NR-GAN: Noise Reduction GAN for Mice Electroencephalogram Signals

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ABSTRACT
To support basic sleep research, several automated sleep stage scoring methods for mice have been proposed. Although these methods can score mice sleep stages accurately based on their electroencephalogram (EEG) and electromyogram (EMG) signals, they are fragile against noise, especially in EEG signals. The simplest solution is to reduce or eliminate noise before scoring. However, a method for reducing noise in biological signals does not exist. Because EEG signals contain many types of noise, predicting all of them is difficult, which inhibits the use of hand-engineered methods such as frequency filters. Additionally, noise reduction methods with deep learning models are not applicable as they require records of noise, and the noise considered here cannot be measured separately from biological signals. In this study, we address this problem using adversarial training, which is a method for deep learning models that does not require noise records as training samples. We propose a new noise-reduction model called "NR-GAN." Its training process requires a set of noisy signals and a set of clear signals. Since these sets can be measured independently, NR-GAN can reduce noise in mice EEG signals.

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CCS Concepts
•Applied computing→Life and medical sciences→ Bioinformatics.

Keywords
Adversarial training; machine learning; biological signal processing; electroencephalogram;

1. INTRODUCTION
Mice sleep consists of three stages: wake, REM, and non-REM. Since the ratio or transition of these stages can diagnose sleep disorders, sleep stage scoring is an essential test in basic sleep research. However, sleep stage scoring, which is conducted by visually inspecting mice electroencephalogram (EEG) and electromyogram (EMG) signals, is very time-consuming and burdensome. To enhance the efficacy of this inspection, several automated sleep stage scoring methods have been proposed [1]–[6]. For example, Suzuki et al. developed a scoring model that employs a support vector machine and achieves a scoring accuracy of almost 95%, which is comparable to the inter-rater reliability among human scorers [2].

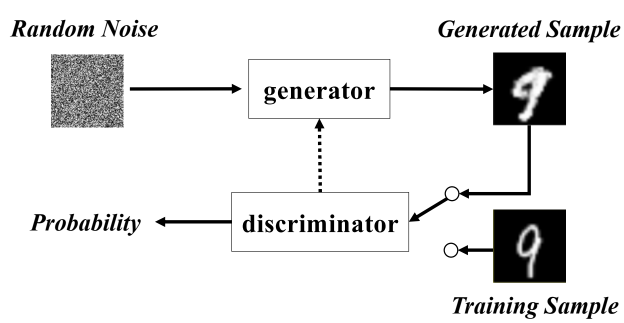


Figure 1. Structure of typical GANs.

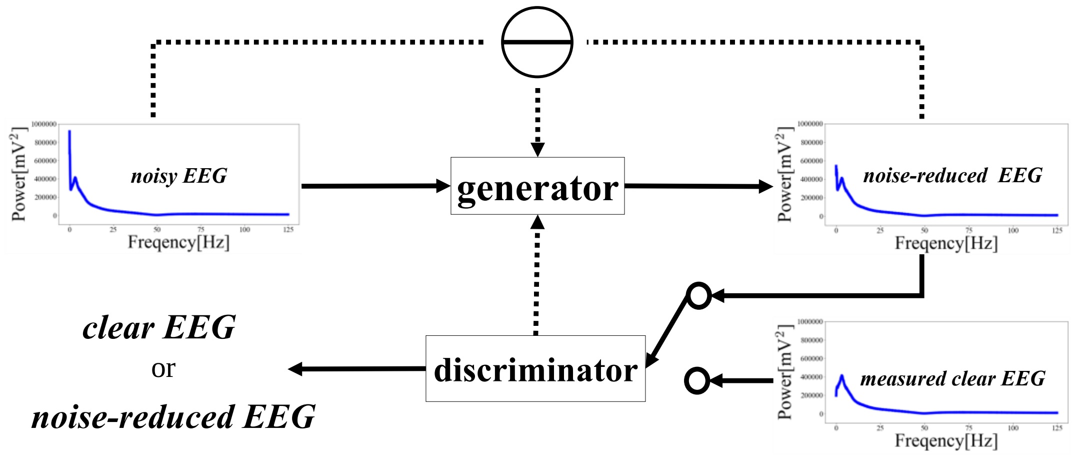


Figure 2. Structure of NR-GAN.

However, these methods cannot be used in sleep research due to their weakness against noise in EEG and EMG signals. Their accuracy quickly degrades, especially when the EEG signals are noisy. Noise is also a problem in manual sleep stage scoring. Typically, scorers conduct noise reduction over biological signals to maintain a high scoring accuracy. A straightforward procedure to enhance the robustness of conventional methods is to employ a noise reduction or elimination method in the preprocessing phases.

Several features of the mice biological signals prevent conventional noise reduction methods from working well. First, EEG and EMG signals can contain many types of noise, whose properties are not clarified. Thus, it is difficult to model all possible types of noise and design noise-reduction methods manually. Second, some of the noise contains frequency components that are essential in sleep stage scoring. For example, noise from motion artifacts contains components between 0 to 1 Hz, which are often observed in EEG signals during non-REM sleep. The presence of artifacts in signals is inconsistent. In other words, the records contain both noisy and clear signals. Thus, noise-reduction methods must adapt processing according to whether the signal is noisy or not. Consequently, it is difficult to employ hand-engineered noise-reduction methods such as frequency filters.

To handle noise and signals, some approaches employ machine learning techniques. Recently, noise-reduction methods using a deep-learning model have been proposed [7] [8]. These methods are known as good noise eliminators for acoustic signals and can handle various types of noise. However, they encounter practical issues in preparing training samples. These approaches model the relationship between the original noisy signals and their clear signal parts directly from their pairs. In the context of noise reduction from sounds, pairs can be easily prepared. For example, artificial noisy sounds for the training process can be synthesized by combining sounds and noises measured separately. By contrast, noise in biological signals cannot be measured separately from signal parts since they occur inside mice or the measurement equipment. Hence, training sets for biological samples cannot be prepared in the same manner as those for acoustic signals. For biological samples, training sets must be prepared by measuring the noisy signals and reducing the noise manually, which is extremely burdensome and impractical.

This research aims to develop a novel noise reduction method for mice biological signals. Specifically, our method does not require prior knowledge or records of noise in biological signals. Herein we focus on adversarial training, which enables deep neural networks to model the relationship without direct pairs of input and output signals. The proposed method, named "NR- GAN," is an expansion of generative adversarial neural networks and is inspired by SimGAN [9]. Although SimGAN was originally proposed for image refinement, we modified the layer organization and the loss function to make it more suitable for noise reduction of EEG signals.

The experimental results show that NR-GAN can locate the noise reduction procedure without prior knowledge or noise records in EEG signals. Compared to a frequency filter optimized for target noises, NR-GAN reduces more noise and affects fewer signal parts. These results indicate that NR-GAN is very effective for noise reduction in mice biological signals.

The rest of this paper is organized as follows. Section 2 explains the architecture and training process of vanilla generative adversarial networks. Section 3 describes NR-GAN and the difference from conventional GAN models. The experiment and evaluation of NR-GAN are presented in Sections 4 and 5, respectively. Section 6 discusses related works. Finally, Section 7 concludes the paper.

2. GENERATIVE ADVERSARIAL NETWORKS

GAN [10] is a signal generation model that consists of two types of neural networks. One is called a generator and the other is called a discriminator (Figure1). The generator plays the main role in a signal generation as it converts random noises and generates artificial signals. By contrast, the discriminator supports the training process of the generator. It learns the features of training samples (examples of signals that should be generated) and calculates the probability of whether the input signal is a training sample or not. The generator is trained based on the output of the discriminator.

In particular, the generator and the discriminator are trained to minimize the following loss functions, L_g and L_d.

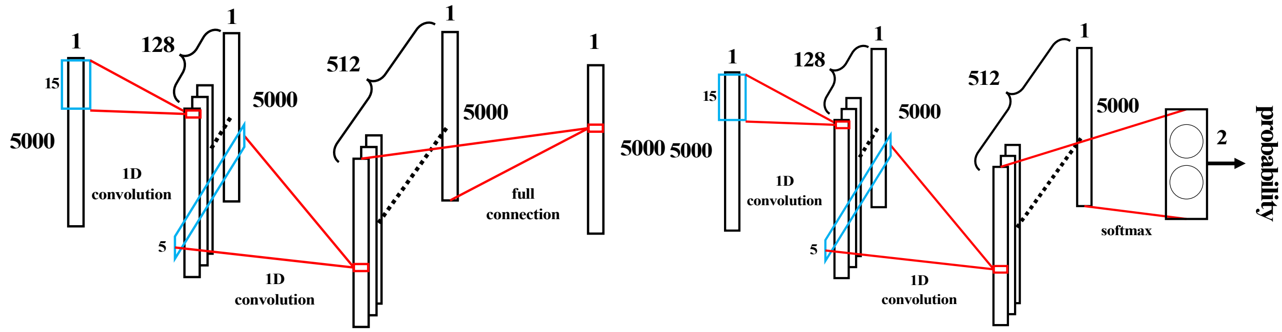


Figure 3. Structure of the generator and discriminator.

$$L_g = \mathbb{E}_{x \sim p_x(x)}\left[log\left(1 - D\big(G(x)\big)\right)\right], \tag{1}$$

$$L_d = \mathbb{E}_{x \sim p_x(x)}\left[log\left(D\big(G(x)\big)\right)\right] + \mathbb{E}_{y \sim p_{data}(y)}\left[log\left(D\big(G(x)\big)\right)\right], \tag{2}$$

x is a random noise with a distribution of px and y is the training sample. G and D are functions represented by the generator and the discriminator, respectively.

Both networks are trained to beat each other. The discriminator is optimized to classify the generated signals and training samples. On the other hand, the generator learns how to output signals that will be misclassified by the discriminator. By repeatedly alternating these processes, the generator can generate signals that are similar to the training samples. Note that the training samples do not need to be associated with the input (random noises). This practical advantage should also be effective in noise reduction of mice EEG signals. For example, we can model the conversion of noisy EEG signals into clear EEG signals by training GANs with measured noisy and clear EEG signals instead of random noise and training samples.

However, typical GANs have a serious issue when applied to noise reduction tasks. The generator can output clear EEG signals unrelated to the inputted noisy EEG signals. The loss function of the generator is designed without considering the similarities and differences between the input and output signals. Thus, it does not always output the clear signal part of the inputted noisy signal.

2.1 SimGAN

SimGAN [11] is an extension of GAN, which was originally proposed to improve the reality of input synthetic images. This model solves the above issue by modifying the loss function of the generator, L_{sg}.

$$L_{sg} = \mathbb{E}_{x \sim p_x(x)}[lof(1 - D(G(x))) + \alpha||x - G(x)||]. \tag{3}$$

The authors added the L1 norm between the input and output signals of the generator. This improvement allows ways to generate signals, which are similar to both the training samples and input signals, to be learned. α is the hyperparameter that determines how much consider that the generator's output signal is similar to its input signal. This approach may also be effective to develop a noise reduction model. However, the structure of SimGAN is optimized for image processing. Hence, the expression is too high, which results in overfitting. Thus, we modified the layer organization and the loss function of SimGAN to prevent overfitting and to increase the compatibly with noise reduction of EEG signals.

3. PROPOSED METHOD: NR-GAN

Conventional sleep stage scoring methods [1, 2] consider only the frequency-domain features of EEG and EMG signals. Hence, so, we converted all the EEG signals, including the training samples, into frequency components. In particular, the 20-s EEG signals obtained with a sampling frequency of 250 Hz were converted into a vector $x\ (= x_1, x_2, \ldots, x_{5000})$ by

$$x_t = \left\|\sum_{z=0}^{4999} X_z^{-i\frac{2\pi tz}{5000}}\right\|^2, \tag{4}$$

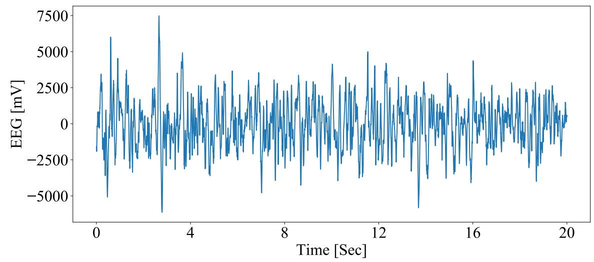
where $X\ (= X_1, X_2, \ldots, X_{5000})$ the raw EEG signal. NR-GAN has one generator and one discriminator like typical GANs or SimGAN (Figure2). The generator generates the clear signal parts from the input noisy EEG signals, while the discriminator evaluates the quality of generated signal parts.

3.1 Structure of Generator and Discriminator

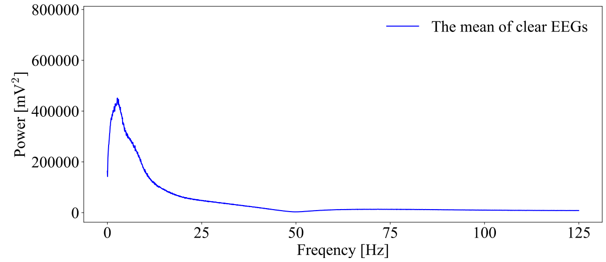
In this research, we adopt a convolutional neural network as a generator of NR-GAN (Figure3(a)). The noisy EEG signals are input into two convolutional layers and converted into the feature values. The first and second convolutional layers have 128 kernels with a 15 width and 512 kernels with a five width, respectively. Each layer calculates the convolution between their input and kernels and activates the results with a parametric-ReLU function

$$f(x) = max(0.2x, x). \tag{5}$$

The extracted feature values are input into a full connection layer with 5,000 neurons to estimate the frequency components of the clear signal part. The discriminator has almost the same structure as the generator, but the full-connection layer is replaced by the softmax layer to calculate the probability of whether the input signals are the training sample. Note that the optimizations of the structure, number of kernels, and other hyperparameters of NR-GAN were performed by a trial and error procedure.



(a) Time domain.



(b) Frequency domain. All clear EEG signals are in blue area.

Figure 4. Example of clear EEG.

3.2 Training

After the training process, the generator converts the noisy EEG signal into a signal that is similar to both the training sample (measured clear EEG signal) and the input. To achieve the above conditions, we chose a loss function close to that of SimGAN. The loss function of the generator and the discriminator, L_{ng} and L_{nd} are defined as

$$L_{ng} = \sum_{x \in S_{ns}} \left[log\left(1 - D\big(G(x)\big)\right) + \alpha \left| |x - G(x)| \right|^2 \right], \quad (6)$$

$$L_{nd} = \sum_{x \in S_{ns}} \left[log\left(D\big(G(x)\big)\right)\right] + \sum_{y \in S_{cs}} \big[log\big(1 - D(y)\big)\big] \quad (7)$$

where S_{ns} and S_{cs} are the set of noisy EEG signals and clear EEG signals, respectively. In this research, we set α to 0.0001. Like typical GANs and SimGAN, the generator and the discriminator are optimized by repeatedly alternating the minimization of L_{ng} and L_{nd}.

3.3 Difference between NR-GAN and SimGAN

Although NR-GAN is inspired by SimGAN, the structures of the generator and the discriminator differ. First, we replaced the 2-D convolution layers into 1-D convolution layers to handle the 1-D frequency components of EEG signals. Second, we omitted several layers of SimGAN to prevent overfitting and to reduce the training time. As mentioned above, SimGAN has too much expression ability for our intent. Finally, we replaced the residential layer into a full connection layer because the residential layer is for very deep neural networks. Hence, it is not suitable for our shallow model. The neurons of the full connection layer are associated with one frequency component, and they can perform processing specialized to a specific frequency component. This improvement may also effectively reduce specific noise frequencies, such as the power supply noise.

Additionally, we changed the training process. We omitted the local adversarial loss and history of the training sample to reduce the computational costs. Besides, we changed the L1-norm in the loss function of the generator into the L2-norm. We could not find a suitable parameter for L1-norm. It might be more sensitive than that of L2-norm.

4. EVALUATION EXPERIMENTS

To verify the efficacy of NR-GAN, we compared its noise reduction performance with that using frequency filters, which is the typical noise reduction method in manual scoring by experts, and original SimGAN architecture.

4.1 Target Noise

In this experiment, we used two types of noises: motion artifacts, 25-Hz power supply noise. Because these noises contain the same frequency components as EEG signals of sleeping mice, they decrease the scoring accuracy. Thus, these noises should be reduced in automated sleep stage scoring.

A motion artifact is a noise caused by motions of the mice themselves, such as turning while sleeping. As mice often move even while asleep, this is one of the most common noises in mice EEG signals. These noises consist of very low-frequency components in the range of 0-0.5 Hz.

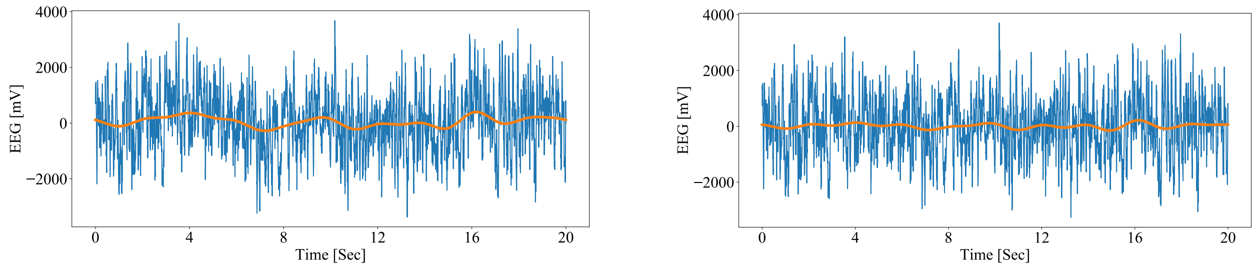
A 25-Hz power supply noise is caused by electromagnetic waves generated by an AC-DC converter. Thus, this noise occurs due to lighting and using measurement instruments.

4.2 Dataset

A dataset of mice EEG signals is provided by the International Institute for Integrative Sleep Medicine (IIIS). From this dataset, we chose the EEG signals of seven mice that could be scored accurately without noise reduction as clear EEG signals. Then we split these signals into 20-s subsequences.

In this experiment, we generated artificial noisy EEG signals by converting the clear EEG signals. It is difficult to develop a generative model for the motion artifact because it depends highly on the mice motion. Thus, we generated the EEG signals with motion artifacts by replacing frequency components between 0 Hz and 0.5 Hz in the clear EEG signals with those of EEG signals that include real motion artifacts. EEG signals with 25-Hz power supply noise were generated by adding 25 Hz frequency components to clear EEG signals. Hence, the amount of 25 Hz frequency components is the same as the peak frequency with EEG signals.

Finally, we received 1800 subsequences of clear EEG signals, 1800 subsequences of artificial noisy signals, and 1800 pairs of clear and noisy EEG signals for each noise. These subsequences and pairs were used in the training and test procedures.



(a) Before. **(b) After.**

Figure 5. Example of motion artifact reduction. Orange line represents the summation of the frequency components between 0 Hz to 0.5 Hz.

4.3 Evaluation Index

In this experiment, the two indices were employed for evaluation: the rate of noise remain R_{nr}, and the rate of signal distortion R_{sd}.

$$R_{nr} = \frac{1}{N}\sum_{i}^{N}\left(\sum_{j\in F_n}\frac{|x_j^i - o_j^i|}{|x_j^i - c_j^i|}\right) \tag{8}$$

$$R_{sd} = \frac{1}{N}\sum_{i}^{N}\left(\sum_{j\in F_c}\frac{|x_j^i - o_j^i|}{|c_j^i|}\right) \tag{9}$$

where x_j^i, o_j^i and c_j^i denote the frequency components of j Hz in i-th input, output, and target EEG signal, respectively. F_n and F_c are the set of noise and other frequencies, respectively. For in- stance, in the case of 25 Hz supply noise, $F_n = \{25\}$ and $F_c = \{0,0.05,...,24.95,25.05,...,125\}$. N is the number of EEG signals.

Table 1. Performance indices of each noise reduction

	For Noisy Spectrum			
	Motion Artifact Noise		25Hz Noise	
	R_{nr}	R_{sd}	R_{nr}	R_{sd}
NR-GAN	48%	44%	5.8%	1.7%
Freq.filter	49%	66%	5.7%	1.7%
SimGAN	1000%	93%	-	-
	For Clear Spectrum			
	Motion Artifact Noise		-	
	-	R_{sd}	-	-
NR-GAN	-	16%	-	-
Freq.filter	-	33%	-	-

4.4 Result

After the training NR-GAN for 50 times for each sample, we got the performance indices shown in Table 1 (They are the mean value of five experiments using different initial synaptic weights).

The results show that NR-GAN can reduce the half of motion artifact noise and almost all 25 Hz power supply noise without distorting EEG signals (Figure 6, 7). These results indicate that NR- GAN has the potential to reduce actual noises in mice EEG signals and enhance the robustness of conventional sleep stage methods.

The changes to the frequency components of the EEG signals containing noises were more pronounced than those of the EEG signals (Figs.6, 7). This indicates that NR-GAN can learn the noise features and reduce them selectively without using prior knowledge or a direct pair of a noisy EEG signal and its clear signal part.

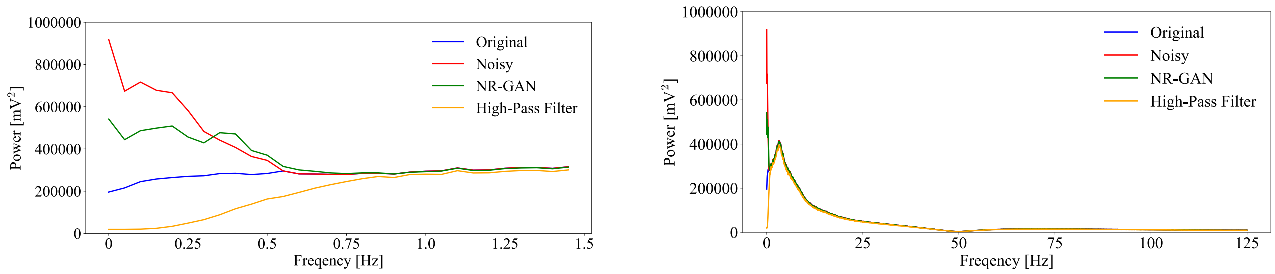
4.5 Comparison with Frequency Filters

To evaluate the noise reduction performance of NR-GAN, we compared it with frequency filters adjusted using prior-knowledge of noise properties. A second-order high-pass filter of 0.5 Hz and a second-order band-stop filter of 25 Hz were used for reducing motion artifact noise and 25 Hz power supply noise, respectively. The comparison shows that the performance of NR-GAN is competitive with frequency filters using prior knowledge. Especially, its rates of signal distortion, R_{sd} are rather better than that of filters. This suggests that NR-GAN can be placed instead of frequency filters since it can reduce "unknown" noise in EEG signals more properly. Although the quantitative performance of NR-GAN and frequency filters are competitive, the tendency of "cleaned-up" signals were different (Figure 6 (a), 7 (a)). The frequency filters tend to reduce also the components of the EEG signal, whereas NR-GAN tries to reproduce the amount of each frequency component (Figure 7 (a)). Besides, the amount of reduced noise is smaller than that of the frequency filters, since NR-GAN reproduce the feature of clear EEG signals with minimum change because of L2-norm in the loss function.

4.6 Processing Result for Clear Signal

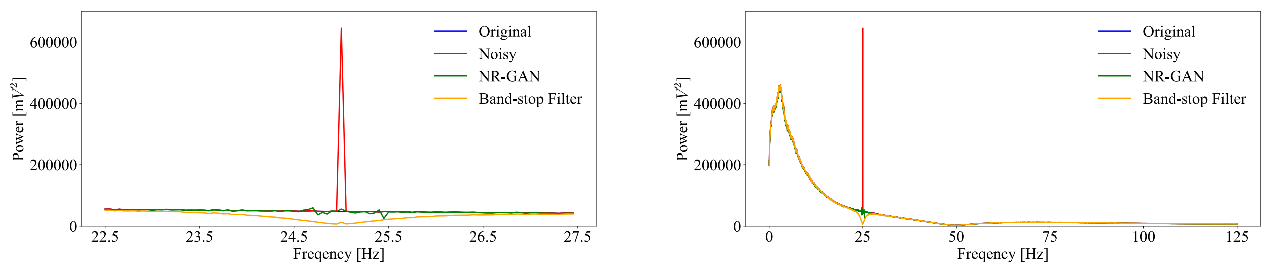
As mentioned in the Introduction section, the mice biological signal records contain both noisy signals and clear signals. Therefore, noise reduction methods have to change the processing when clear signals are input.

To verify the processing, we inputted the clear EEG signals to NR-GAN and a frequency filter, which is optimized for motion artifact noise (Table 1, Figure 8). The results show that NR-GAN reduced the frequency components of less than 0.5 Hz by 16 %. The reduction amount is about half of that of the frequency filter (33%); however, NR-GAN could not change its process according to the presence of noise. This shortcoming is thought to be caused by inappropriate training samples for this task. In the training process, NR-GAN provided only the noisy signals as input. Therefore, NR- GAN did not need to learn the way for evaluating the noisiness of the input signal. At least, NR-GAN achieved superior performance than frequency filters without providing clear EEG signals as input in its training sample. This indicates that NR-GAN is suitable for mice EEG signals.



(b) Noise area (0 to 0.5 Hz). **(b) Whole area.**

Figure 6. Example of motion artifact noise reduction.



(c) Noise area (25 Hz). **(b) Whole area.**

Figure 7. Example 25-Hz power noise reduction.

4.7 Comparison with SimGAN Architecture

Our proposed method, NR-GAN, is inspired by SimGAN architecture. Needless to say, the structure of NR-GAN is optimized for mice EEG signals; however, we have to show its advantages comparing to SimGAN. Here, we compared the noise reduction performance between NR-GAN and SimGAN using motion artifact noise.

In this experiment, the property of SimGAN is decided, referring to its original paper [9]. Although the structure is almost the same, we adjusted several layers to make SimGAN suitable for 1-D input and noise reduction tasks. For example, the kernel size in the convolutional layer has changed to 1×100.

After 50 epochs training, we applied SimGAN to noisy EEG signals containing motion artifact noise. The index R_{nr} and R_{sd} were 1000% and 93%, respectively (Table 1), which indicates that SimGAN can not reduce noise at all. Perhaps, this is caused by the structure of SimGAN, especially its output (last) layer. NR-GAN employs a full connection layer, whereas SimGAN uses ResNet block [12] as its output layer. Therefore, it is difficult for SimGAN to change the process according to the frequency components. In this experiment, the target noise mainly consists of frequency components of less than 0.5 Hz, which may be a favorable condition for NR-GAN.

The many types of noise in mice EEG signals have specific frequency components. Therefore, NR-GAN is more effective than SimGAN, especially for noises. Besides, NR-GAN was superior to SimGAN also in terms of computational cost. SimGAN takes three times longer than NR-GAN.

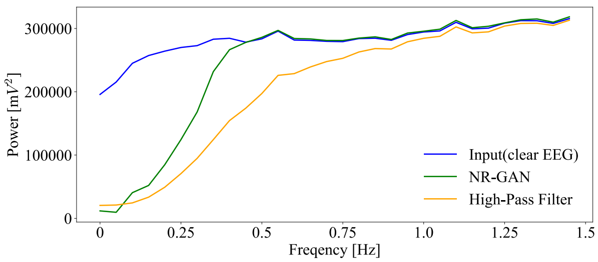
From the above, NR-GAN is thought to be more practical than SimGAN for reducing noise in mice EEG signals.

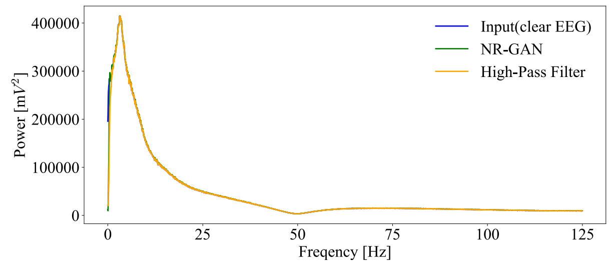
5. DISCUSSION

Using the squared difference between input and output signals as a part of the loss function, NR-GAN aims to locate the noise feature without prior knowledge or records. However, this improvement also causes some limitations of NR-GAN.

First, NR-GAN cannot handle signals containing large noise. In this case, the noisy signals and their signal parts are far apart in the frequency domain. Noise reduction is not correctly implemented because the NR-GAN assumption is not satisfied. In the future, we will clarify the detailed relationship between the signal-to-noise ratio of the input signals and the performance of NR-GAN.

Second, the performance of NR-GAN is easily affected by the value of hyper-parameter α, which is in the loss function of the generator (Eq. 6). Since α controls the amount of noise reduction, it must be set very carefully. The experiment suggests that α also influences the balance of adversarial loss and the L2 norm between input and output signals. In the future, we plan to develop a parameter optimization method based on this balance.





(d) Noise area (0-0.5 Hz). **(b) Whole area.**

Figure 8. Example of motion artifact reduction performed for clear EEG signal.

6. RELATED WORK

6.1 Automated Sleep Stage Scoring

To support basic sleep research, several studies have examined automated sleep stage scoring methods for mice EEG and EMG signals [1] [2]. MASC [2], which is an SVM-based method, achieved a scoring accuracy of almost 95%, which is the same level as manual scoring by experts for clear EEG signals (Table II). However, this method is not robust against the noise in EEG signals, and the accuracy drops by more than 2%. The frequency components between 0 Hz and 30 Hz of mice EEG signals were extracted as feature values. Thus, it cannot handle the EEG signals where the noises include these frequency components. As mentioned above, noises such as motion artifacts are commonly observed in EEG signals. Consequently, this method cannot be used in practical research.

6.2 Deep Learning Model to Reduce Noise in Acoustic Signals

Noise reduction methods for acoustic signals based on a deep learning model have been proposed [7] [8]. Yong Xu et al. [7]. proposed a deep neural network that models the relationship between noisy sounds and their clear sound parts. Then it converts the latter from the former. Also, Michelsanti et al. [8] employed pix2pix architecture for noise reduction. Pix2pix is an extension of GANs, which is very suitable for modeling signal conversions.

Experiments revealed that these proposed methods can reduce various noises such as traffic noise and they are superior to other conventional noise reduction methods.

However, these methods require direct pairs of noisy sounds and their clear sound parts. Hence, they are not applicable to address the issue in this study.

6.3 Other GANs Architecture for Signal Conversion

Several GAN architectures to model signal conversion have been proposed. For example, CycleGAN [13] and Disco-GAN [14] can learn signal conversion without using pairs of input and output signals. CycleGAN and DiscoGAN consist of two GAN architectures to model the signal conversion and its inverse conversion. Thus, the input and output signals have to be in a one-to-one correspondence. In the context of noise reduction for mice EEG signals, the clear EEG signal parts can be associated with multiple noisy EEG signals. Consequently, they are not applicable to address the issue in this study.

7. CONCLUSION

Herein we propose a novel noise reduction method, NR-GAN. NR-GAN is suitable for mice biological signals, especially EEG signals. Unlike conventional noise reduction methods, NR-GAN does not require prior knowledge or records of the noise itself. Thus, training samples can be easily prepared. Consequently, NR-GAN is well suited to reduce noise in biological signals and can be employed in an automated sleep stage scoring system.

The experimental results show that NR-GAN can reduce more than half of the noises commonly observed in mice EEGs without distorting clear signals. Hence, NR-GAN achieves the same level of noise reduction as frequency filters tuned to the noise frequencies by trial and error processes. These results suggest that NR-GAN can work in lieu of frequency filters and improve the efficiency of manual noise reduction.

Future research will work to improve NR-GAN. First, we will evaluate the noise reduction ability using various types of noises, such as white noise. We also plan to improve the structures of the generator and discriminator. For example, incorporating the structure for acoustic noise reduction should enhance our model.

8. ACKNOWLEDGEMENT

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