 3.5: Calculation process of automatic sleep stage determination by conditional probability of Gaussian distribution. (A) showed the raw sleep data of an epoch; (B) showed the procedures to obtain the conditional probability of Gaussian distribution of segment k+2; (C) was the calculation repeated among the consecutive segments for one epoch.



(A) Visual inpection

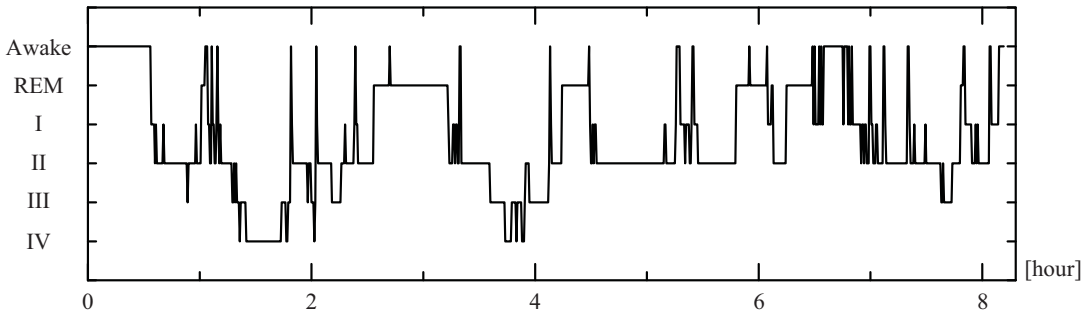


(B) Automatic sleep stage determination by Gaussian distribution

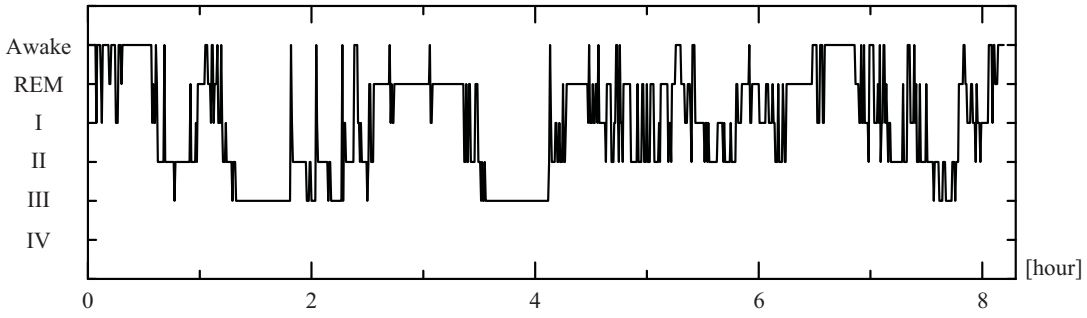


(C) Automatic sleep stage determination integrated by Cauchy distribution

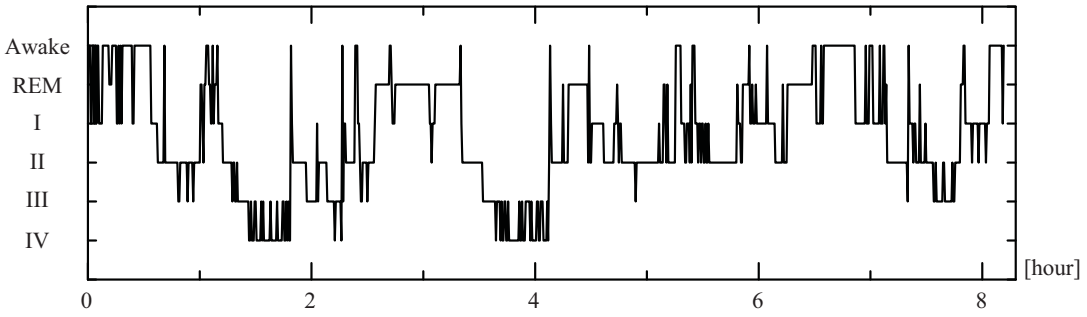
Figure 3.6: The automatic determination result of subject B by Cauchy distribution, Gaussian distribution compared with visual inspection. (A) Visual inspection by qualified clinician. (B) Determination by conditional probability of Guassian distribution. (C) Determination by conditional probability of Cauchy distribution.



(A) Visual inpection



(B) Automatic sleep stage determination by Gaussian distribution



(C) Automatic sleep stage determination integrated by Cauchy distribution

Figure 3.7: The automatic determination result of subject F by Cauchy distribution, Gaussian distribution compared with visual inspection. (A) Visual inspection by qualified clinician. (B) Determination by conditional probability of Guassian distribution. (C) Determination by conditional probability of Cauchy distribution.

Table 3.1: Evaluation of accuracy comparing with visual inspection
(Gaussian distribution, Subject B)

		Automatic determination								
		O(W)	**C(W)**	**REM**	**I**	**II**	**III**	**IV**		
Visual Inspection	**O(W)**	29	3	3	1	0	1	0	37	78.38%
	C(W)	7	106	13	3	0	0	0	129	82.17%
	REM	5	0	127	17	0	0	0	149	85.23%
	I	40	12	17	67	24	0	0	160	41.88%
	II	10	0	33	76	225	25	0	369	60.98%
	III	1	0	1	3	3	40	0	48	83.33%
	IV	0	0	0	4	4	93	0	101	0.00%
									Total : 59.82%	

Table 3.2: Evaluation of accuracy comparing with visual inspection
(Cauchy distribution, Subject B)

		Automatic determination								
		O(W)	**C(W)**	**REM**	**I**	**II**	**III**	**IV**		
Visual Inspection	**O(W)**	19	12	1	1	1	2	1	37	51.35%
	C(W)	8	107	0	14	0	0	0	129	82.95%
	REM	9	0	93	47	0	0	0	149	62.42%
	I	41	17	1	74	27	0	0	160	46.25%
	II	8	3	2	64	253	39	0	369	68.56%
	III	0	0	0	0	6	39	3	48	81.25%
	IV	0	0	0	1	3	57	40	101	39.60%
									Total : 62.94%	

Table 3.3: Evaluation of accuracy comparing with visual inspection
(Gaussian distribution, Subject F)

		Automatic determination								
		O(W)	**C(W)**	**REM**	**I**	**II**	**III**	**IV**		
Visual Inspection	**O(W)**	54	11	6	7	0	0	0	78	69.23%
	C(W)	4	52	1	0	0	0	0	57	91.23%
	REM	1	0	152	21	3	0	0	177	85.88%
	I	14	15	30	38	4	0	0	101	37.62%
	II	12	0	72	82	231	25	0	422	54.74%
	III	0	0	0	0	5	90	0	95	94.74%
	IV	0	0	0	0	0	53	0	53	0.00%
									Total : 62.77%	

Table 3.4: Evaluation of accuracy comparing with visual inspection
(Cauchy distribution, Subject F)

		Automatic determination								
		O(W)	**C(W)**	**REM**	**I**	**II**	**III**	**IV**		
Visual Inspection	**O(W)**	30	27	5	14	0	2	0	78	38.46%
	C(W)	1	53	0	3	0	0	0	57	92.98%
	REM	0	1	131	31	14	0	0	177	74.01%
	I	3	24	8	60	6	0	0	101	59.41%
	II	3	0	18	66	294	40	1	422	69.67%
	III	0	0	0	0	3	59	33	95	62.11%
	IV	0	0	0	0	0	16	37	53	69.81%
									Total : 67.55%	

3.4 Discussion

3.4.1 Cauchy distribution

In our method, Cauchy distribution is adopted as the probability distribution instead of Gaussian distribution. Comparing with Gaussian distribution, Cauchy distribution has similar shape which can be represented by location ± scale. In addition, it has infinite variance where the tails are much heavier.

During the long-term recording of human overnight sleep, it is inevitably contaminated by artifacts, such as blink artifacts, body movement, electrodes artifact, etc. Artifacts always cause problem either in the computerized analysis or the human visual analysis. For example, the electrodes artifact shows similar characteristics as the slow wave (0.5-2 Hz), and it is predominant in the deep sleep (stage III and IV). Then the value of R_{s1} of those epochs will be closer to the distribution in stage III and IV, far from the distribution of the actual stage. It will cause mis-determination. Then the value of the conditional probability corresponding to the mis-determined stage affects the predicted probability for next segment in Equation 3.1.

Due to the definition, Gaussian distribution has exponentially decreasing tail whereas Cauchy distribution has ratio decreasing tail. In Equation 2.3, the conditional probability was calculated by ratio. When artifact occurred, the values of some parameters would locate at the tails of distribution. By ratio, the mis-determined stage would be an exponential value (10^{-10}-10^{-20}) when using Gauss distribution. The effect of mis-determination will be seriously transferred to the following segments. But when using Cauchy distribution, the affect could be abated because it has heavier tails and the value located at the tail would be 10^{-2}-10^{-3}.

The periodogram of EEG has similar characteristic as Cauchy distribution [91]. Cauchy distribution may have significance for neurophysiological signal analysis especially for EEG. Therefore, we chose Cauchy distribution for modeling the parameter distribution on histogram. The heavier tail of Cauchy distribution showed its effectiveness to abate the effect of mis-determination caused by artifact contamination. On the other hand, Cauchy distribution also showed consistent determination results where the recording data was not contaminated with artifacts.

3.4.2. Automatic sleep stage determination

The automatic determination processing in Figures 3.4 and 3.5 showed that the proposed methodology was sensible to the sleep stage changing in every 5-second segment. The final decision making of each epoch was as close as the way when clinician made their visual inspection. The discrimination of sleep stage was appreciably satisfied. For both test subjects, the recognition of the stage awake, light sleep and deep sleep stages are good. Compare with other sleep stages, the recognition of stage REM was not as good as other sleep stages. In Toranomon hospital, a belt around the chin was utilized in order to avoid EMG artifact. The amplitude of chin-EMG was in low level. The distribution of high frequency activity in chin-EMG could not separate stage REM well from other sleep stages. Besides, the subjects we investigated are the patients suffered from breathing disorders during sleep. The sleep patterns of those subjects after the treatment of Continuous Positive Airway Pressure (CPAP) are slightly different with the normal and healthy person. The disorders of REM sleep behavior will cause intermittent atonia in REM sleep. The amplitude of slow wave activity is difficult to distinguish stage III and stage IV because they are the persons over 50 years old. Stage III and IV are mixed in those subjects.

3.5 Conclusion

We developed an automatic sleep stage system by a multi-valued decision making method based on conditional probability of Cauchy distribution. Due to the infinite variance of Cauchy distribution, the effect of the mis-determination caused by artifacts could be abated. The performance of the expert knowledge-based automatic sleep stage determination system was improved to deal with the sleep data contaminated with artifacts for clinical practice.

Chapter 4

Automatic Sleep Stage Determination with Automatic Parameter Selection

4.1 Introduction

With the development of modern electrical measurement and recording techniques, the dynamic behavior in sleep can be observed. There are two sleep states: rapid eye movement (REM) sleep and non rapid eye movement (NREM) sleep. The NREM sleep consists of stage I, stage II, stage III and stage IV. Another stage of awake is often included, during which a person falls asleep. For normal and healthy persons, those types of sleep stages corresponding to certain frequency bands and amplitudes follow a fairly well-behaved cyclic pattern throughout the night. Sleep stage scoring is an important task for inspecting neurophysiological diseases of subjects. The most well-known criteria for sleep stage scoring were published by Rechtschaffen and Kales in 1968 [16]. Currently, sleep stage scoring has been widely used for evaluating the condition of sleep and diagnosing the sleep related disorders in hospitals and institutions.

Automatic sleep stage determination can free the clinicians from the heavy task of visual inspection on sleep stages. Rule-based waveform detection method, according to Rechtschaffen and Kales criteria, has been frequently utilized in many studies. The limitations of Rechtschaffen and Kales criteria have been noticed [85]. The insufficiency is that it only includes typical characteristic waveforms of healthy and normal persons for staging. Besides, EOG (electrooculogram) signal was investigated to process stage determination [80] [81]. A changeable transition probability of sleep stages based on body movement was developed to interpret the human sleep [73] [74].

Although various methodologies have been developed, effective technique is still needed for clinical application. Sleep data adopts long-term recording. It is inevitably being affected by various artifacts [93] [94]. Individual differences are also commonly existed, even under the same recording condition [98]. For same sleep data, different clinician may also have different scoring result [99] [100]. For the patients with

sleep-related disorders, their sleep data has particular characteristics. Therefore, the recorded sleep data containing complex and stochastic factors will increase the difficulties for the computerized sleep stage determination techniques to be applied for clinical practice.

In this study, sleep stage determination is considered as a multi-valued decision making problem in the field of clinics. The main methodology, explained in Chapter 2, has been proved to be successful for sleep stage determination. The aim of this study is to develop a flexible technique adapting to different cases of sleep data, which can meet the customized requirements in hospitals and institutions. The method includes two modules: expert knowledge database construction and automatic sleep stage determination. Visual inspection by a qualified clinician is utilized to obtain the probability density function of parameters during the learning process of expert knowledge database construction. A process of parameter selection is introduced in order to make our algorithm flexible. Automatic sleep stage determination is manipulated based on conditional probability.

4.2 Method

4.2.1 Data acquisition

The sleep data investigated in this study was recorded in the Department of Clinical Physiology, Toranomon Hospital, at Tokyo, Japan. Eight subjects of an average age about 50 years old, were participated. These patients had breathing disorder during sleep (Sleep Apnea Syndrome). Their overnight sleeping data were recorded after the treatment of Continuous Positive Airway Pressure (CPAP) based on the polysomnographic (PSG) measurement. The PSG measurement used in Toranomon Hospital included four EEG (electroencephalogram) recordings, two EOG recordings and one EMG (electromyogram) recording.

The subjects were same with Table 2.1 in Chapter 2. The recording condition have been described in detail in Chapter 2, subsection 2.2.1 Subjects and sleep data.

4.2.2 Visual inspection

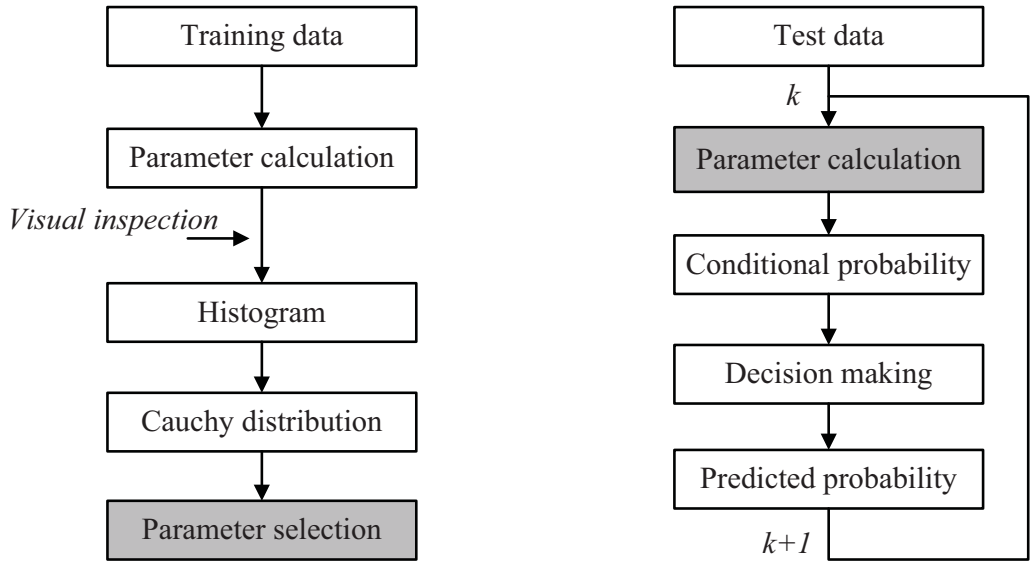
A qualified clinician F.K. in Toranomon hospital scored sleep stages on the overnight sleep recording of subjects. The clinician made the visual inspection based on the Rechtschaffen and Kales criteria and clinical experience through an epoch-by-epoch approach.

The PSG recording of subjects were divided into consecutive 30-second epochs. Each epoch was assigned by a single sleep stage. In the case of multiple stages presented in a certain epoch, the stage taking major portion of the epoch was scored. In total, seven types of stages were inspected, stage awake with eyes opened, stage awake with eyes closed, stage REM, stage I, stage II, stage III and stage IV. Stage awake was classified into open eyes state and close eyes state. Stage I and stage II were identified with light sleep. Stage III and stage IV were identified with deep sleep.

The detail explanation of visual inspection work by qualified clinician was in Chapter 2, subsection 2.2.2 Visual inspection.

4.2.3 Multi-valued decision making

The block diagram of multi-valued decision making method (Chapter 2) is illustrated in Figure 4.1. It consists of two modules. Figure 4.1 (A) is a learning process of expert knowledge database construction. Visual inspection is adopted. Figure 4.1 (B) shows the algorithm of automatic sleep stage determination iterating through the consecutive segments. An automatic parameter selection process is developed to obtain an adaptive expert knowledge database. The selected parameters are adopted to manipulate the automatic sleep stage determination algorithm.



(A) Expert knowledge database construction (B) Automatic sleep stage determination

Figure 4.1: Black diagram of processing. (A) Expert knowledge database construction to obtain the probability density function of optimal parameters. (B) Automatic sleep stage determination integrated with the selected optimal parameters.

4.2.3.1 Expert knowledge database construction with optimal parameters

- **Parameter calculation**

The overnight sleep recording from subjects was divided into consecutive 30-second epochs for training purpose. Each epoch was subdivided into 5-second segments. A set of characteristic parameters, extracted from the periodogram of EEGs, EOGs and EMG, were calculated for each segment. In order to obtain the parameter values, the periodogram was derived by taking 512-point FFT (Fast Fourier Transform) with Hanning window for EEGs and EOGs, whereas 1024-point FFT with Hanning window for EMG. The frequency resolution for all the channels was 0.2Hz. There are three types of parameters: ratio, amplitude and amount. The description of each parameter is given in Table 4.1.

Totally, 20 parameters were calculated as candidates. Ratios include $R^{O}_{\omega 1}$, $R^{O}_{\omega 2}$, $R^{O}_{\omega 3}$, $R^{O}_{\omega 4}$, $R^{C}_{\omega 1}$, $R^{C}_{\omega 2}$, $R^{C}_{\omega 3}$, and $R^{C}_{\omega 4}$. Amplitudes include $A^{O}_{\omega 1}$, $A^{O}_{\omega 2}$, $A^{O}_{\omega 3}$, $A^{O}_{\omega 4}$, $A^{C}_{\omega 1}$, $A^{C}_{\omega 2}$, $A^{C}_{\omega 3}$, and $A^{C}_{\omega 4}$. Amounts include $S^{L}_{\omega 5}$, $S^{R}_{\omega 5}$, $S^{LR}_{\omega 5}$, and $S^{M}_{\omega 6}$. The superscript C stands for C3/A2 or C4/A1, O for O1/A2 or O2/A1, L for LOC/A1, R for ROC/A1, LR for LOG/ROC and M for chin-EMG channel. The subscripts indicate the frequency bands which are given in the notation under Table 4.1. The parameters of consisted segments were taken average to derive the parameter value of one epoch.

Table 4.1 Parameter description

Parameter	Description
Ratio (%)	Maximum value of the ratios of the summation of periodogram with the certain frequency bands ($\omega 1$, $\omega 2$, $\omega 3$, $\omega 4$) to the frequency band (T) in EEG channels (*C3/A2, C4/A1* and *O1/A2, O2/A1*) between two hemispheres.
Amplitude (μV)	Maximum value of the square root of the summation of periodogram with the frequency bands ($\omega 1$, $\omega 2$, $\omega 3$, $\omega 4$) in EEG channels (*C3/A2, C4/A1* and *O1/A2, O2/A1*) between two hemispheres.
Amount (μV^2)	Summation of periodogram with the frequency band ($\omega 5$) in EOG channels (*LOC/ROC, LOC/A1, ROC/A1*), with the frequency band ($\omega 6$) in EMG channel (*chin-EMG*)

* $\omega 1$: 0.5-2 Hz; $\omega 2$: 2-7 Hz; $\omega 3$: 8-13 Hz; $\omega 4$: 25-35 Hz;
$\omega 5$: 2-10 Hz; $\omega 6$: 25-100 Hz; T: 0.5-25 Hz.

- **Histogram and probability density function**

The epochs were classified into sleep stage groups according to the visual inspection by clinician. The histogram for each parametric variable was created for each sleep stage. The probability density function was approximately evaluated using histogram with Cauchy distribution. The procedures of how to obtain the histogram and probability density function of Cauchy distribution have been explained in Chapter 2 and Chapter 3.

- **Parameter selection**

The distance of the *pdfs* between stage *i* and stage *j* was calculated by

$$d(i,j)=|a_i-a_j|. \quad (4.1)$$

The larger distance indicates smaller overlap between the *pdfs*. It is measured by

$$d(i,j)>max(3b_i,3b_j). \quad (4.2)$$

When the distance is larger than three times of the deviations of the probability density functions of both stages, the parameter is selected.

- **Transitional probability matrix**

In addition, a transitional probability matrix of sleep stage change was calculated for the training data as in Chapter 2. The consisted segments of one epoch were considered having the same scoring result. The transitional probability between sleep stages was obtained. It designated the probabilities of stage change between two conjoint segments.

4.2.3.2 Automatic sleep stage determination with optimal parameters

The overnight sleep recordings of subjects were divided into the same length of epochs and segments as the training data. The values of selected parameters were calculated for each segment.

Initially, predicted probability of first segment for various sleep stages shared the probability equally with a value of *1/n*. *n* is the number of the types of sleep stages. The automatic sleep stage determination is iterated though the calculation of conditional probability (Equation 2.2) and predicted probability (Equation 2.4) among

the consecutive segments. The decision (Equation 2.3) is made based on the value of conditional probabilities. The sleep stage for each epoch is determined by choosing the stage which takes up the greatest portion in one epoch. The detail explanation of the automatic sleep stage determination was in Chapter 2.

4.3 Results

4.3.1 Probability density function

The overnight sleep recordings of two subjects (Subject D and Subject H) were utilized as the training data for expert knowledge database construction. The *pdfs* of the selected parameters are illustrated in Figure 4.2. The horizontal axis indicates the types of stages, the vertical axis is the value of parameters, "●" denotes the location of Cauchy distribution, and "○" denotes the scale of Cauchy distribution.

Totally, 8 parameters were selected. In the ratio of $\omega 1$ (0.5-2Hz) in EEGs, S3 and S4 of deep sleep had lager location values separated from other stages. S3 and S4 were slightly separated from each other among the training subjects of elder persons. The amplitude of $\omega 2$ (2-7Hz) in EEGs, REM and light sleep (S1, S2) showed relatively large location values comparing with others. The ratio of $\omega 3$ (8-13Hz) in EEGs can be the evidence for C(W). EEGs (O1/A2, O2/A1) showed predominant rhythmic alpha activity when the subjects were falling to sleep with the eyes closed. The amplitude of $\omega 4$ (25-35Hz) in EEGs indicated that stage awakes of O(W) and C(W) were separated from other stages. The amount of $\omega 5$ (2-10Hz) in EOGs, S2 showed larger location value comparing with other stages. In the amount of $\omega 6$ (25-100Hz) in EMG, REM had the smaller location value comparing with other sleep stages. In stage REM, EMG voltage was in the lowest level. The combination of those selected parameters was utilized for manipulating the automatic sleep stage determination.

4.3.2 Sleep stage determination

The overnight sleep recordings of another two subjects (Subject B and Subject F) were analyzed, which were different from the training data. The calculation process for one epoch is illustrated in Figure 4.3.

In Figure 4.3, the forepart of sleep recording showed REMs in EOGs. In the latter part of sleep recording, EEGs showed high amplitude. The level of EMG was rather low. According to the conditional probabilities with underline, the first two segments were determined by REM. The middles were stage I and the latter parts were O(W). In this case, the stage result of previous epoch was referred. The last two segments in previous epoch were REM. Then, REM was determined as the result for this epoch. The transition from REM to awake can be estimated. Through the visual inspection, awake occurred after this epoch.

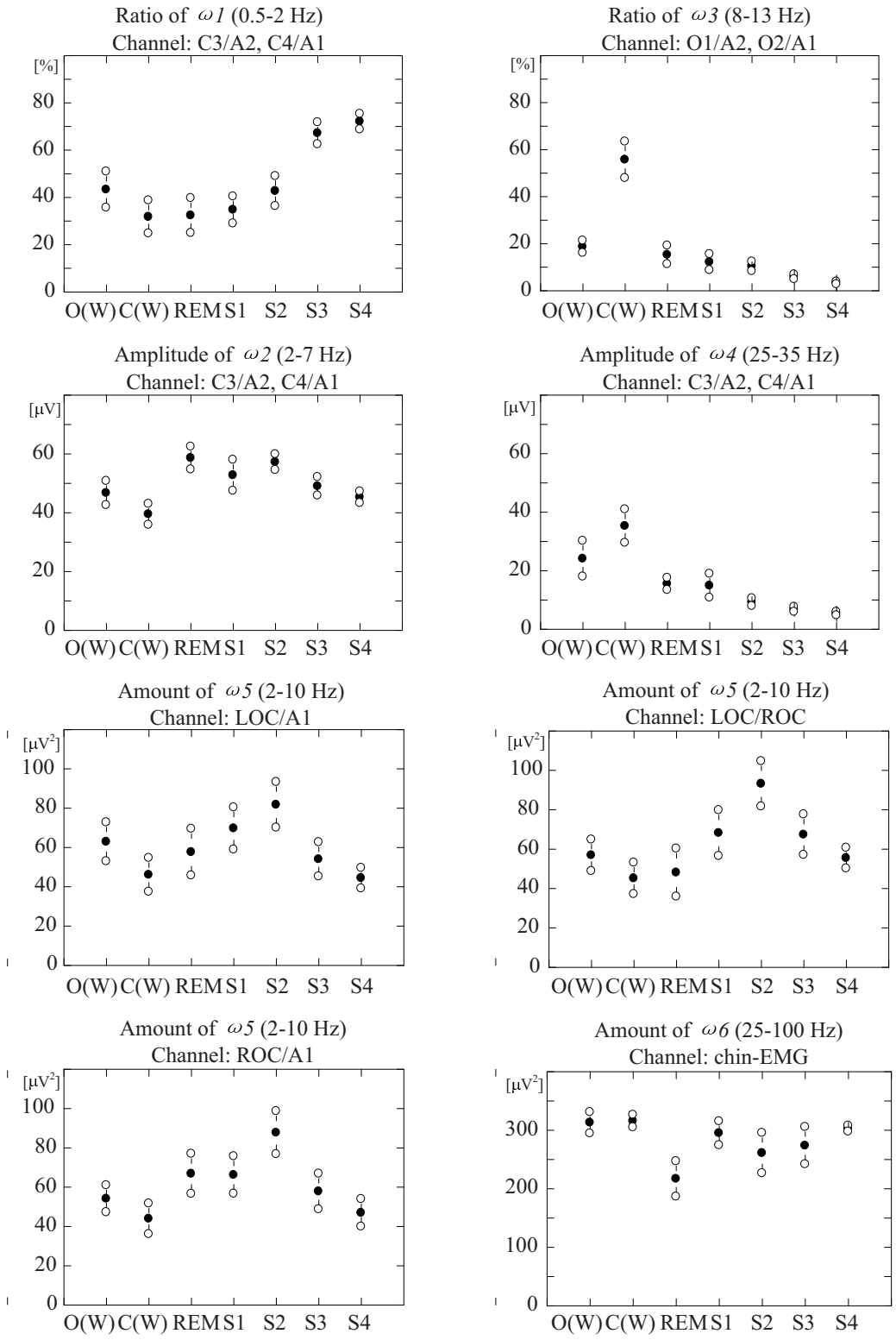
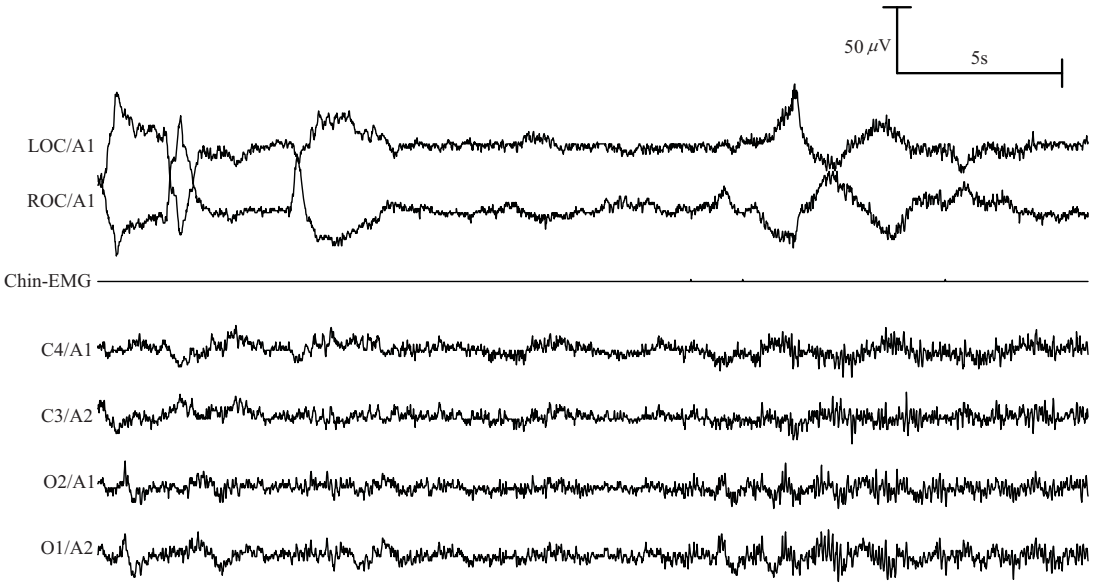


Figure 4.2: Parameter distributions. The x-axis denoted the sleep stages, the closed circles denoted the location parameter and the open circles denoted the scale parameter.



(A) Raw sleep data

	K		K+1		K+2		K+3		K+4		K+5	
Stage	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	3.8e-4	3.8e-6	3.4e-4	8.9e-6	5.8e-4	2.0e-5	9.9e-4	2.9e-5	1.9e-3	**0.48**	0.47	**0.98**
C(W)	0.02	0.04	0.04	0.07	0.07	0.04	0.05	0.16	0.16	0.02	0.02	1.5e-3
REM	0.67	**0.92**	0.92	**0.92**	0.91	0.04	0.04	0.03	0.03	0.06	0.06	1.5e-3
S1	0.28	0.03	0.03	5.7e-3	0.01	**0.91**	0.86	**0.81**	0.77	0.44	0.42	0.01
S2	0.01	6.8e-6	1.4e-3	2.1e-5	3.7e-4	5.8e-7	0.04	1.2e-5	0.03	4.2e-7	0.02	5.3e-8
S3	3.9e-6	7.3e-8	9.3e-8	1.5e-12	6.9e-8	1.5e-12	1.8e-9	6.4e-13	3.8e-8	1.2e-11	1.4e-9	8.3e-16
S4	7.4e-13	8.4e-16	8.7e-10	1.4e-16	1.8e-14	6.8e-21	1.8e-14	9.2e-19	7.7e-15	4.4e-18	1.4e-13	2.6e-18
Result	REM		REM		S1		S1		O(W)		O(W)	
Automatic determination	REM											

(B) Automatic sleep stage determination

Figure 4.3 Calculation process of automatic sleep stage determination for a 30-second epoch. (A) Raw sleep data under PSG measurement including two EOG channels, one EMG channel and four EEG channels. (B) Automatic sleep stage determination based on conditional probability. The line names are sleep stages. The column names are conditional probability and predicted probability for each 5-second segment. Underline is the maximum value of conditional probability. The decision making result is given for each segment. The automatic sleep stage determination for current epoch is showed.

4.3.3 Accuracy evaluation

Automatic sleep stage determination result of two test subjects were evaluated in Table 4.2. The accuracy of stage wake (combined open and close eyes awake), stage REM, light sleep (combined sleep stage I and II) and deep sleep (combined sleep stage III and IV) were given respectively for Subject B and Subjct F.

The discrimination of sleep stage was appreciably satisfied. The average accuracy of two test subjects showed that stage awake was 85.8%, stage REM was 76.2%, light sleep (stage I and stage II) was 80.6% and deep sleep (stage III and stage IV) was 95.7%.

Table 4.2: Evaluations of sleep stage determination for two subjects

	Subject B	Subject F	Average
StageWake	84.3%	87.4%	85.9%
StageREM	73.2%	79.1%	76.2%
Stage I/II	80.7%	80.5%	80.6%
Stage III/IV	93.3%	98.0%	95.7%

4.4 Discussion

4.4.1 Parameter selection

Unlike the rule-based method, our method is expert knowledge-based. The visual inspection by a qualified clinician takes an important role during the learning process of expert knowledge database construction. The clinician made visual inspection not only referring to Rechtschaffen and Kales criteria, but also considering the artifacts and surrounding circumstance in clinical practice. We considered that the visual inspection has covered both Rechtschaffen and Kales criteria and clinical experiences.

The visual inspection by a qualified clinician, thus, can be reliable to construct the knowledge database of probability density functions of parameters and manipulate the automatic sleep stage determination.

Parameter selection was one component included in our learning process of expert knowledge database construction. The principle of parameter selection is to decrease the positive error and negative error of sleep stage determination. In our study, one parameter is not expected to distinguish all the sleep stages from each other. The pdfs of some stages may be overlapped. If the *pdf* of the stage is separated from others, this parameter can be selected. The next parameter would be selected if it can distinguish the stages in the overlapped part of previous parameters. A distance of three times of the deviation, which covers 99% of the *pdf*, is adopted for measurement. The combination of the selected parameters is optimized for manipulating the automatic sleep stage determination algorithm.

4.4.2 Clinical application

The aim of our study is to develop flexible methodology of sleep stage determination which can adapt to the customized requirements in hospitals and institutions. Therefore, sleep data from clinics is worth for investigation and analysis. In this study, the patients were from Toranomon hospital. Toranomon hospital is named for the diagnosing and treatment of Sleep Apnea Syndrome. A qualified clinician F.K. from Toranomon hospital made visual inspection on sleep stages. According to the visual inspection, expert knowledge database was constructed. The result of automatic sleep stage determination showed close agreement comparing with the visual inspection. Our system can satisfy the sleep stage scoring requirement in Toranomon hospital. In addition, our method is flexible to learn from any clinicians. Accordingly, the developed automatic sleep stage determination system can be optimized to meet the requirements in different hospitals and institutions.

The sleep recording data of 2 subjects are utilized for training. During the learning process of expert knowledge database construction, visual inspection by clinician is required. It is not convenient always learning from large amount of data, which will bring heavy burden to clinician. Therefore, we practice on few data for training. The sleep recording data of 7 subjects which were different from training data have been tested. All subjects were patients with Sleep Apnea Syndrome in Toranomon hospital.

Their sleep data was recorded after the treatment of CPAP. 2 of them were inspected by clinician. The results of those 2 subjects were evaluated and analyzed. The results of other tested subjects were also satisfactory. The evaluation of the reliability and effectiveness for clinical practice is important for automatic sleep stage determination technique [101]. Increasing the test data amount with various kinds of patients will be followed in future works.

4.5 Conclusion

An expert knowledge-based method for sleep stage determination was presented. The process of parameter selection enhanced the flexibility of the algorithm for clinical practice. The developed automatic sleep stage determination system can be optimized to different sleep disorder cases by learning few sleep data with visual inspection by qualified clinician.

Chapter 5

Automatic Sleep Stage Determination Integrated with Amendment Function

5.1 Introduction

Human sleep has been described by several stages, REM (rapid eye movement) stage and four non-REM stages of stage I, II, III and IV. Another stage of awake is often included, during which a person falls asleep. The most well-known staging criteria were published by Rechtschaffen and Kales (Rechtschaffen and Kales criteria) in 1968. It defines rules for sleep stage determination by characteristic waveforms and activities in sleep EEGs (electroencephalogram), EOGs (electrooculogram), EMG (electromyelogram) as well.

The computerized sleep stage recognition techniques desired based on Rechtschaffen and Kales criteria can be found in many studies. Although Rechtschaffen and Kales criteria is a worth reference for sleep stage discrimination, this technique seems not be sufficient enough to support the description of sleep process demanded for clinical practice [85]. Rechtschaffen and Kales criteria include rules of typical waveforms from healthy persons [16]. However, sleep stage scoring is used for evaluating the condition of sleep and diagnosing the sleep related disorders in hospitals. The subjects are patients suffered by sleep disorders. Additionally, the typical waveforms shown in Rechtschaffen and Kales criteria are under ideal recording condition. The sleep data under usual recording condition at hospitals are inevitably contaminated by various artifacts [93] [94]. The surrounding circumstances may be variable in different hospitals. Therefore, the conventional rule-based technique designed only according to Rechtschaffen and Kales criteria would have limitation for clinical practice.

An expert knowledge-based methodology has been presented in our previous study in order to overcome the above limitation [87]. Since qualified clinician made visual inspection referring to the staging criteria and considering the surrounding circumstance in the hospital, the visual inspection by qualified clinician was reliable

to deal with the sleep data contaminated with artifacts from real clinics [92]. Moreover, a parameter selection function has been developed to make our algorithm flexible [102] [103]. By learning from few subjects with visual inspection, our automatic sleep stage determination can be optimized for various cases of sleep data. In real clinics, clinician adopts additional rules to smooth the sleep stage scoring result especially for the continuity of stage II and onset/offset of stage REM [104] [105]. The corresponding EEGs, EOGs and EMG may have few or no characteristics of the sleep stages which have been smoothed by the clinician. The automatic determination algorithm would be difficult to detect the sleep change and continuity only according to the characteristics of sleep data.

In this study, a modification process is presented to enhance the performance of our automatic sleep stage determination system on sleep stage changing and continuity. The sleep stage is determined automatically based on the expert knowledge-based method of conditional probability. The modification is manipulated incorporating sleep-related event detection to modify the decision by the expert knowledge-based method. The continuity of stage II and onset/offset of stage REM are detected automatically. The modification algorithm mimics the humanized inspection by clinician.

5.2 Method

5.2.1 Sleep data acquired from hospital

Four subjects were analyzed in this study across the patients having breathing disorders during sleep (Sleep Apnea Syndrome). The subjects were male, aged 49 to 61 years old. Their overnight sleeping data were recorded after the treatment of CPAP (Continuous Positive Airway Pressure) based on the polysomnographic (PSG) measurement from the department of Clinical Physiology, Toranomon Hospital, Tokyo, Japan. The PSG measurement included electroencephalogram (EEG), electromyogram (EMG), electrooculogram (EOG) and other signal types.

The subjects were same with Table 2.1 in Chapter 2. The recording condition have been described in detail in Chapter 2, subsection 2.2.1 Subjects and sleep data.

5.2.2 Visual inspection by clinician

5.2.2.1 Sleep stages

The clinician scored sleep stages according to the knowledge and experience covering the Rechtschaffen and Kales criteria. The overnight sleep recording was divided into consecutive 30s epochs. The clinician made visual inspection through an epoch-by-epoch approach. Totally, seven types of sleep stages were visually inspected, including awake with eyes closed, awake with eyes opened, REM sleep and non-REM sleep of stage I, II, III and IV. Stage awake was classified into open eyes state and close eyes state according to the alpha activity (8-13Hz) on EEGs of O1/A2 and O2/A1 channels and the existence of eye movements on EOGs. Stage I and II were identified as light sleep. Deep sleep of stage III and IV were scored based on a relatively different presence of slow wave activity within an epoch.

The detail explanation of visual inspection work by qualified clinician was in Chapter 2, subsection 2.2.2 Visual inspection.

5.2.2.2 Sleep related events

The related events, investigated in this study, are corresponding to the change and continuity of stages. Here, the continuity of stage II and onset/offset of stage REM were inspected by clinician based on the indicators of sleep EEGs, EOGs and EMG. The principle is summarized as below [106].

- Continuity of stage II
  - Stage II is indicated by K-complex and sleep spindle in sleep EEGs.
  - If the occurrence of K-complex or sleep spindle is less than 3-min to previous occurrence, the interval sleep recordings are smoothed by stage II.

- Detection of stage REM onset and offset
  - The epoch where K-complex or sleep spindle is observed and EMG is as low as stage REM level is judged by stage REM onset.
  - Although REMs can not be observed, stage REM is considered to be continued until EMG level becoming higher.
  - The epoch where EMG level became higher is judged by stage REM offset.

5.2.3 Characteristic parameters

The overnight sleep recording data is divided into 30-second epochs. Each epoch was subdivided into still smaller segments of 5-second. In order to calculate the parameter values, the periodogram was derived by taking 512-point FFT (Fast Fourier Transform) for EEGs and EOGs, whereas 1024-point FFT for EMG. The parameters included, the ratio of EEG components R_{s1} (0.5-2 Hz) and R_{α} (8-13 Hz) in C3/A2, C4/A1 and O1/A2, O2/A1 channels, the amplitude of EEG components A_{s2} (2-7 Hz) and A_h (25-35 Hz) in C3/A2 and C4/A1 channels, the amount of EOG components S_{LR}, S_{LOC} and S_{ROC} (2-10 Hz) in LOC/ROC, LOC/A1 and ROC/A1 channels, the amount of EMG components $S_{chin\text{-}EMG}$ (25- 100 Hz) in chin-EMG channel.

The detail description of parameter definition was in Chapter 2, subsection 2.2.3 Expert Knowledge Database Construction.

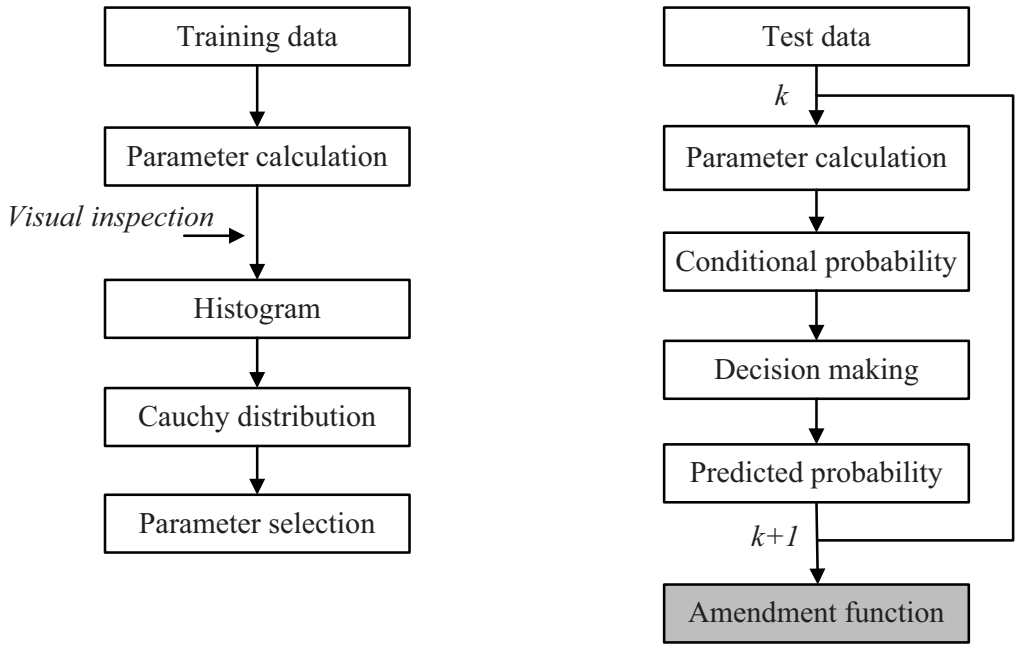
5.2.4 Expert knowledge-based method

The block diagram of multi-valued decision making method is illustrated in Figure 5.1. It consists of two modules. Figure 5.1 (A) is a learning process of expert knowledge database construction. Visual inspection is adopted. Figure 5.1 (B) shows the algorithm of automatic sleep stage determination iterating through the consecutive segments.

During the learning process of Figure 5.1 (A), training data of the overnight sleep recording were divided into consecutive 30s epochs. Each epoch was sub-divided into 5s segments. The extracted characteristic parameters of sleep EEGs, EOGs and EMG were calculated for each segment. According to the visual inspection, each epoch was scored by a single stage. The consisted segments of one epoch were considered having the same scoring result. The *pdf* of parameter of each stage was derived by approximately evaluated using histogram with Cauchy distribution. In addition, the transitional probability between sleep stages was counted and calculated to obtain a probability transition matrix *T*.

During the test process of Figure 5.1 (B), test data of the overnight sleep recording were divided into same length of epochs and segments as the training data. Initially, the predicted probability of first segment for various sleep stages shared the probability equally with a value of *1/n*, where *n* is the number of the types of sleep stages. A joint *pdfs* of parameters for various sleep stages was calculated. The conditional probability of segment *k* was calculated based on the Bayesian rule. The decision making of sleep stage were carried out according to the maximum value of conditional probability, which indicated the most possible stage for current segment based on the parameter values. The predicted probability of next segment *k+1* was calculated based on conditional probability and probability transition matrix. The automatic sleep stage determination was iterated by calculating the conditional probability and predicted probability among the consecutive segments.

The detail explanation of expert knowledge-based automatic sleep stage determination was in Chapter 2, subsection 2.2.2 Expert knowledge database construction and subsection 2.2.3 Automatic sleep stage determination.



(A) Expert knowledge database construction (B) Automatic sleep stage determination

Figure 5.1: Black diagram of processing. (A) Expert knowledge database construction to obtain the probability density function of Cauchy distribution for parameters. (B) Automatic sleep stage determination integrated with amendment function.

5.2.5 Amendment function

In Figure 5.1 (B), an amendment function is developed to modify the decision making result by expert knowledge-based method. The amendment function was to modify the decision making of sleep stage by the expert knowledge-based method. It included the continuity of stage II and onset/offset of stage REM.

The continuity of stage II was measured by a data length of 3-min. If the data length between two decisions of stage II was less than 3-min, the decision of sleep stage during interval sleep recordings were amended to stage II.

The continuity of Stage REM was amended by detecting the onset and offset. Stage REM may start or end with stage awake and stage II. If stage awake or stage II occured before and after the determined stage REM, the onset and offset are detected. The interval sleep recordings between the onset and offset were amended to stage REM.

5.3 Results

5.3.1 Sleep stage determination and stage II amendment

The procedures of sleep stage determination and amendment of stage II are showed in Figure 5.2. Figure 5.2 showed the procedures of sleep stage determination and smoothing of stage II.

In Figure 5.2 (A), K-complex can be observed in the last segment. The other segments showed mixed frequency and low voltage of EEGs. According to the maximum value of conditional probability in Figure 5.2 (B), the calculation process of last segment was illustrated. For the 5-second segment, characteristic parameters were calculated. Based on the expert knowledge database of probability density functions of parameters, joint probability of parameters for each sleep stage was obtained. The joint probability was utilized to calculate the conditional probability. For this segment, the maximum value of conditional probability was corresponded to stage II. In Figure 5.2 (C), the former four segments were judged by stage REM and last two segments were judged by stage II. The decision making results included stage II. The length to the previous stage II was less than 3min. The continuity of stage II was manipulated. The final determination result for this epoch was stage II, same as the visual inspection by clinician.

5.3.2 Sleep stage determination and stage REM amendment

Stage REM was amended between the detected onset and offset. The procedures of sleep stage determination and detection of stage REM onset/offset are shown in Figure 5.3 and Figure 5.4 respectively.

In Figure 5.3 (A), the consisting segments showed mixed frequency and low voltage of EEG. Rapid eye movements were not observed in EOGs. The calculation repeated with conditional probability and predicted probability was showen in Figure 5.3 (B). Based on the conditional probability, the decision making results were stage I in Figure 5.3 (C). The next epoch was stage REM and the previous epoch was stage II. The stage REM onset was detected as in Figure 5.3 (D). Finally, this epoch was scored to stage REM onset in Figure 5.3 (E).

In Figure 5.4, similar situation occurred after the determined stage REM. The decision making results of the consisting segments contained stage I and stage II. The next segment was stage awake. This epoch was scored to stage REM offset. The decision of sleep stages between the onset and offset epochs were amended. The final determination results were consistent with the visual inspection by clinician.

5.3.3 Accuracy evaluation

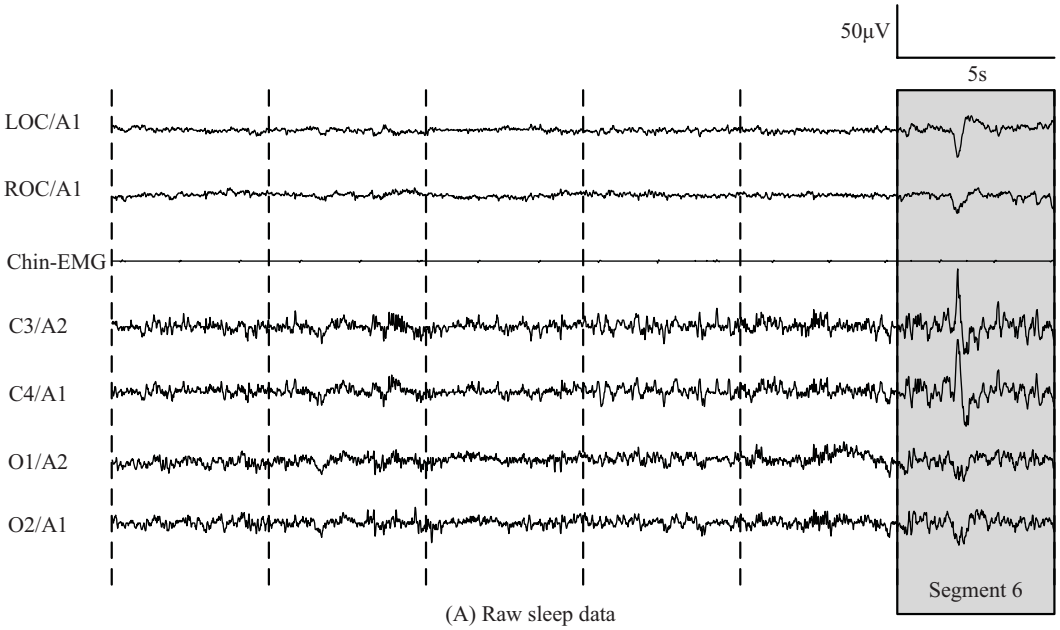
The result of two subjects (Subject B and Subject F), which were different from the training subjects (Subject D and Subject H), had been evaluated. The determination results of subject B and F are showed in Figure 5.5 and Figure 5.6 respectively.

The stage scoring results by visual inspection, automatic sleep stage determination without and with amendment function are illustrated respectively. The horizontal axis is time and vertical axis is sleep stages. The grey cycles showed that the recognition of stage II and stage REM was improved with amendment function. The hypnogram presented well comparing with visual inspection on sleep change and continuity detection.

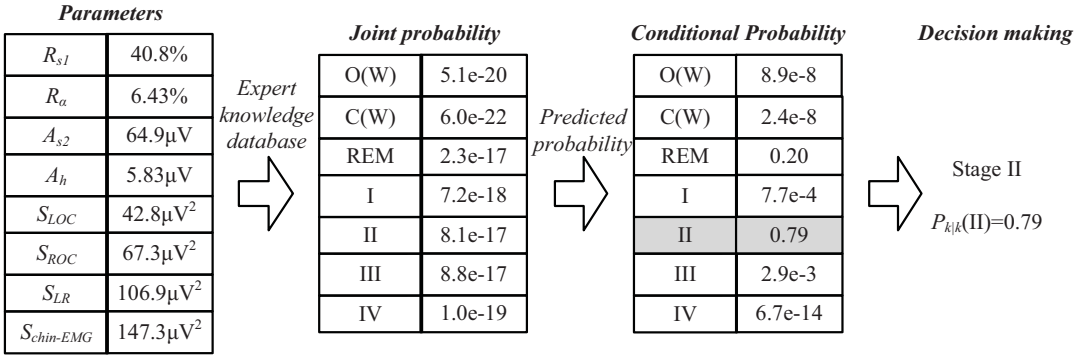
The accuracies of two subjects are shown in Table 5.1 and Table 5.2 respectively. The columns represent the result of automatic determination and the lines represent the visual inspection by clinician. The light sleep of stage I and II were combined as well as deep sleep of stage III and IV. The grey parts showed the agreements on stage awake, REM, light sleep and deep sleep. Those were divided by the total amount of the sleep stages scored by visual inspection to calculate the accuracy.

For subject B, the agreement epochs of stage II was 345 after amendment while 294 before amendment. The agreement epochs of stage REM was 137 after amendment while 123 before amendment. The accuracy of stage awake was 85.2%, stage REM 77.4%, light sleep 88.5%, and deep sleep 93.9%. The total accuracy for this subject was 86.9%.

For subject F, the agreement epochs of stage II was 336 after amendment while 253 before amendment. The agreement epochs of stage REM was 109 after amendment while 87 before amendment. The accuracy of stage awake was 83.7%, stage REM 73.2%, light sleep 87.9%, and deep sleep 83.9%. The total accuracy reached 84.4%.



(A) Raw sleep data



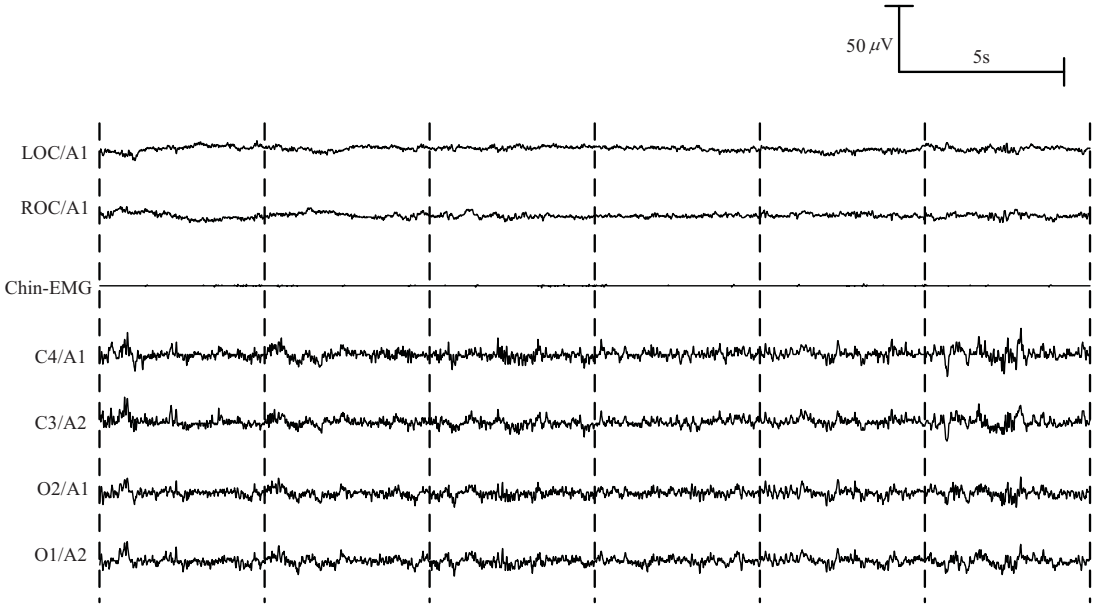
(B) Calculation process for segment 6

Decision making	REM	REM	REM	REM	II	II
Amendment	II	II	II	II	II	II

Automatic determination:	Stage II

(C) Automatic sleep stage determination integrated with amendment function

Figure 5.2: Sleep stage determination and stage II amendment. (A) A 30s epoch of raw sleep data, divided into 5s segments; (B) Calculation process containing parameters, joint probability, conditional probability; (C) Automatic sleep stage determination with amendment of stage II continuity.



(A) Raw sleep data

Stage	K		K+1		K+2		K+3		K+4		K+5	
	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	9.0e-4	1.8e-3	2.8e-3	6.7e-4	1.4e-3	4.2e-5	7.3e-4	1.3e-5	3.1e-4	2.5e-6	3.3e-4	9.8e-3
C(W)	0.01	1.6e-6	0.01	5.2e-7	0.01	3.8e-8	0.01	2.8e-6	0.01	3.3e-9	6.3e-3	6.8e-9
REM	0.03	5.3e-3	7.3e-3	1.2e-3	3.2e-3	2.3e-3	4.3e-3	0.15	0.15	0.14	0.14	0.35
I	0.91	**0.99**	0.93	**0.99**	0.94	**0.99**	0.94	**0.67**	0.63	0.33	0.32	**0.42**
II	0.04	5.3e-5	0.04	2.4e-3	0.04	3.4e-4	0.04	0.17	0.20	**0.52**	0.53	0.22
III	1.4e-7	2.6e-9	1.8e-7	1.9e-10	8.0e-6	6.6e-10	0.1e-6	1.6e-10	5.8e-4	1.3e-8	1.7e-3	7.8e-7
IV	6.2e-13	3.3e-18	3.2e-11	1.1e-17	2.3e-12	1.2e-19	7.9e-12	5.4e-19	1.9e-12	4.5e-21	1.6e-10	6.1e-17

(B) Calculation process

Decision making	I	I	I	I	II	I

(C) Decision making for segments

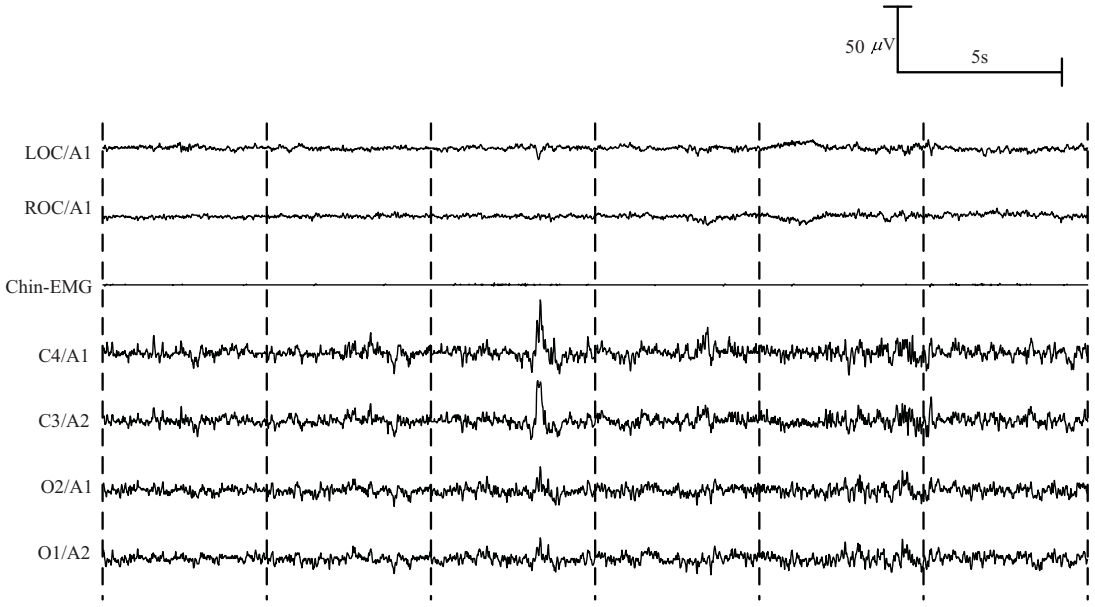
Amendment	REM	REM	REM	REM	REM	REM

(D) Amendment of stage REM

Automatic determination	Stage REM onset

(E) Automatic determination for an epoch

Figure 5.3: Sleep stage determination and stage REM amendment. (A) A 30s epoch of raw sleep data, divided into 5s segments; (B) Calculation process repeated with conditional probability and predicted probability; (C) Decision making result of sleep stage for segments; (D) Detection of stage REM onset; (E) Determination result of sleep stage for an epoch.



(A) Raw sleep data

Stage	K		K+1		K+2		K+3		K+4		K+5	
	$P_{k\|k-1}$	$P_{k\|k}$	$P_{k+1\|k}$	$P_{k+1\|k+1}$	$P_{k+2\|k+1}$	$P_{k+2\|k+2}$	$P_{k+3\|k+2}$	$P_{k+3\|k+3}$	$P_{k+4\|k+3}$	$P_{k+4\|k+4}$	$P_{k+5\|k+4}$	$P_{k+5\|k+5}$
O(W)	6.4e-4	1.4e-6	2.3e-4	1.1e-7	2.7e-4	3.8e-7	1.7e-4	2.6e-5	2.6e-4	4.0e-4	1.1e-3	5.4e-7
C(W)	0.01	8.8e-8	5.5e-3	4.4e-9	4.8e-3	6.9e-10	2.1e-3	2.3e-7	3.6e-3	1.1e-6	0.01	3.0e-8
REM	0.06	**0.48**	0.47	0.11	0.11	3.3e-4	1.2e-3	7.0e-4	1.7e-3	6.8r-4	2.7e-3	8.6e-4
I	0.86	0.27	0.26	0.21	0.21	1.1e-3	8.4e-3	0.12	0.11	**0.98**	0.93	**0.50**
II	0.06	0.24	0.26	**0.67**	0.67	**0.99**	0.98	**0.87**	0.88	0.01	0.05	0.49
III	8.6e-5	1.7e-9	8.1e-4	4.7e-9	2.2e-3	3.0e-5	3.3e-3	5.4e-7	2.9e-3	1.1e-6	4.5e-5	4.4e-9
IV	4.5e-10	2.2e-18	2.1e-11	1.3e-19	5.7e-11	3.3e-17	3.6e-7	3.3e-14	6.5e-9	1.4e-14	1.3e-8	4.7e-16

(B) Calculation process

Decision making	REM	II	II	II	I	I

(C) Decision making for segments

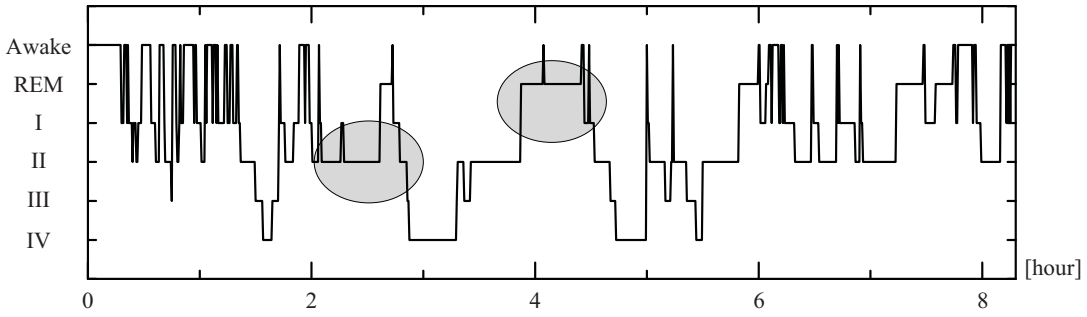
Amendment	REM	REM	REM	REM	REM	REM

(D) Amendment of stage REM

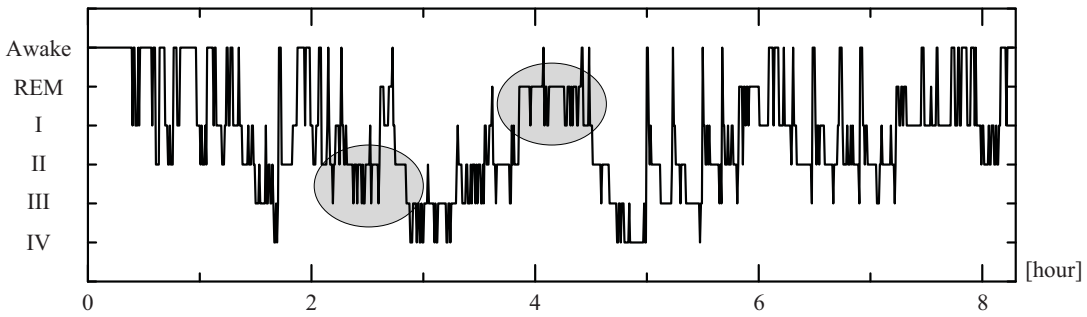
Automatic determination	Stage REM offset

(E) Automatic determination for an epoch

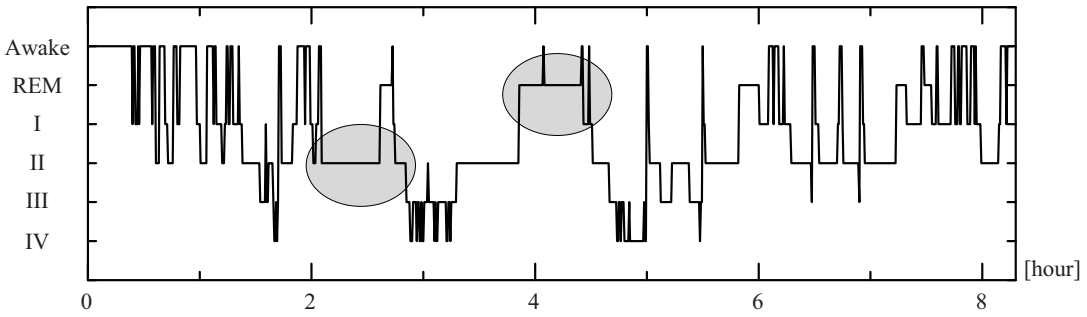
Figure 5.4: Sleep stage determination and stage REM amendment. (A) A 30s epoch of raw sleep data, divided into 5s segments; (B) Calculation process repeated with conditional probability and predicted probability; (C) Decision making result of sleep stage for segments; (D) Detection of stage REM offset; (E) Determination result of sleep stage for an epoch.



(A) Visual inpection

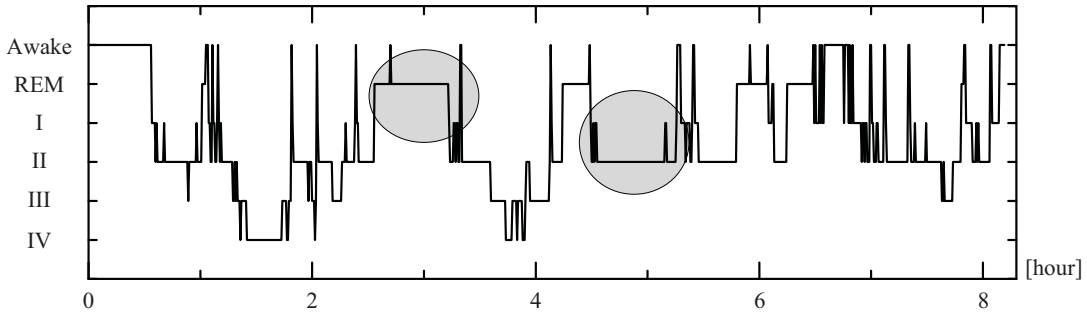


(B) Automatic sleep stage determination without amendment function

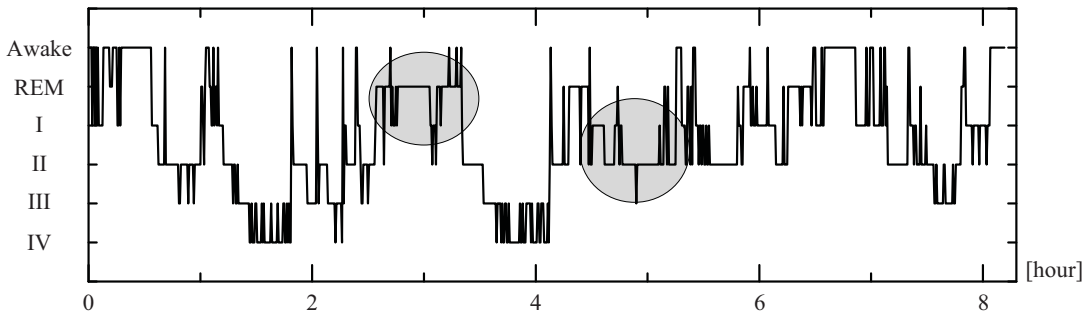


(C) Automatic sleep stage determination integrated with amendment function

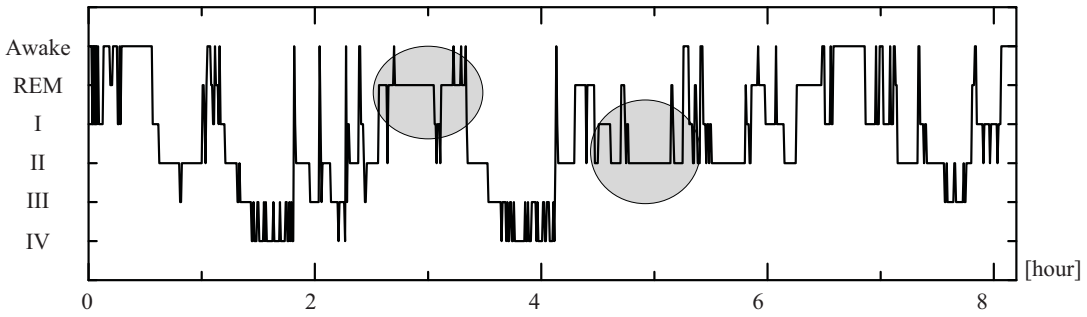
Figure 5.5: The automatic determination result of subject B with and without amendment function compared with visual inspection. (A) Visual inspection by qualified clinician. (B) Automatic determination without amendment. (C) Automatic determination with amendment.



(A) Visual inpection



(B) Automatic sleep stage determination without amendment function



(C) Automatic sleep stage determination integrated with amendment function

Figure 5.6: The automatic determination result of subject F with and without amendment function compared with visual inspection. (A) Visual inspection by qualified clinician. (B) Automatic determination without amendment. (C) Automatic determination with amendment.

Table 5.1: Accuracy evaluation for subject B. Automatic sleep stage determination integrated with amendment function comparing with the visual inspection.

		Automatic determination						
		Awake	REM	I	II	III	IV	Accuracy
Visual Inspection	Awake	**115**	4	13	3	0	0	115/135 (85.2%)
	REM	0	**137**	14	26	0	0	137/177 (77.4%)
	I	24	8	**53**	**16**	0	0	463/523
	II	2	11	**49**	**345**	14	1	(88.5%)
	III	0	0	0	9	**53**	**33**	139/148
	IV	0	0	0	0	**16**	**37**	(93.9%)
Total accuracy: 854/ 983 = 86.9%								

Table 5.2: Accuracy evaluation for subject F. Automatic sleep stage determination integrated with amendment function comparing with the visual inspection.

		Automatic determination						
		Awake	REM	I	II	III	IV	Accuracy
Visual Inspection	Awake	**139**	2	20	4	1	0	139/166 (83.7%)
	REM	6	**109**	34	0	0	0	109/149 (73.2%)
	I	45	7	**72**	**36**	0	0	465/529
	II	1	2	**21**	**336**	9	0	(87.9%)
	III	0	0	0	18	**27**	**3**	125/149
	IV	0	0	1	5	**55**	**40**	(83.9%)
Total accuracy: 838/993 = 84.4%								

5.4 Discussion

5.4.1 Stage amendment

We engaged in the expert knowledge-based method for automatic sleep stage determination which can be effective for clinical practice. At the hospital, the clinician made visual inspection on stage II and stage REM with additional rules, not only based on the characteristics of sleep EEGs, EOGS and EMG [107] [108]. In 2001, supplements and amendments to the staging criteria of R&K were published by Japanese Society of Sleep Research, in which the additional rules for stage II and stage REM was summarized [106]. Those rules were widely utilized in hospitals. We developed the expert knowledge-based method with amendment function to mimic the visual inspection work on sleep stage scoring in clinics.

We developed our automatic sleep stage determination method integrated with amendment function to modify the decision by the knowledge-based method. In the results of Figure 5.2, 5.3 and 5.4, the decision making results showed the most possible stage according to the characteristics of the sleep data in every 5s segment. Stage was changed sensitively. If we count the stage which occupied major portion within the 30s epoch, the determination result for Figure 5.2 would be stage REM, for Figure 5.3 stage I and for Figure 5.4 stage II. After the detection of continuity of stage II and onset/offset of stage REM, decision making results were modified. Finally, consistent results with the visual inspection can be obtained. With a modification process, the recognition accuracy of stage II and stage REM were improved satisfactory.

5.4.2 Clinical application

Since our algorithm mimicked the visual inspection by clinician, our system can be applicable for clinical practice. The cyclic pattern of stage change and continuity is one of the purposes of sleep stage scoring. Clinician would measure the effect of the treatment and make further inspection for the patients by referring to the computerized sleep stage determination result on the sleep cyclic rhythm of stage change and continuity. The developed amendment function enhanced the performance of expert knowledge-based method on stage change and continuity detection.

5.5 Conclusion

We developed an automatic sleep stage determination system with the abilities of sleep related events detection. Our system can mimic the inspection work by clinicians and establish a reliable and objective evaluation technique on sleep recording. The performance of expert knowledge-based automatic sleep stage determination was improved on the sleep stage continuity and change detection with the amendment function.

Chapter 6

Conclusions and Future Study

6.1 Conclusions

Sleep stage scoring has been widely used for evaluating the condition of sleep or diagnosing the sleep related disorders in the sleep laboratories and hospitals. Computerized sleep stage scoring is proposed to manage the large amount of data, an overnight sleep generates, as well as to minimize the amount of time required to score and analyze sleep stages.

The ultimate objective of this work is to develop an effective and reliable automatic sleep stage technique for clinical practice. Since rule-based method according to Rechtschaffen and Kales criteria had limitation in real clinics, expert knowledge-based method can be new to be applied in clinics.

In **Chapter 2**, an expert knowledge-based method has been introduced. The expert knowledge is the visual inspection by a qualified clinician. The clinician made visual inspection not only based on Rechtschaffen and Kales criteria, but also considering the circumstance in the hospital. The automatic sleep stage determination based on visual inspection can have the same reliable result of sleep stage scoring on the actual sleep data.

In **Chapter 3**, Cauchy distribution is adopted to estimate the probability density function of parameter on the histogram. The affect of artifacts can be abated by using Cauchy distribution comparing with Gaussian distribution.

In **Chapter 4**, a parameter selection process is introduced during the learning process of expert knowledge database construction. For various cases of sleep data, optimal parameters can be selected automatically. The performance of automatic sleep stage determination can be adaptive with the optimal parameters.

In **Chapter 5**, an amendment function is added after the determination of sleep stages by knowledge-based method. The continuity of stage II can be traced. The onset/offset of stag REM can be detected. With the amendment function, the performance of automatic sleep stage determination can be improved.

As a conclusion, the developed automatic sleep stage determination in this thesis can be an assistant tool for clinical practice enabling a further inspection by clinician. The clinician can be free from the heavy task of visual inspection. The performance of our system is adaptive to meet the different requirement in hospitals and institutions.

6.2 Research Contributions

Current research work makes the following major contributions:

1. The expert knowledge-based automatic sleep stage determination can overcome the limitation by the conventional rule-based methods. The visual inspection by a qualified clinician is the reliable sleep stage scoring result for real clinics at the hospital. The obtained parameter distributions for sleep stage, which is learning from the visual inspection and actual sleep data, can reflect the actual distribution of parametric variable. The distributions are reliable to manipulate the automatic sleep stage determination algorithm on the actual sleep data from the hospital.

2. The mathematical model of Cauchy distribution on the histogram can abate the affect of artifacts to our automatic sleep stage determination technique. Cauchy distribution has ratio decreasing tail whereas Gaussian distribution has exponentially decreasing tail. The heavier tails allow the affect of mis-determination to be minimized in conditional probability during the transition between data segments.

3. Amendment process is presented which mimic the visual inspection by qualified clinician. With the amendment function, the sleep stage recognition result was improved. The accuracy of agreement on stage II and stage REM was increased remarkable. The final result showed close agreement with the visual inspection by clinician.

4. Parameter selection process is presented as a component in the learning process of expert knowledge database construction. For variable cases of sleep data, optimal parameters can be selected automatically. The result of automatic sleep stage determination can meet the customized requirement in different hospitals.

5. The developed automatic sleep stage determination in this thesis has strong performance for clinical practice. By learning from different clinicians, our system is flexible to be utilized in real clinics.

6.3 Future Study

Current research works are focused on the methodology developments. The future research works will consider the clinical application in the hospital. To be close to our ultimate purpose, our automatic sleep stage determination system needs to be applied in real clinics at the hospital. Such application can evaluate the reliability of our system. During the application, the methodology can be developed to solve the actual problems encountered. The future research plan is as below.

1. **Realization of automatic algorithm for sleep stage determination by using expert knowledge-based method.**

The current automatic sleep stage determination algorithm will be modified to adapt to the real-time automatic determination. In order to realize the real-time determination, automatic feedback algorithm needs to be considered especially for the amendment function, and automatic expert database construction needs to be developed for real requirements in hospital.

2. **Expert knowledge-based method of automatic sleep stage determination for different sleep-related diseases.**

The current automatic sleep stage determination algorithm was tested for the patients with Sleep Apnea Syndrome after CPAP treatment. In future, more sleep data from the patients with different sleep-related diseases will be analyzed and tested to develop the expert knowledge-based method. Other sleep signals besides EEGs, EOGs and EMG will also be considered according to the requirements in hospital.

3. Evaluation of the reliability and effectiveness of expert knowledge-based automatic sleep stage determination system for clinical practice.

The reliability and effectiveness is important to evaluate the automatic determination technique for clinical practice. With the permission of hospital, we may compare the results by using our method and by using the commercial system in the hospital. Based on the comparison, the performance of the current method can be evaluated. Furthermore, the current method can be developed by considering the comparison with other methods to be a usable technique for clinical practice.

4. Sleep engineering related works.

The sleep problem seems popular in the modern society. Especially, the persons, whose work condition requires much concentration, are easy to feel tense, tiredness, pressure if they did not have enough sleep or rest. In future, experimental works for healthy persons will be carried out. The evaluation of healthy person's sleep can be an interesting topic for human daily life and work.

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Publications

A. Journal paper

[1] Bei Wang, Xingyu Wang, Junzhong Zou, Fusae Kawana and Masatoshi Nakamura: "Automatic determination of sleep stage through bio-neurological signals contaminated with artifacts by a conditional probability of the knowledge base", *Artificial Life and Robotics*, 2008, Vol. 12, pp. 270–275.

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[3] Bei Wang, Takenao Sugi, Fusae Kawana, Xingyu Wang and Masatoshi Nakamura: "Expert knowledge-based automatic sleep stage determination by multi-valued decision making method", *IEEJ transactions on Electronics, Information and Systems*, Vol. 129, No. 4, Sec. C. (accepted)

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B. Proceedings of international conferences

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[2] Bei Wang, Takenao Sugi, Fusae Kawana, Xingyu Wang and Masatoshi Nakamura: "Multi-valued decision making of sleep stages determination based on expert knowledge", *Proceedings of SICE Annual Conference 2008*, Chofu, Japan, August 20-22, 2008, 3194-3197.

[3] Bei Wang, Takenao Sugi, Fusae Kawana, Xingyu Wang and Masatoshi Nakamura: "Conditional probability of Cauchy distribution in automatic sleep stage determination for sleep data with artifacts", *Proceeding of International Conference on Control, Automation and Systems*, Seoul, Korea, October 14-17, 2008, 530-533.

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C. Proceedings of domestic conferences

[1] Masatoshi Nakamura, Bei Wang, Takenao Sugi, Fusae Kawana and Xingyu Wang: "Automatic sleep stage determination by multi-valued decision making method based on expert knowledge", *Proceeding of the 33rd Annual Meeting of Japanese Society of Sleep Research*, Fukujima, Japan, June 25-26, 2008.

[2] Masatoshi Nakamura, Bei Wang, Takenao Sugi, Fusae Kawana and Xingyu Wang: "Automatic Sleep stage determination system with sleep-related events detection ability by multi-valued decision making method", *Proceeding of the 38th meeting of Japan society of clinical neurophysiology*, Kobe, Japan, November 12-14, 2008.

Index of publications corresponding to the chapters

Chapters	Journal	Conference
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Chapter 3 Automatic Sleep Stage Determination by Conditional Probability of Cauchy Distribution	A[1], A[5]	B[1], B[3]
Chapter 4 Automatic Sleep Stage Determination with Automatic Parameter Selection	A[2]	B[4]
Chapter 5 Automatic Sleep Stage Determination Integrated with Amendments	A[4]	C[2]