A Machine Learning Framework for Space Medicine Predictive Diagnostics with Physiological Signals

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***Abstract*— Prognostics and health management (PHM) in the context of space missions focuses on the fundamental issues of system failures in an attempt to predict when the failures may occur, and links these issues to system life cycle management. Space missions that are targeting for aerospace exploration or aviation also pose great challenges on the health conditions of people involved, such like astronauts, crew members, aviators, etc. Considering the inherent risks of space missions and the difficulty of direct communications between crew and ground support medical specialists, we see that greater autonomy in medical operations for crew is required. Namely, there is an urgent call for an effective onboard medical system to predict and prevent health problems in a timely manner, rather than following reactive approaches which are inherent to conventional medicine.**

Interdisciplinary research is underway to develop computer-based, self-diagnosis and self-directed treatment programs for the crew to autonomously predict, prevent, and manage potential health problems of two types: physiological and psychological. Predictive diagnostics aims at identifying negative health trends with concerned premonitory symptoms followed by predicting the future health condition and raising alarms in case of emergency. These alarms will startup devices that are capable of quickly reacting to an acute disease by delivering therapy or notifying a caregiver, thus avoiding fatal consequences likely to occur. Acute diseases such as cardiovascular and epileptic seizures are found to be frequently incident in-flight medical events, where the aftermath of seizures such as dyspnoea or serious physical injuries usually does the most harm to the subject. Consequently, a predictive diagnostics system that is able to provide early and actionable real-time warnings of impending health problems would play an extremely crucial role in aerospace medicine. In this process, the diagnostic determination is based on the differences between current health status and the predefined normal status. Besides, considering the underlying concepts in predictive diagnostics of aerospace medicine in which every crew member is unique, the development of a processing strategy specially designed for each individual on a subject-by-subject basis is not only necessary but also feasible. The highly autonomous predictive diagnostics system in aerospace medicine would then be able to perform real-time health assessment followed by a comparison of inspection results with a crew member's health baseline, where the health baseline refers to a normal health state in which the crew member is identified as a physically and mentally healthy person to meet in-flight specific requirements.

On the Information Technology side, machine learning techniques have made tremendous progress recently in medical diagnosis and health data analytics. We consequently initiate an effort on bringing machine learning based disease prediction technology as predictive diagnostics applications in the context of aerospace medicine. In space missions the physiological and psychological health conditions of crew are subject to continuous monitoring, in which electroencephalogram (EEG), electromyogram (EMG) and electrocardiogram (ECG) signals can be critical. EEG is broadly used to study the nervous system, monitoring of sleep stages, biofeedback and control, and diagnosis of epilepsy. Considering EEG has long been employed in crew selection and training, and recently been widely recognized as an effective means for disease diagnosis and prediction, in this paper we mainly focus on EEG in our investigation for aerospace medicine.

After introduction of EEG and its applications in predictive diagnostics, we explore and extract amplitude-frequency patterns in EEG to provide distinctive features as health indicators. To further achieve predictive diagnostics for aerospace medicine, we propose a machine learning based framework involving physiological signals for automatic health monitoring and disease prediction. This framework incorporates feature extraction as front end, and employs state-of-the-art data mining and classification mechanism to proactively distinguish between normal and abnormal health conditions in real time. Automatic disease prediction for crew members can therefore be timely provided for proper actions. To illustrate the effectiveness of our proposed paradigm, we employ epileptic seizure prediction as a case study. It is shown through experiments that the proposed predictive diagnostic system leads to promising prediction results. As an application of the disease prediction framework on physiological sources other than EEG, we have further discussed its employment on measuring and diagnosing disrupted neuromuscular characteristics and muscle fatigue for astronauts and aviators with EMG signals. We expect the framework described in this paper will result in a positive impact on enhancing the medical operation autonomy in aerospace medicine.

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1. INTRODUCTION TO ELECTROENCEPHALOGRAM

Aerospace medicine, also known as aviation medicine or flight medicine, is a preventive or occupational medicine in which the patients or subjects are pilots, aircrews, or persons involved in spaceflight. This field of expertise focuses on treating or preventing conditions to which aircrews are particularly vulnerable physically or mentally. Such capability is a critical component of aviation safety, as it applies medical knowledge to the human factors for risk reduction in aviation and aerospace [1].

In aerospace medicine, cardiovascular diseases are a major health problem worldwide and a leading cause of mortality and morbidity in industrialized nations, making them a major concern for aeromedical disposition and aircrew standards. Besides cardiac diagnosis, aerospace medicine specialists are typically required to relate the neurologic condition to aviation safety and to accomplish an appropriate aeromedical disposition. Traumatic brain injury (TBI), a common cause of neurologic disability among people between 20 and 55 years of age, is frequently encountered in avionics and aerospace. The evaluator in aerospace medicine is not as much concerned with acute management as with the possibility of persistent residual neurologic impairment. A major aeromedical worry following TBI is the risk of seizures. A seizure is an abnormal, paroxysmal excessive discharge of cerebral neurons. Epilepsy, a major aeromedical issue which we will investigate in detail in this paper, is a chronic condition characterized by a tendency for recurrent (two or more), unprovoked seizures. Not all seizures signify epilepsy, though. It is noted that all persons have a constitutional or genetically determined threshold for seizures, which when exceeded, leads to a clinical event. This threshold is not only individual-dependent, but also affected by hormonal influences, sleep deprivation, and other factors. It also fluctuates with time of day [1]. Fatigue is another omnipresent risk in all modes of transportation, particulary in aviation. In avionics and aerospace environments, cognitive performance degrades with sleep loss, often referred to as a fatigue effect [2]. Pilot fatigue associated with jet lag is a major concern in aviation, especially with travel across multiple time zones. Involved flight crews often experience disrupted circadian rhythms and sleep loss. Studies have reported episodes of fatigue and the occurrence of uncontrolled sleep periods (microsleeps) in pilots [3]. When flight crewmembers remain at their destination only for a short period, they would not have the opportunity to adjust physiologically to the new time zone or altered work schedule before getting on another assignment; therefore, their risk for fatigue drastically increases. Similarly, astronauts can also experience performance decrements and fatigue in space, which may lead to considerable risk no matter how well they are trained [4].

To address the above issues in aerospace medicine, the electroencephalogram (EEG) signal comes as a handy technique for rescue. EEG is a medical test used to measure the electrical activity of the human's brain. EEG can help diagnose a number of conditions, including epilepsy, sleep disorders and brain tumours. The EEG is typically described in terms of rhythmic activity and transients [5]. The rhythmic activity is further divided into bands by frequency as shown in Figure 1. During past decades, EEG has been engaged as part of the medical screening of candidates for aircrew training [6], [7]. Furthermore, studies on military personnel have gained insight on the role of interictal EEG in the diagnosis of epilepsy [8].

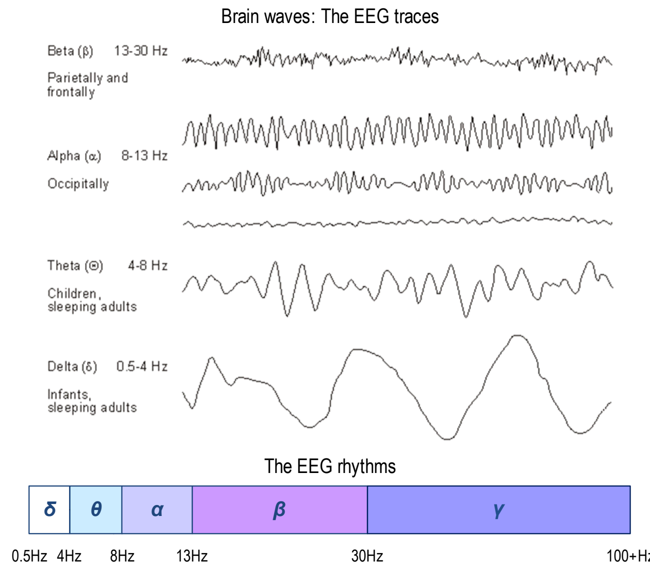

Figure 1. Typical rhythmic activities in an EEG signal.

Standard EEG instrumentation settings used are lowpass filtering at 75 Hz, and paper recording at 100 $\mu V/cm$ and 30 mm/s for 10-20 minutes over 8-16 simultaneous channels. On the other hand, monitoring of sleep EEG and detection of transients related to epileptic seizures may call for multichannel EEG acquisition over several hours. Special EEG techniques include the use of needle electrodes, the use of naso-pharyngeal electrodes, the recording of intracranial EEG from an exposed part of the cortex, and the use of intracerebral electrodes. Evocative techniques for recording EEG include initial recording at rest (eyes open vs. eyes closed), hyperventilation (after breathing at 20 respirations per minute for 2-4 minutes), photic stimulation (with 1-50 flashes of light per second), auditory stimulation with loud clicks, sleep (of different stages), and pharmaceuticals or drugs [5].

As an example, Figure 1 shows the traces of EEG signals together with the rhythms. EEG rhythms are associated with various physiological and mental processes. The alpha rhythm is the principal resting rhythm of the brain, which is common in wakeful, resting adults, especially in the occipital area with bilateral synchrony. The alpha wave is replaced by slower rhythms at various stages of sleep. Theta waves appear at the beginning stages of sleep, while delta waves appear at deep-sleep stages. High-frequency beta waves appear as background activity in tense and anxious subjects. The depression or absence of the normal (expected) rhythm in a certain state of the subject could indicate abnormality. The presence of delta or theta (slow) waves in a wakeful adult would be considered to be abnormal. Focal brain injury and tumors may lead to abnormal slow waves in the corresponding regions. Unilateral depression (left-right asymmetry) of a rhythm could indicate disturbances in cortical pathways. Spikes and sharp waves could indicate the presence of epileptogenic regions in the corresponding parts of the brain. There are a few events and transients that might occur in EEG signals, which are summarized in Table 1 [5].

EEG is broadly employed in the study of the nervous system, disease diagnosis and detection, as well as sleep monitoring, which are critical to the health conditions of crew or astro-

Table 1. Main events and transients existing in EEG signals.

EEG events	Distinctive characteristics
K-complex	Transient complex waveform with slow waves
	Occurring spontaneously or in response to a stimulus during sleep
Lambda (λ) waves	Monophasic, positive, sharp waves associated with visual exploration
	Occurring in the occipital location
Mu (μ) rhythm	Rhythm with an arcade or comb shape in the central location
	Occurring as a group of waves in the frequency range of 7-11 Hz
Spike	Transient with a pointed peak
	Occurring with a duration in the range of 20-30 ms
Sharp wave	Transient with a pointed peak
	Occurring with a duration in the range of 70-200 ms
Spike-and-wave rhythm	Rhythm
	Occurring as sequence composed of surface-negative slow waves and associated spikes
Sleep spindle	Episodic rhythm
	Occurring maximally over the fronto-central regions during certain stages of sleep
Vertex sharp transient or V-wave	Sharp potential that is maximal at the vertex and is negative in other areas
	Occurring spontaneously during sleep or in response to a sensory stimulus during sleep or wakefulness

nauts. In aerospace medicine, EEG has been considered as an essential metric to assess the health conditions of people involved in space missions. With in-flight medical operation autonomy being emphasized nowadays, a self-diagnosis system which can automatically diagnose and manage the potential medical emergencies is urgently required for flight safety's sake. The application of EEG data in predictive diagnostics under an autonomous, proactive, and real-time scenario consequently attracts greater interests, and expects to play a more and more significant role for the advancement of aerospace medicine.

2. Applications of EEG in Predictive Diagnostics

Mission design for future human exploration spaceflight (including the moon, asteroids, and Mars), with their inherent risks and communications delays, requires a shift in aerospace medicine from a telemedicine paradigm to that of medical autonomy. As interactive medical ground support may be not accessable in a space mission, an automatic clinical decision-making process for crew health monitoring and diagnostics may be required to assist the onboard Crew Medical Officer (CMO), if such a dedicated personnel is available. Predictive diagnostics, consequently, is a specific data analysis methodology supported with a toolset including a set of algorithms and computing capabilities, such as data mining, machine learning, pattern recognition, and other advanced computing techniques. Predictive diagnostics provides early and actionable real-time warnings of impending health problems that would have otherwise gone undetected. Based upon the differences between real-time health status and predefined normal status, predictive diagnostics detect and isolate abnormal circumstances and negative trends, in the context of flight operating conditions of the crew members. An underlying thesis in predictive diagnostics in aerospace medicine is that every crew member is unique. As a result, it requires the development of a distinctive data set for each individual. This personalized data set should covers at least the following areas: medical history, genetic predisposition, recent medical events, baseline health assessments, etc. Vital signs in terms of operational and emotional contexts (e.g. extra-vehicular activity, melancholy), should also be included. In aerospace medicine the system would further be required to perform real-time health assessment followed by a systematic comparison of assessment results with a crew members health baseline, a health pattern corresponding to a ”normal” health state in which the crew member is identified as a physically and mentally healthy person who can meet in-flight specific requirements. Predictive diagnostics could then recognize potential alarming incidents and provide notifications of developing problems to the CMO [9].

In [10], Sirven *et al.* made a great effort to analyze the frequency of neurologic events during commercial airline flights and to assess whether onboard emergency medical kits are adequate for in-flight neurologic emergencies. By reviewing the Mayo In-flight Advisory Report which contains a record of all in-flight events from 1995 to 2000 for a US airline, the authors found that neurologic symptoms are the most common medical complaint requiring air-to-ground medical support, even surpassing cardiovascular and gastrointestinal symptoms. Among the incidence of neurologic symptoms, seizures are considered to be the most frequently encountered events, second only to dizziness. They therefore suggested adding anti-epileptic drugs to the onboard medical kit and providing greater emergency medical training for in-flight personnel so as to potentially reduce the number of distractions for in-flight neurologic incidents.

In fact, epilepsy is one of the most common neurological disorders worldwide, second only to stroke. Around 1% of the world's population is affected by various types of epilepsy. Two thirds of patients, nevertheless, can achieve sufficient seizure control with the help of anti-convulsive medication, and another 8-10% people could get benefit from resective surgery. However, for the remaining 25% of patients, no adequate treatment is currently available [11]. There are several major phases of seizures. As defined by the epilepsy foundation of America [12], preictal is a period of time before the seizure onset occurs, which can last from minutes to days. Ictal is the period during which the seizure takes place. Postictal is the period after the seizure ends, which can sometimes take several hours. Interictal is the time between seizures. In Figure 2, the preictal-postictal stage transition for

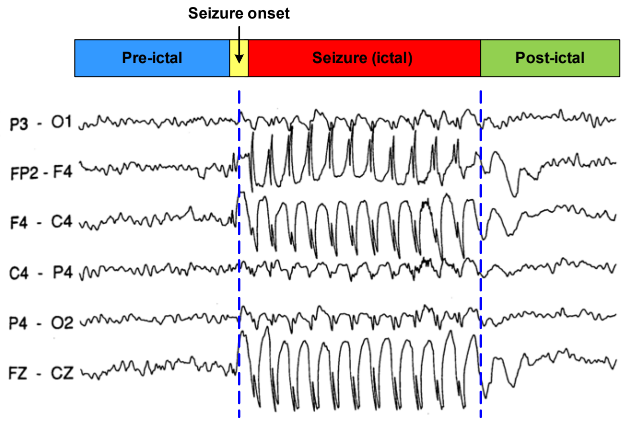

Figure 2. EEG preictal-postictal transition.

an example seizure cycle is illustrated, where the note on the left, e.g, "P3-O1" indicates the channel to which the signal belongs. Recent clinical studies have found premonitory symptoms for seizures from a certain portion of patients with epilepsy [13], [14]. There are also evidences showing that the interictal-ictal transition is not abrupt. During this period of time, the person with epilepsy manifests changes in medical measurements such as cardiovascular, metabolic, and EEG recordings [15]. These changes will help a neurologist to predict an upcoming seizure.

The most common way for epilepsy diagnosis is through analysis of EEG, which has therefore been widely employed in epilepsy diagnosis as well as prediction [11], [16], [17], [18]. Epileptic seizure onset detection algorithms aim to raise alarms as soon as a seizure occurs on a patient from examining his/her EEG data [17]. These alarms will startup devices that are capable of quickly reacting to a seizure by delivering therapy or notifying a caregiver, thus alleviating fatal consequences of seizures. An even more important issue in the context of predictive diagnostics under aerospace environment is the challenge of predicting epileptic seizures, which is approached by searching for distinctive changes in the EEG before seizure onsets. An epileptic seizure prediction algorithm should be able to forecast an upcoming seizure prior to seizure onset by raising an alarm. The time interval after an alarm within which a seizure is expected to take place is called Seizure Prediction Horizon (SPH) in the context of seizure prediction characteristic. SPH ranges from several minutes to a few hours [19]. If a seizure occurs within the SPH, the alarm is regarded as a correct prediction; otherwise, it is counted as a false alarm. Due to its high interest in aerospace medicine, epileptic seizure prediction issue will be explored as a case study later in the paper.

EEG rhythms associated with various physiological and mental processes produce high dimensional feature data which are used to be hard for computers to handle. During the past years, fortunately, sophisticated machine learning tools have been developed to alleviate the computational burden caused by feature classification in a very high dimensional data space. Current seizure prediction approaches mostly adopt a two-step strategy: extracting measurements from EEG signals along the time line, and then determining their categories to be either preictal or interictal within a binary classification framework. The machine learning based approaches have been employed in state-of-the-art seizure prediction and detection algorithms [17], [20]. The reduced requirements on computational resources and the subject-specific strategy taken in the machine learning based seizure prediction methods make them applicable components in the aeromedical predictive diagnostics framework.

3. Amplitude and Frequency Properties in EEG

In this section we first observe the primary amplitude-frequency modulation components in an EEG signal, and then introduce the feature extraction process that we will use in our proposed framework.

Amplitude-frequency modulation signal representation

A narrow-band signal, whose bandwidth is sufficiently small, can be viewed as a monocomponent amplitude and frequency modulating (AM-FM) signal. Among the frequencies spanning over the signal spectrum, there is one frequency bin assuming a majority of the signal energy. The two determining parameters in an AM-FM signal are *amplitude* and *phase*. A *monocomponent* AM-FM signal is described by Equation (1) [21],

$$x(n) = A(n)cos\big[\Theta(n)\big], \tag{1}$$

where $A(n)$ denotes the instantaneous amplitude of the monocomponent signal and $\Theta(n)$ denotes its instantaneous phase.

The kth EEG rhythm $s_k(n)$ as shown in Figure 1 could be formulated as an AM-FM term by Equation (2):

$$s_k(n) = A_k(n)cos\big[\Theta_k(n)\big], \tag{2}$$

with the EEG rhythm being characterized by two sequences:

- $A_k(n)$ – Amplitude of rhythm;
- $\Theta_k(n)$ – Phase of rhythm.

Teagers proposed to employ a *multicomponent* AM-FM model in exploring amplitude-frequency modulation patterns in speech resonances [22]. Likewise, considering the multiple characteristic bands of EEG, we can also interpret it as a multicomponent AM-FM signal. An EEG signal can thus be written as a linear combination of amplitude and frequency modulated components which we call the primary components,

$$\begin{aligned} s(n) &= \sum_{k=1}^{K} A_k(n)cos[\Theta_k(n)] + \eta(n) \qquad (3)\\ &= \sum_{k=1}^{K} A_k(n)cos\Big\{\Big[\Omega_c(k)n + \sum_{r=1}^{n} q_k(r)\Big]\Big\} + \eta(n), \end{aligned}$$

where $A_k(n)$ denotes the instantaneous amplitude of the kth primary component and $\Theta_k(n)$ denotes its instantaneous phase. With the backward difference between $\Theta_k(n)$ and $\Theta_k(n-1)$, the instantaneous frequency sequence is defined as $\Omega_k(n) = \Omega_c(k) + q_k(n) = \frac{2\pi}{f_s} f_c(k) + q_k(n)$, where f_s is the sampling frequency, $q_k(n)$ is the frequency modulation component. Note $\eta(n)$ takes into account additive noise and errors of modeling, especially those errors due to finite summation. The dominant rhythms in an EEG signal are therefore captured by the primary AM-FM components in the corresponding frequency bands. Depending on applications, the number of primary components required for processing may vary. For the epileptic seizure prediction purpose in

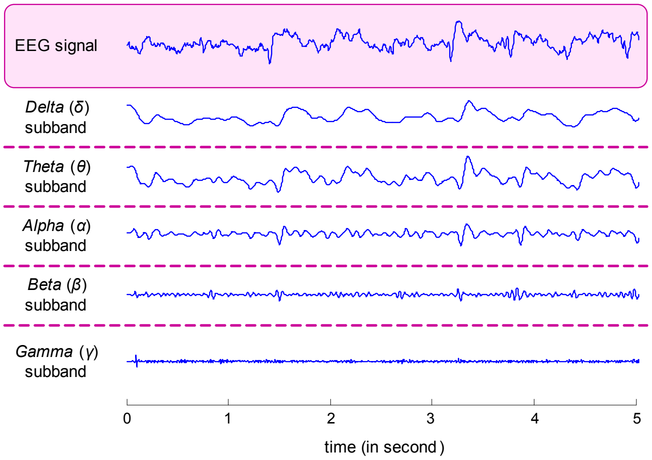

Figure 3. Detection of the present rhythms in a 5-second long EEG epoch.

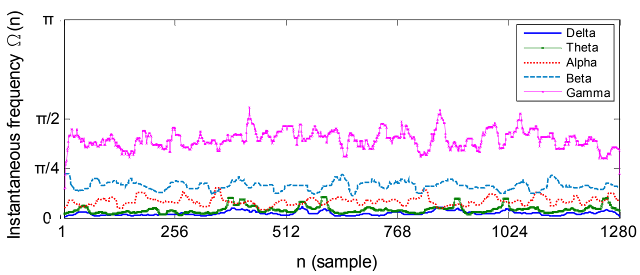

Figure 4. The instantaneous frequency estimate $\Omega(n)$ in the detected EEG rhythms.

our case study shown later, the necessary components are identified as the existing constituent brain waves.

Figure 3 gives an example of a 5-second long EEG signal and the present rhythms detected through band-pass filtering. In Figure 4, instantaneous frequencies of these subbands have been shown. From Figure 4, it is obvious that a primary component dominates the frequency variation in each subband, and this principal value differs from one subband to another. Similar observations could be found for the instantaneous amplitude quantities. An effective feature extraction process can therefore be considered as to identify and estimate these constituent primary components from the AM-FM EEG representation.

Feature Extraction

A common approach of getting those inclusive components in EEG signals is through nonlinear signal decomposition. Consequently, we employ the multi-band AM-FM model on the EEG signal to extract the averaged instantaneous envelope (AIE) and averaged instantaneous frequency (AIF) feature vectors. The process of computing the AIE and AIF features is summarized as follows:

1. *Signal segmentation*: The EEG signal in each channel is segmented into 5 second epochs with no overlap.
2. *Signal decomposition*: Each epoch is divided into 5 subbands: *delta* (0-4 Hz), *theta* (4-8 Hz), *alpha* (8-13 Hz), *beta* (13-30 Hz), and *gamma* (>30 Hz) through a bank of 48th ordered finite impulse response (FIR) filters, where a 48-point Hanning window is applied before the filtering process.
3. *Multi-band demodulation*: Teager's energy separation algorithm [21] is employed to obtain the instantaneous envelope (IE) sequence $|A(n)|$ and the instantaneous angular frequency (IF) $\Omega(n)$ one epoch after another for each subband signal.
4. *Sequence smoothing*: A 21-point median filter is applied to remove the abrupt impulses in the epochs of IE and IF sequences, where the order 21 is empirically determined.
5. *Spatio-temporal averaging*: This process is conducted on each subband epoch by following a two-step calculation:

- *Temporal averaging*: The averaging operation is undertaken on the smoothed IE and IF sequences first to remove the fluctuations over time.
- *Spatial averaging*: These temporal IE, IF mean values are then averaged across different channels to compensate for possible channel variability.

The short-term parameter sets AIE and AIF are generated from the characteristic bands of EEG signals on an epoch-by-epoch basis as described. They capture the dominant amplitude and frequency components in the concerned temporal span and spatial range of these bands. The dimension of AIE and AIF feature vectors depend on the number of subbands that are included, which is set to be five for both AIE and AIF vectors in this paper. The number of data samples extracted from a fixed set of EEG data depends also on the epoch length, which is empirically set to be 5 second. In order to enrich the information contained in the feature vectors, we have concatenated AIE and AIF vectors one after the other to constitute a new vector AIEF, which has a dimension of ten. Moreover, it is revealed through a pilot study on small amount of data that all three sets of feature vectors can achieve higher discriminative performance when they are with a duration of 5 minute.

4. Disease Prediction with Machine Learning Approach

This section focuses on our machine learning based disease prediction methodology. Main approaches in this application domain and the evaluation metrics are described. Finally, a working framework which includes signal processing, data mining, and statistical classification modules are proposed and shown in detail.

Machine learning based approaches

Over the past few years, there has been growing interest in the use of analytical methods to deal with disease diagnosis and prediction problems. One of such method is machine learning. Machine learning is a branch of artificial intelligence in which the computers "learn" from past data samples with statistical, probabilistic and optimization techniques to identify the underlying patterns existing in large, noisy and complex data sets, and to automatically extract useful information from the data [23]. The major focus of machine learning research is to make intelligent decisions on unseen data, which makes it a suitable tool for medical diagnosis and disease prediction in the growing trend towards personalized, predictive medicine.

Within machine learning, there are two main approaches that one can take: supervised and unsupervised learning. In supervised learning, the training data includes examples of the input vectors along with their corresponding target vectors. Existing or new algorithms can be employed to assign new, previously unseen data to one of the predefined categories with a given accuracy. On the other hand, in unsupervised learning, the goal can be three-fold: (1) clustering: to discover groups of similar examples within the data, (2) density estimation: to determine the distribution of data within the input space, and (3) visualization: to project the data from a high-dimensional space down to two or three dimensions [24]. One specific form of supervised pattern recognition is classification, which concerns with the automatic discovery of regularities in the data that can be used to classify the data into different predefined categories. In disease prediction for subjects, for example, the health indicators extracted from the physiological data of the particular individual are referred as "data samples", while the categories to which they may be assigned to are noted as "labels". A decision function for "classifier" is then built, which can capture the relationship between each data sample and its corresponding label with the possible highest accuracy [25].

Supervised machine learning techniques that have been employed in disease prediction task include, but are not limited to, artificial neural network [26], [27], [28], decision trees [29], mixture Gaussian models [30] and support vector machine (SVM) [31], [32].

SVM is a specific type of supervised machine learning method, aiming to classify data points by maximizing the margin between classes in a high-dimensional space [33], [34]. SVM in its basic form is a non-probabilistic binary linear classifier. Suppose there is a set of training data with each data point labeled as belonging to one of two different classes, an SVM will learn from these data a separation boundary to assign unseen data in the test stage into one category or the other with the possible highest accuracy. Namely, an SVM model is a representation of data points in some space, where the data of different categories can be divided by a clear gap with a margin as wide as possible. For prediction purpose, new data points are mapped into the same space first, the SVM classification algorithm will then determine the category for each point in virtue of the side of gap it falls into in the concerned space. SVM can also efficiently perform non-linear classification by way of what is called the kernel trick: mapping of input data points into high-dimensional spaces by some methods. The popular software packages to implement an SVM include Libsvm [35], SVMlight [36], and SVMTorch [37], etc.

Evaluation methodology

In general, disease prediction is a binary classification task. The output data is to be classified either as abnormal, which indicates an upcoming disease onset, or as normal, when the subject's health condition is fine. The performance of prediction is usually measured in terms of sensitivity and specificity. Sensitivity, which is known as recall rate as well, is a measurement of the proportion of actual positives which are correctly identified as such. Specificity measures the proportion of negatives which are correctly identified.

In a disease detection test that screens people for a disease, each subject taking the test either has or does not have the disease. The test outcome could be positive or negative, which indicates that the subject is sick or not sick respectively. The test results for each subject in this setting might be as follows:

- *True positive (TP)*: Sick people correctly diagnosed as sick
- *False positive/alarm (FP/FA)*: Healthy people incorrectly identified as sick
- *True negative (TN)*: Healthy people correctly identified as healthy
- *False negative (FN)*: Sick people incorrectly identified as healthy

The sensitivity, specificity, and the overall accuracy are calculated in the following manner:

$$\begin{aligned} Sensitivity &= \frac{\sum TP}{\sum TP + \sum FN} \\ Specificity &= \frac{\sum TN}{\sum FA + \sum TN} \\ Accuracy &= \frac{\sum TP + \sum TN}{\sum TP + \sum FA + \sum FN + \sum TN} \end{aligned} \tag{4}$$

On the other hand, the specificity in disease prediction tasks is by usage referred to as $1 - Specificity$, namely, the smaller the better, while sensitivity indicates the same meaning as defined in (4). In general, for this type of task, the data falling into the two classes are typically unbalanced in number. The overall accuracy in this scenario sometimes cannot make good trade-off with the loss due to missing detection and false alarm errors; consequently, the F_β measure turns out to be a standard choice. F_β is a performance metric for binary classification functions that is weighted on the harmonic mean for the classifier's TP, FN, and FA, whose definition is denoted by Equation (5):

$$F_\beta = \frac{(1+\beta^2) \cdot TP}{(1+\beta^2) \cdot TP + \beta^2 \cdot FN + FA}, \tag{5}$$

where β is a weighting factor.

Working framework

PHM is a research methodology for system health management during a space mission, which focuses on predicting the time at which a system component will encounter failures to avoid detrimental consequences on operation safety. Another crucial issue associated with the security of space mission is the health conditions of people involved therein, including aviators, astronauts, etc. Aerospace medicine predictive diagnostics which aims to forecast the potential disease onsets a person might experience in the context of space scenarios, such as heart attack, convulsion, muscular fatigue, etc, makes efforts to develop self-diagnosis and self-directed medical management for crew members. Nowadays, the computer-based data analytics techniques have been employed in this field. Data mining and machine learning approach, as a new branch of data processing method, is thereby involved in predictive diagnostics for aerospace medicine. The machine learning based methods in the science of predictive diagnostics can be taken to determine whether a subject is in a healthy status or an impending disease, for example, cardiovascular disease or epileptic seizure, is foreseen. As an initial effort, we propose a machine learning based framework making use of physiological measurements to provide automatical health monitoring and disease prediction for crew members on a subject-by-subject basis. In this framework, the amplitude-frequency feature extraction is employed in the front end to offer discernible health-related characteristics. The SVM classifier is applied to distinguish between the abnormal and normal health status. Standard cross-validation training and classification are systematically carried out.

The physical monitoring of the proposed predictive diagnostics system under aeromedical scenario is conducted through observing physiological data continuously. For each targeted subject, two models will be built: One is for the normal state,

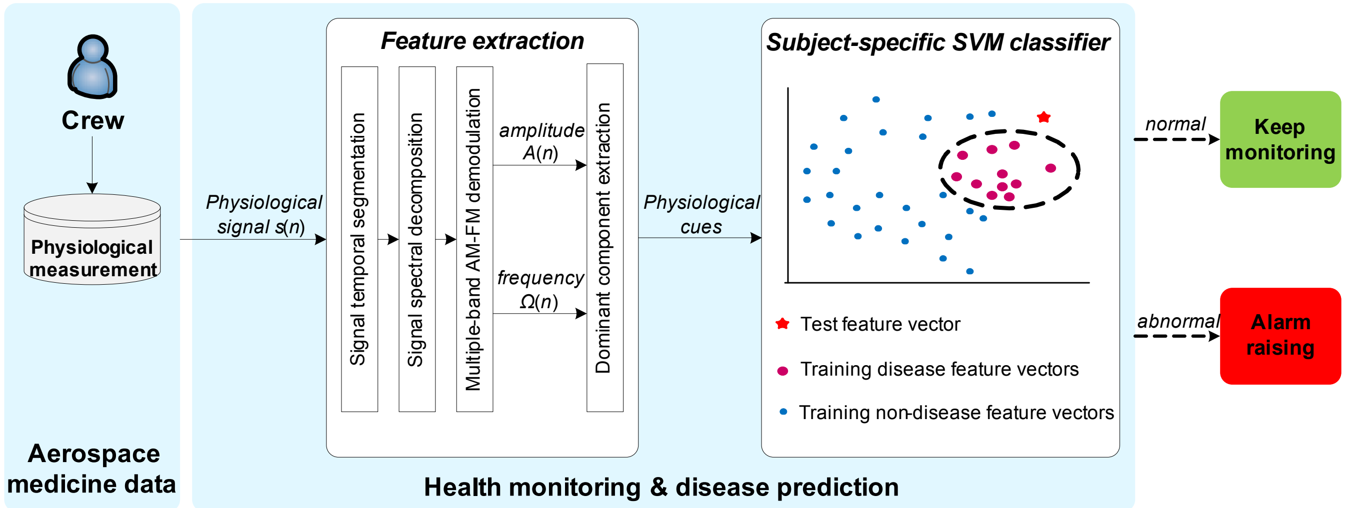

Figure 5. A paradigm of machine learning based disease prediction system in aerospace medicine scenario.

and the other is for the pre-seizure state where there is an upcoming disease. A subject-specific binary classification is conducted continuously to classify the input feature vectors into normal or pre-disease groups [17], [32]. Once pre-seizure observations for acute diseases are found to last for a certain period, alarms are to be raised to clinical caregivers immediately. For diseases characterized by chronic symptoms due to fatigue, such as muscular fatigue and stiffness, if detected, awareness should also be raised. In our previous work on epileptic seizure prediction with EEG data, a binary classification scheme is implemented with SVM, where non-linear decision boundaries are generated to separate the data by using radial basis function (RBF) kernel [38]. Similar approaches can be applied to other physiological data, e.g., ECG and EMG, for disease prediction and potential pattern classification purposes.

Figure 5 gives an overall illustration of the described paradigm for the machine learning based disease prediction system in a typical aerospace medicine scenario. The paradigm mainly contains three modules: aerospace medical data acquisition, feature extraction, and SVM-based classification. The input data are physiological measurements from the crew members on a continuous-time basis, where the medical recordings could be provided by the EEG, ECG, EMG, etc. These time-varying sequences are then processed by a series of signal processing steps, producing respective health profiles of the concerned subject, which are named feature vectors in pattern recognition terminology. Through implementing these sequentially connected procedures, which include temporal segmentation, spectral decomposition, and multi-band demodulation, on the physiological signal $s(n)$, its instantaneous amplitude and frequency sequences, $A(n)$ and $\Omega(n)$ respectively, are picked out. The most dominant amplitude and frequency components present in $s(n)$ are then extracted as the physiological cues. To provide subject-centric medical management, SVM classifiers are trained separately for each subject. A separation boundary is learned from past data sets of the subject regarding whether the concerned disease is present or not. Once a set of unseen data samples come, the categories they should fall into will be decided accordingly. In case an impending disease is forecasted, alarms will be raised to notify the concerned parties; otherwise, the system keeps monitoring health condition of the respective subject.

This infrastructure built for predictive diagnostics in aerospace medicine applications provides necessary signal processing steps to handle various physiological signals. The SVM-based pattern recognition module, on the other hand, is also replaceable with other machine learning tools when necessary. As a result, this integrated and portable structure will make the proposed framework extendable to new application scenarios.

5. Case study: Epileptic Seizure Prediction

In this section, our machine learning based disease prediction framework is evaluated on 19 out of 21 patients in the Freiburg EEG data set. The remaining two patients are discarded due to lack of observed seizures. The SPH is set to be 50 minutes in this case study.

Like most pattern classification problems, the two essential components in the machine learning based disease prediction system demonstrated by Figure 5 are feature extraction and binary classification. In this case study, the physiological data under the aerospace medicine scenario refer to EEG signals from the Freiburg database. During the feature extraction process, where there are four successive procedures including signal division and demodulation, the dominant amplitude and frequency components existing in an EEG signal are extracted as feature vectors along the time line. These feature vectors are then taken as physiological cues to detect potential negative health trend for disease prediction purpose. More details about the indicated feature extraction process could be found in Section 3. In the remaining paragraphs of this section, we will focus on the evaluation metrics and performance analysis of the studied epileptic seizure predictor.

Database

The investigated Freiburg EEG database [39], is a popular epileptic seizure data set. It is a publicly available intracranial EEG data set, which contains invasive EEG recordings of 21 patients suffering from medically intractable focal epilepsy. The data were recorded during an invasive pre-surgical epilepsy monitoring at the Epilepsy Center of the University Hospital of Freiburg, Germany. The epileptic focus was located in neocortical brain structures for 11 patients, in the hippocampus for eight patients, and in both structures for two patients. In order to obtain a high signal-to-noise ratio with fewer artifacts, and to record directly from focal areas, intracranial grid-, strip-, and depth-electrodes were utilized. The EEG data were acquired using a Neurofile NT digital video EEG system with 128 channels, a 256 Hz sampling rate, and a 16-bit analogue-to-digital converter.

For each of the patients, there are two sets of data that contain EEG signals from ictal and interictal stages, respectively. For prediction purposes, at least 50 minutes preictal data were retained prior to each epileptic seizure. As for the interictal states, approximately 24 hours of EEG recordings without seizure activity were provided. At least 24 hours of continuous interictal recordings were available for 13 patients. For the remaining patients, interictal invasive EEG data consisting of less than 24 hours were joined together, so as to end up with at least 24 hours of interictal recordings per patient. For each patient, the recordings of three focal and three extra-focal electrode contacts were available.

Performance metrics

In machine learning, one of the most common tasks is data classification. Suppose there are data points belonging to two different classes, the goal is to determine which one of the two classes a new data point will be in. A classifier is said to assign a feature vector $\boldsymbol{x} \in \mathbb{R}^d$ to class w_i if $g_i(\boldsymbol{x}) > g_j(\boldsymbol{x})$ for all $j \neq i$. In binary classification task, suppose $g(\boldsymbol{x}) \equiv g_1(\boldsymbol{x}) - g_2(\boldsymbol{x})$, we assign the point to w_1 if $g(\boldsymbol{x}) > 0$, otherwise, assign it to w_2. In linear discriminant study, $g(\boldsymbol{x})$ is a linear function $g(\boldsymbol{x}) = \boldsymbol{w}^T \cdot \boldsymbol{x} + b$, where $\boldsymbol{w}$ indicates the normal vector to the hyperplane, $\cdot$ denotes the dot product. A hyperplane is a set of points that satisfy $\boldsymbol{w} \cdot \boldsymbol{x} + b = 0$. The parameter $b/\|\boldsymbol{w}\|$ determines the offset of the hyperplane from the origin along the normal vector $\boldsymbol{w}$ [40].

For a linear SVM classifier, a data point is viewed as a d-dimensional vector, a hyperplane to separate such points is of $(d-1)$-dimension. There are many choices for the separation hyperplane, the best one is that can divide the two classes with the possible largest margin. Given a set of training data which contains N points $\{(\boldsymbol{x}_i, y_i) | \boldsymbol{x}_i \in \mathbb{R}^d, y_i \in \{-1, 1\}\}_{i=1}^N$, where each $\boldsymbol{x}_i$ is a d-dimensional real vector. After scaling on both $\boldsymbol{w}$ and b, for $y_i = 1$, there is $\boldsymbol{w}^T \cdot \boldsymbol{x}_i + b \geq 1$, for $y_i = -1$, $\boldsymbol{w}^T \cdot \boldsymbol{x}_i + b \leq -1$ holds. The maximum-margin hyperplane which can divide the points with $y_i = 1$ from those with $y_i = -1$ is to be searched for. To perform nonlinear classification, kernel trick is always applied to maximum-margin hyperplanes by replacing every dot product in the linear function $g(\boldsymbol{x})$ with a nonlinear kernel function. The resulting decision function becomes $g(\boldsymbol{x}) = \boldsymbol{w}^T \phi(\boldsymbol{x}) + b$, where a kernel function is defined as a function that corresponds to a dot product of two feature vectors in some expanded feature space $k(\boldsymbol{x}_i, \boldsymbol{x}_j) \equiv \phi(\boldsymbol{x}_i)^T \phi(\boldsymbol{x}_j)$. The algorithm in other respects is similar with that for linear classifiers. As a result, the original input space is mapped to some higher-dimensional feature space where the training set is separable. If the kernel used is a Gaussian radial basis function $k(\boldsymbol{x}_i, \boldsymbol{x}_j) = exp(-\gamma \|\boldsymbol{x}_i - \boldsymbol{x}_j\|^2)$, with $\gamma > 0$, the respective feature space is a Hilbert space of infinite dimensions [41]. To deal with noisy data set where mislabeled points might exist, there is a call for a trade off between a large margin and a small error penalty. The soft margin method which can split the examples as cleanly as possible while at the meantime maximize the separation gap is thereby introduced. Generally speaking, the effectiveness of an SVM depends on the following three factors: choice of kernel function, the kernel's parameters, and the soft margin parameter C. A common choice for kernel function is Gaussian kernel, where there is only one parameter γ to be tuned. The optimal $[C, \gamma]$ set is often found via grid search, in which each combination of C and γ parameters is typically checked by cross validation, and the parameters with best cross validation accuracy among the rounds are picked out in the end. These fine-tuned parameters are then employed in the final model for classifying new data.

We measure the performance of our machine learning based disease prediction framework in terms of sensitivity and specificity. Sensitivity refers to the number of seizures that have been predicted correctly. Once an alarm of seizure has been raised in the preictal stage, and there is seizure occurring in the subsequent SPH, it is regarded as a correct prediction. Specificity in the seizure prediction task is related with the number of false alarms generated during the interictal period per hour. We set the weighting factor β in Equation (5) to be 2 in this case study. In each cross-validation training round, the target function is optimized by choosing SVM cost parameter C and RBF kernel parameter γ through a 21×21 grid search, where $log_2 C$ and $log_2 \gamma$ range from -10 to 10, respectively. The parameter set $[C, \gamma]$ chosen in the training stage is subsequently adopted in the respective evaluation round.

Experiments and results

In this case study, the patient-specific binary classification of feature vectors is implemented with SVM through employing the Libsvm software package [35]. Nonlinear decision boundaries are generated to separate the preictal and interictal data by applying RBF kernel. In order to estimate the prediction performance in an in-sample optimization and out-of-sample evaluation manner, 5-fold cross validation is applied to obtain the optimal parameters during the training stage. Suppose N_S 50-minute preictal records and N_{NS} 1-hour interictal records are included in a patient's data. In measuring the prediction sensitivity, one classifier is trained from $N_S - 1$ preictal records, and another classifier is trained from all N_{NS} interictal records. The predictor is then tasked with determining the class of samples in the withheld preictal record. This process is repeated N_S times until all preictal records are tested. True positive and false negative measurements are counted in the process. To estimate the predictor's specificity, the classifiers are trained from the N_S preictal records and $N_{NS} - 1$ interictal records, respectively. The withheld interictal record is used as testing data, and this process is repeated N_{NS} times such that all interictal records are tested. The false alarms which have occurred are noted as well.

Two sets of parallel experiments have been conducted. One set is to maximize the overall accuracy, noted as Exp$_{Acc}$, while the other one that optimizes the F_2 measurement is noted as Exp$_{F2}$. In Table 2, the epileptic seizure prediction performance on a patient-specific basis in Exp$_{Acc}$ is indicated in detail. The results recorded here are from the best performing feature sets among AIE, AIF and AIEF parameter sets. To achieve accurate prediction, for each subject, these selected feature sets are immediately re-evaluated in Exp$_{F2}$ tests, whose results are recorded in Table 3. For the final results given in Table 3, the overall sensitivity obtained across all patients is 95.2%, where 18.0% relative improvement over the Exp$_{Acc}$ result has been achieved. In specific, 79 out of 83 seizures in the evaluation set have been successfully

Table 2. Sensitivity and specificity results in Exp_{Acc} experiments.

Patient Id.	Seizure No.	Interictal Hr.	Sen. (%) (Exp_{Acc})	FA/hr (Exp_{Acc})
01	4	24	100	0.000
02	3	24	33.3	0.042
03	5	24	100	0.042
04	5	24	100	0.000
05	5	24	80.0	0.792
06	3	24	100	0.083
07	3	25	100	0.000
09	5	24	100	0.042
10	5	25	100	0.287
11	4	24	25.0	0.000
12	4	25	100	0.000
14	4	24	25.0	0.084
15	4	25	50.0	0.280
16	5	24	80.0	0.083
17	5	24	100	0.125
18	5	26	100	0.463
19	4	24	100	0.369
20	5	25	40.0	0.608
21	5	25	80.0	0.722
Total			Mean	
19	83	461	80.7	0.212

Table 3. Sensitivity and specificity results before and after post-processing in Exp_{F2} re-evaluation experiments.

Patient Id.	Sen. (%)	FP/hr (before filtering)	FA/hr (after filtering)
01	100	0.000	0.000
02	66.7	0.042	0.000
03	100	0.042	0.000
04	100	0.000	0.000
05	100	0.917	0.708
06	100	0.083	0.042
07	100	0.000	0.000
09	100	0.042	0.000
10	100	0.287	0.082
11	75.0	0.332	0.166
12	100	0.000	0.000
14	100	0.797	0.294
15	100	0.440	0.200
16	100	0.708	0.208
17	100	0.125	0.083
18	100	0.463	0.232
19	100	0.369	0.041
20	60.0	0.892	0.284
21	100	0.963	0.401
Total	Mean		
19	95.2	0.342	0.144

predicted, and for 16 out of the 19 patients, all seizures are correctly forecasted in advance. The specificity of the epileptic seizure prediction algorithm is inspected through measuring the average false alarms occurring per hour. Considering the observation that a majority of isolated positive detections happen to be falsely generated alarms, we employ a simple one-step post-processing scheme to filter out these single positives. The FA/hr results before taking this two-in-a-row filtering step for individual patients are 0.342, which is worse than that for Exp_{Acc}. As a consequence of the post-processing, 0.144 FAs per hour specificity result has been finally achieved.

The data set we used for this case study contains only invasive EEG recordings, however, the proposed working framework under aerospace medicine scenarios can also work on scalp EEG and other physiological information sources, such as ECG and EMG.

6. FURTHER DISCUSSION

It is known that the ECG signal has been widely used to measure and monitor the activity of heartbeat. In this section, we would rather focus on another physiological measurement, electromyogram (EMG) signal, which can reflect electrical activity produced by skeletal muscles, and has been viewed as an important means to indicate human's physical status. The long-duration spaceflight and absence of gravity greatly impacts astronauts' neuralmuscular system. As recently reported in [42], the subtle neuromotor control system would be compromised and neuromuscular activation characteristics would be disrupted as a result of long-term spaceflight. Due to the inherent coherence with EEG signals, the machine learning based disease prediction framework developed in this paper could also be extended to EMG signals, in applications such as neuromuscular abnormality diagnosis and muscular fatigue prediction.

It is noted that the disrupted neuralmuscular activation is typically associated with abnormal forces, while muscle force is closely related to the amplitude of EMG signals. Therefore, the extracted forces of particular joints such as knees and elbows during a specific astronaut's operation task can also be taken as physiological cues in the outlined framework. In our previous work [43], the combined techniques of Kalman filter and nonlinear normalization have been successfully employed to estimate human joint forces. For this propose, the EMG signal is first band-pass and notch filtered to remove most of the power energy in the low frequency range (caused by fatigue, tissue filtering properties and the differential amplification process), and then nonlinear normalized as described in Equation (6),

$$EMG_N = 100\frac{e^{(EMG_L\xi)} - 1}{e^{-100\xi} - 1}, \tag{6}$$

where $EMG_L = EMG$ is linearly normalized to 100% of the maximum, $EMG_N = EMG$ is non-linearly normalized to 100% of the maximum. ξ is a user-specific parameter. Then, by passing EMG_N through a Kalman filter, we can get a rough estimate of the joint force; this is because in larger muscles where the firing rate has a lower dynamic range, the relationship between force and the amplitude of EMG signal can be described by the above nonlinear equation [44]. When applying the proposed framework on EMG signals to detect abnormal neuromuscular characteristics and to predict muscular fatigue, the force estimate parameters could also be incorporated to enhance the amplitude-frequency feature set.

7. CONCLUSION

In order to improve the medical operation autonomy of aerospace medicine, a machine learning based framework for predictive diagnostics with physiological signal has been proposed in this work. One important issue in aerospace medicine is to develop diagnostic programs that can autonomously predict, prevent, and manage potential health problems of individual crew members timely. Predictive diagnostics science is therefore aimed to identify negative trends of specific subject by forecasting upcoming onset of concerned disease in order to provide sufficient time for urgent action. Due to the broad use of EEG in health monitoring, disease detection and diagnosis, it has been taken as an essential physical indicator for people working in space missions. We therefore focus on EEG in this initial research effort on bringing machine learning based disease prediction technology as predictive diagnostics applications under the field of aerospace medicine. By means of the powerful data processing capability of machine learning, the hard-to-discern trends underlying each person's real-time physiological measurements are dig out, and then by comparing with predefined normal status from respective profile, timely diagnostic decisions can be achieved. In the proposed framework, distinctive amplitude-frequency attributes in physiological signals are first explored and parameterized into compact yet comprehensive form. Up-to-date support vector machine approach is then applied on both normal and abnormal health data to determine a separation boundary, enabling an effective classifier for future data. Disease prediction on a subject-by-subject basis is thus achieved automatically. The effectiveness of the suggested paradigm has been demonstrated through experimental results on a real-world EEG data set for epileptic seizure prediction. We further discuss the application of proposed framework on processing other physiological data such as EMG signal as an extension of the case study. In consequence, we expect the herein introduced framework will provide new perspective in promoting the predictive diagnostics in aerospace medicine.

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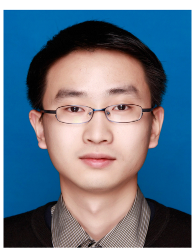

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