Region-of-Interest Extraction of fMRI data using Genetic Algorithms

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***Abstract*—Functional connectivity, which is indicated by time-course correlations of brain activities among different brain regions, is one of the most useful metrics to represent human brain states. In functional connectivity analysis (FCA), the whole brain is parcellated into a certain number of regions based on anatomical atlases, and the mean time series of brain activities are calculated. Then, the correlation between mean signals of two regions is repeatedly calculated for all combinations of regions, and finally, we obtain the correlation matrix of the whole brain. FCA allows us to understand which regions activate cooperatively during specific stimulus or tasks. In this study, we attempt to represent human brain states using functional connectivity as feature vectors. As there are a number of brain regions, it is difficult to determine which regions are prominent to represent the brain state. Therefore, we proposed an automatic region-of-interest (ROI) extraction method to classify human brain states. Time-series brain activities were measured by functional magnetic resonance imaging (fMRI), and FCA was performed. Each element of the correlation matrix was used as a feature vector for brain state classification, and element characteristics were learned using supervised learning methods. The elements used as feature vectors, i.e., ROIs, were determined automatically using a genetic algorithm to maximize the classification accuracy of brain states. fMRI data measured during two emotional conditions, i.e., pleasant and unpleasant emotions, were used to show the effectiveness of the proposed method. Numerical experiments revealed that the proposed method could extract the superior frontal gyrus, orbitofrontal cortex, cuneus, cerebellum, and cerebellar vermis as ROIs associated with pleasant and unpleasant emotions.**

I. INTRODUCTION

In recent years, higher brain functions such as recognition and emotion have been studied using noninvasive functional brain imaging systems. Functional magnetic resonance imaging (fMRI) [1], [2] and functional near-infrared spectroscopy (fNIRS) [3], [4] are being used to measure brain activities associated with them. fMRI uses a nuclear magnetic resonance phenomenon to visualize brain functions. Compared with other noninvasive imaging modalities, fMRI has higher spatial resolution. Therefore, fMRI has been rapidly adopted as a measurement method in brain functional studies. fMRI can measure brain activity by capturing changes in cerebral blood flow. The brain replenishes necessary oxygen and saccharides by increasing blood flow in particular areas depending on neural activity. It becomes possible to estimate brain function because blood flow changes are associated with neuronal activity.

There have been many studies to investigate the functions of specific regions based on the theory of functional localization. They have focused on which brain regions activated in response to specific stimuli. We refer to this conventional method as activation study. In emotion studies, brain regions activated while feeling pleasant and unpleasant emotions have been investigated based on activation study [5], [6]; however, comparisons of brain states that considered cooperative relations between brain regions associated with pleasant and unpleasant emotions, have not been performed enough. Nevertheless, the brain does not activate independently in every region. It exchanges information and cooperatively activates among each region. It is known that many regions are involved in some automatic and simple functions, such as facial recognition [7]. Even if the brain regions are spatially separated and not connected directly via nerves, they often cooperatively work. This is referred to as a functional brain network.

In recent years, a functional network analysis method has been proposed and developed [8], [9]. Sala-Llonch et al. [8] used fMRI to measure human brain activity during a memorization task and a resting state, and the functional network was analyzed using a temporal correlation between the brain activities of two brain regions as a connectivity measure. Similarly, Van-Den-Heuvel et al. [9] measured human brain activity using fMRI and investigated a resting-state functional network using graph theoretical analysis. Furthermore, Bullmore and Sporns have revealed that the functional brain network formed a complex network consisted of many nodes and edges [10]. Although they have introduced graph theoretical metrics to quantitatively analyze characteristics of the functional brain network, however, it is difficult to search for all networks because there are many regions in the brain.

Therefore, this paper proposes a method that efficiently searches for more important brain function networks using a genetic algorithm (GA) [11], [12], which is an optimization method inspired by evolutionary processes. In addition, the proposed method estimates the regions of interest (ROI) related to pleasant and unpleasant emotions by extracting an important brain function network to classify pleasant and unpleasant emotions.

II. Proposed method

A. Concept: feature selection for fMRI data using GA

In this section, we describe the concept of our proposing method. The functional network is a connection between brain regions that indicates similar brain activity. Generally, similarity of brain activity, i.e., the degree of coupling between brain regions, is calculated by the correlation coefficient of time-series brain activity data. If a brain region is considered a node and connections between brain regions are considered edges, the functional network is considered a weighted undirected graph. In addition, the correlation matrix between multiple regions can be regarded as an adjacency matrix of such graphs. In this study, connectivity between multiple regions is used as a characteristic vector to classify brain state expressed by a weighted undirected graph. However, it is not realistic to use all regions as the feature vector because there are hundreds of brain regions defined by theory of functional localization. To classify brain state, we can find a brain region related to a specific problem or stimulus by understanding the important connectivity between brain regions. In addition, identifying a brain region related to a specific problem or stimulus will provide new neuroscience knowledge. Thus, this study defines an optimization problem that searches the combination of feature vectors that obtains maximum classification accuracy of the brain state using connectivity between regions as the feature vector. A framework to solve this problem is proposed in this paper.

B. Problem formulation

The target problem can be formulated as the following optimization problem.

1) Design variables: Design variable x_k selects or deselects each element a_{ij} of adjacency matrix A in an weighted undirected graph of functional brain network illustrated in Fig.1. A diagonal component is not selected because its correlation is always 1.0 regardless of given data. In a brain region divided into n units, the number of design variables is $(n^2 - n)/2$ because the adjacency matrix is symmetric. Therefore, the design variables $\boldsymbol{x}$ can be expressed as follows:

$$\boldsymbol{x} = (x_1, x_2, \dots, x_d) \tag{1}$$

$$x_k \in \{0, 1\} \tag{2}$$

In addition, anatomical automatic labeling (AAL) [13], which parcellates the brain into 116 anatomical regions, is used in this study. In other words, $d = (116^2 - 116)/2 = 6670$. How variables are lined up is shown in Fig.1.

2) Objective function: The objective function is an classification accuracy of the data set in the feature space constructed using the selected feature vector, which is defined by a design variable. A combination of feature vectors is optimized such that an classification accuracy with any classifier becomes maximum. The objective function $f(\boldsymbol{x})$ can be defined as follows:

$$f(\boldsymbol{x}) = E_{\text{classification}}(\boldsymbol{x}) \tag{3}$$

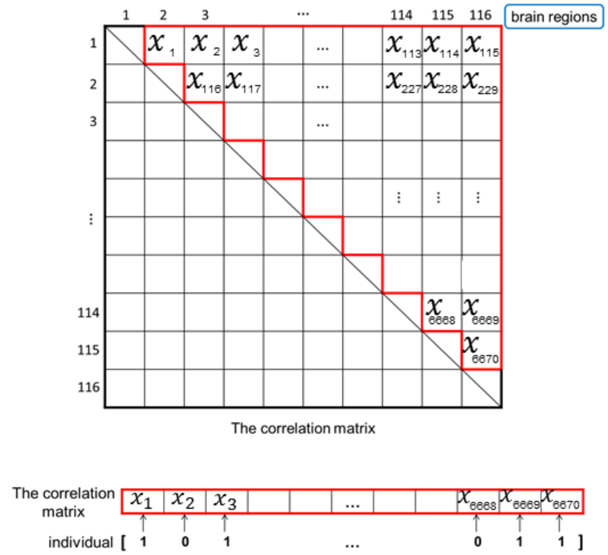


Fig. 1. Representation of the design variables

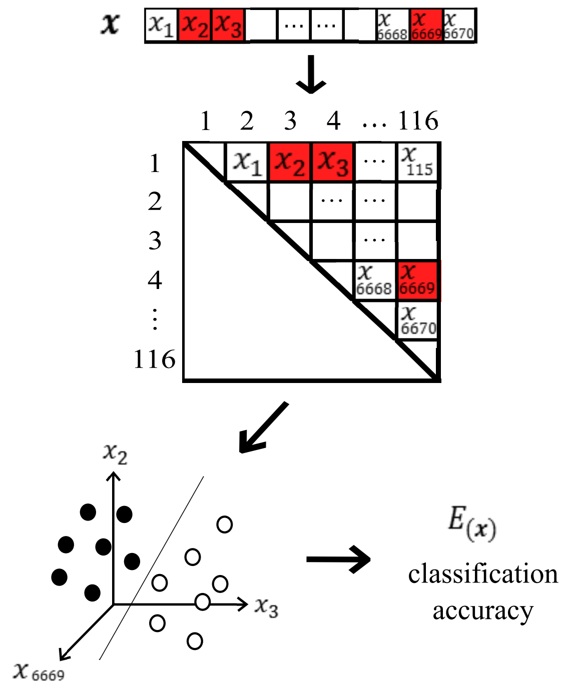


Fig. 2. Procedure of Objective Function Evaluation

If $x_k = 1$, the corresponding element of the adjacency matrix is utilized as a feature vector for the classification. Thus, $E_{\text{classification}}(\boldsymbol{x})$ is an classification accuracy of distinguishing a dataset using all the feature vectors chosen ($\forall x_k = 1$, $k = 1, 2, \dots, d$). This evaluation process is illustrated in Fig.2.

3) Constraints: In this study, our goal is to obtain the highest classification accuracy using as few feature vectors as possible. Therefore, it is expected that the prominent feature vector will be obtained for classification. Therefore, we limit the number of the selected feature vectors as follows:

$$g(\boldsymbol{x}) = \Sigma_{k=1}^{d} x_k - M \leq 0 \tag{4}$$

Here, $g(\boldsymbol{x})$ is a constraint on $\boldsymbol{x}$, and M is the upper limit of the number of feature vector choices. Note that M is set by the user.

4) Optimization problem: From the above, the target optimization problem can be formulated as follows:

$$\text{maximize } f(\boldsymbol{x}) \tag{5}$$

$$\text{subject to } x_k \in \{0, 1\}, \ g(\boldsymbol{x}) \leq 0 \tag{6}$$

C. GA implementation

The optimization problem defined in the previous section is solved using a GA. In this study, we used the GA implemented in Distributed Evolutionary Algorithms in Python (DEAP) library [14].

III. FMRI DATA ANALYSIS BY PROPOSED METHOD

In this study, we conducted an experiment in which pleasant and unpleasant images were shown to subjects. The important functional brain networks for emotion classification were extracted using the proposed method with fMRI data. Moreover, the ROIs associated with pleasant and unpleasant emotions were estimated using these networks.

A. EXPERIMENTAL METHOD

1) Participants: Fifteen healthy right-handed subjects (ten men and five women) participated in this experiment. Their mean age was 22.1 years (standard deviation: 1.3). All participants gave written informed consent to participate in this experiment.

2) Experimental environment: fMRI data were acquired with a 1.5 T Echelon Vega scanner (Hitachi, Ltd., Tokyo, Japan). Functional volumes were collected using a gradient-echo echo-planer imaging (GE-EPI) sequence. We also employed a Rf-spoiled steady state gradient echo (RSSG) sequence to obtain T1-weighted structural images. The MR imaging parameters are shown in TABLE I.

TABLE I
MR IMAGING PARAMETERS

Parameter	functional imaging	T1 anatomical imaging
TR [ms]	3000	9.4
TE [ms]	40	4.0
FA [˚]	90	8
FOV [mm]	240 × 240	256 × 256
Matrix size [pixel]	64 × 64	256 × 256
Thickness [mm]	5.0	1.0
Number of slices	20	194

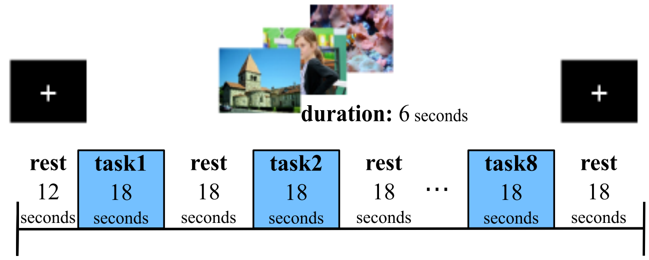


Fig. 3. Experimental design

3) Stimulation image: The Nencki Affective Picture System (NAPS) data set was used for stimulation images in this experiment. NAPS is a data set that includes emotion images used in psychology experiments, and a theme and a valence value (inducibility), arousal value (awakening), and approach-avoidance value (rule) were assigned to each image. Here, the valence represents the degree of pleasant and unpleasant emotion for the image, arousal represents the awakening degree of emotion obtained by looking at the images, and approach-avoidance represents the degree of being drawn into the images [15]. In this experiment, a valence value greater than 5 was used for pleasant images, and a valence value of 2.5 or less was used for unpleasant images. There was a difference between the valence degree of the images and the degree of pleasant which participants feel actually. Therefore, each image was evaluated with seven levels of pleasant emotion by the participants before the experiment was conducted. In this pre-evaluation, pleasant images were evaluated twice. As a result, 24 images with high mean valence values were chosen as pleasant images for use in two experimental sessions. In addition, 24 images were selected randomly as unpleasant images for use in the two experimental sessions. The stimulation images were chosen in these ways because the pleasant emotions were difficult to be exposed while the unpleasant emotions could be easily expressed.

4) Experiment procedure: Brain activity at the time at which pleasant and unpleasant images were presented was measured by fMRI. Fig.3 shows the experimental design. This experiment consisted of two sessions. One session used a block design in which a rest and a task were shown alternately. Each session consisted of four blocks of pleasant task and four blocks of unpleasant task. For each pleasant/unpleasant task block, three pleasant/unpleasant images were randomly presented. The first rest time was 12 s, and the other rest times and the task times were 18 s. A fixation point was displayed during the rest time, and images were displayed for 6 s per image during the task. To obtain the participants' subjective evaluations, the images used in the experiment were evaluated by participants in seven stages after fMRI data collection.

B. ANALYSIS METHOD

1) Extraction of correlation matrix: The initial six images were discarded from analysis in order to eliminate the non-equilibrium effects of magnetization. As a result, 136 images were used for analysis. Functional brain networks were analyzed using Conn [16] in order to analyze the functional connectivity. SPM8 (Welcome Department of Cognitive Neurology) [17] was used to preprocess the fMRI data. All functional images were realigned to correct for head movements, and adjustment between the functional images of the subjects' brains and anatomical images was performed using a least square approach to regress out 6 head motion parameters (3 translations and 3 rotations) implemented in SPM8. Individual brain image was coordinated to match the Montreal Neurological Institute (MNI) standard brain and was smoothed with a Gaussian kernel of 8 mm (full-width half-maximum). Then the image was band-pass filtered (0.008 – 0.09 [Hz]), and the artifacts caused by head movement and the blood oxygenation level dependent (BOLD) signal of white matter and cerebrospinal fluid were regressed out from the BOLD signal of each voxel. The BOLD signal during a task period was extracted to calculate a temporal correlation during the task. The brain region was specified based on AAL [13], and the average BOLD signal for every region was calculated. Finally, temporal correlation between brain regions were calculated, and the population correlation coefficients were estimated by Fisher z-transformation. The correlation matrix (adjacency matrix), which was divided for each brain region, was then extracted. These steps are summarized in Fig.4.

2) Extraction of important functional brain networks: All negative correlation of the correlation matrix extracted became 0, and we analyzed only positive correlation. An important functional brain network for emotion classification was extracted using the proposed method with the correlation matrix. In this study, a support vector machine (SVM) [18] was used for emotion classification. The classification accuracy was evaluated by 10-fold cross validation. The GA was performed with 10 trials with two constraint settings ($M = 5$ and 10), and the extracted functional brain networks were compared. TABLE II shows the SVM parameters. TABLE III shows the parameters of the GA.

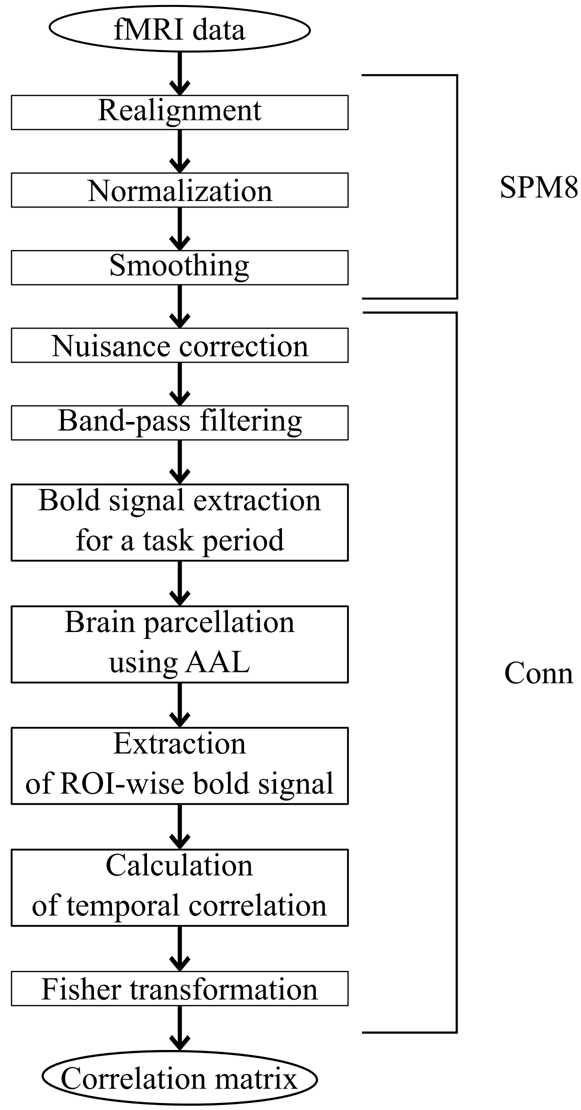


Fig. 4. Extraction step of the correlation matrix

TABLE II
SVM PARAMETERS

Parameter	Value
Label	Pleasant / unpleasant
SVM	C-SVM
Kernel	RBF
Cost	1000
Gamma	0.001
Test	10 fold

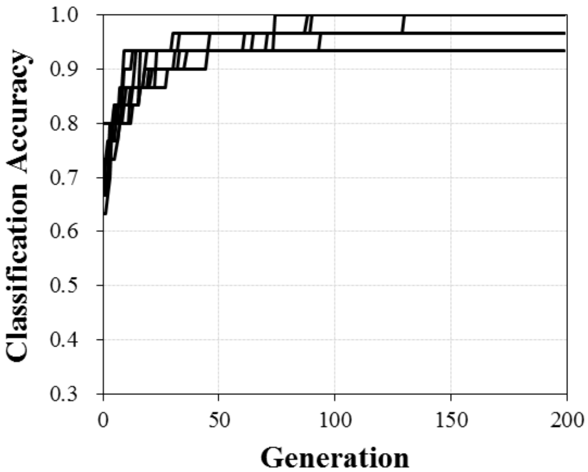
TABLE III
GA PARAMETERS

Parameter	Scale
Population Size	100
String Length	6670
Number of Generation	200
Tournament Size	2
Crossover Rate	1.0
Mutation Rate	1/6670

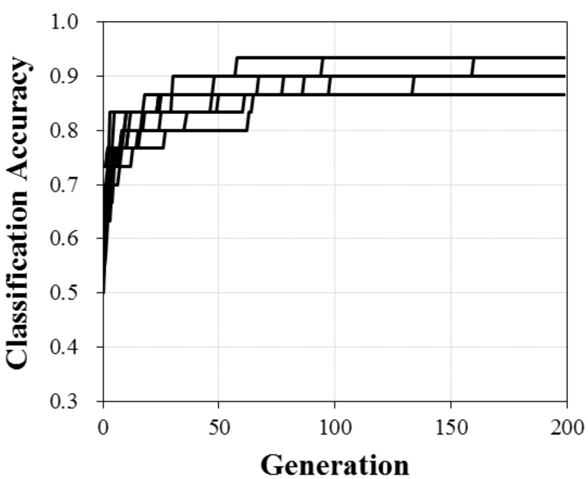
IV. RESULTS

Fig.5 shows the fitness history of the GA runs. The figure indicates that each run of GA converged within 200 generations. TABLE IV and V show the brain regions whose functional connections were selected by GA optimization with the two constraint conditions ($M = 5$ and 10). The classification accuracy for each run is also shown in TABLE IV and V. The best classification accuracy was 100% with $M = 10$, and was 93.3% with $M = 5$. Furthermore, the brain connections (nodes as regions and edges as functional connections) selected with the highest classification accuracy for $M = 5$ and 10 are mapped on the surface of the brain in Fig.6 and Fig.7, respectively.

As can be seen in Fig.6, the superior frontal gyrus (SFGmed and SFGdor), orbitofrontal cortex (ORBsup and ORBmed), cuneus (CUN), cerebellum (CRBL), and cerebellar vermis (Vermis) were extracted in many runs. We define these five regions as important for emotion classification. These regions were also selected with $M = 5$, as shown in Fig.7. In Fig.7(a), the superior occipital gyrus (SOG) was selected with $M = 5$ case instead of CUN with $M = 10$. Two of the five important regions were also selected.



(a) $M = 10$



(b) $M = 5$

Fig. 5. Fitness history

V. DISCUSSION

The proposed method extracted five and ten brain connections at high classification accuracy (93.3% and 100%) among 6670 connections. This indicates that the proposed method is effective for feature selection in emotion classification. Here

TABLE IV

BRAIN REGIONS WHOSE FUNCTIONAL NETWORKS WERE SELECTED BY GA OPTIMIZATION AND CLASSIFICATION ACCURACY ($M = 10$). N/A INDICATES THE SOLUTION WAS NOT OBTAINED.

	trial 1	trial 2	trial 3	trial 4	trial 5
1	ORBmid.R CUN.R	ORBmid.R IOG.R	PreCG.R FFG.L	PreCG.R PCG.L	MFG.R IFGtriang.R
2	ROL.R DCG.R	IFGoperc.L CRBLCrus1.R	ORBsup.L OLF.L	PreCG.R PoCG.L	ORBmid.R PoCG.R
3	OLF.L ORBsupmed.L	CUN.L FFG.L	IFGoperc.L IFGtriang.L	ORBsup.L MFG.L	ORBinf.R FFG.R
4	SFGmed.L CRBL9.R	CUN.R Vermis6	IFGtriang.L PCL.R	ORBsup.R MOG.L	ROL.L CAU.L
5	PHG.L CAU.R	LING.L CRBLCrus1.R	ROL.R PHG.R	ORBmid.L Vermis9	CUN.L SOG.R
6	PHG.R STG.R	MOG.L CAU.L	SFGmed.L MOG.L	IFGtriang.L PHG.R	SOG.L PAL.R
7	LING.L Vermis7	MOG.L Vermis10	ACG.L CRBL9.L	DCG.L PHG.R	SOG.R PAL.L
8	PoCG.R CRBL10.L	FFG.R TPOmid.L	HIP.R ANG.L	PHG.R STG.R	PoCG.R PAL.L
9	TPOmid.L Vermis6	THA.R vermis8	CUN.R vermis8	AMYG.L PUT.R	PCL.L Vermis45
10	CRBL3.L Vermis6	CRBLCrus1.L vermis12	LING.L CRBL6.R	STG.R CRBL45.L	THA.L CRBL3.L
Accuracy [%]	100	100	100	96.7	93.3

	trial 6	trial 7	trial 8	trial 9	trial 10
1	SFGdor.L OLF.L	MFG.L Vermis9	SFGdor.L IFGtriang.R	PreCG.L SMG.L	SFGdor.R CAL.L
2	SFGdor.R TPOmid.R	MFG.R ITG.L	ORBmid.L Vermis9	PreCG.R Vermis6	ORBsup.R SFGmed.R
3	ORBsup.R IOG.L	ORBmid.L Vermis9	ORBinf.R CRBL8.L	MFG.R IFGtriang.R	ORBmid.L CRBL6.L
4	IFGtriang.R ACG.R	ORBmid.R SMA.R	INS.L AMYG.L	ORBmid.L CRBLCrus2.L	ROL.R IOG.R
5	SFGmed.R CRBLCrus1.L	ROL.R CUN.L	CUN.L CRBL6.L	ROL.R TPOmid.R	SFGmed.L Vermis9
6	DCG.R CAL.L	REC.R MOG.L	CUN.R STG.R	OLF.L CRBLCrus2.R	ORBsupmed.L LING.R
7	HIP.L ANG.R	PCG.R CRBLCrus1.L	LING.L CRBL6.L	SFGmed.R Vermis6	CAL.L MOG.L
8	CUN.R STG.R	CUN.R ANG.R	PoCG.L Vermis6	SPG.L STG.L	CUN.R ANG.R
9	LING.L FFG.L	ANG.R Vermis12	CRBLCrus1.R CRBLCrus2.L	TPOmid.L Vermis6	CRBL7b.L CRBL10.R
10	SOG.R CRBL9.R	CRBL6.R CRBL10.R	CRBL6.R CRBL8.R	N/A	N/A
Accuracy [%]	93.3	96.7	96.7	96.7	100

we investigate the reason that the five important regions were derived.

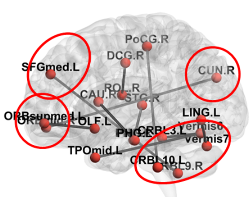
The dorsolateral prefrontal cortex, which is included in SFG, is considered to play an important role in predicting emotion stimulus [19]. Therefore, derivation of SFGmed and SFGdor suggests that the proposed method could find brain regions associated with emotional reaction.

The orbitofrontal cortex is considered related to the evaluation of affective value (valence) and controlling behavior associated with reward and punishment stimuli [20] [21]. Moreover, it has been reported that this region is activated when perceiving beauty in paintings [22]. On the other hand, this region also activates when avoiding harmful stimuli [23].

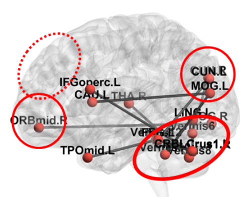
TABLE V
BRAIN REGIONS WHOSE FUNCTIONAL NETWORKS WERE SELECTED BY GA OPTIMIZATION AND CLASSIFICATION ACCURACY ($M = 5$)

	trial 1	trial 2	trial 3	trial 4	trial 5
1	IFGoperc.L	OLF.R	ORBsup.R	SFGdor.R	MFG.L
	SOG.R	PoCG.R	LING.L	MOG.R	SMG.R
2	ROL.R	CUN.R	ORBsupmed.L	ROL.R	MFG.R
	PoCG.L	ANG.R	HIP.R	PoCG.L	IFGtriang.R
3	CUN.R	CUN.R	SOG.R	ACG.L	OLF.L
	ANG.R	TPOsup.R	IOG.L	CRBLCrus1.L	Vermis45
4	SOG.R	IOG.R	IOG.R	PHG.R	CUN.L
	PCL.R	CRBL10.R	HES.R	STG.R	MOG.L
5	IPL.R	PCL.R	TPOmid.L	CUN.R	STG.R
	CRBL10.L	ITG.R	Vermis6	Vermis6	Vermis10
Accuracy [%]	86.7	90.0	93.3	93.3	90.0

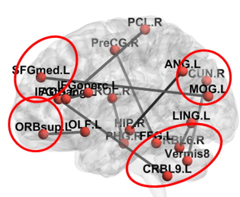
	trial 6	trial 7	trial 8	trial 9	trial 10
1	ROL.R	ORBmid.L	MFG.L	PreCG.L	ORBsup.R
	SMA.R	Vermis7	CRBL10.R	ACG.R	SOG.L
2	ROL.R	IFGoperc.L	INS.R	SFGdor.R	ORBmid.L
	Vermis6	PUT.L	SMG.L	TPOmid.R	Vermis9
3	REC.L	PHG.R	PCG.L	INS.R	REC.L
	HIP.L	STG.R	PoCG.L	SMG.L	CRBL3.L
4	DCG.R	LING.L	CUN.R	CUN.R	INS.R
	SMG.L	CRBL6.L	ANG.R	ANG.R	SMG.R
5	LING.R	ANG.R	MTG.R	CRBL45.R	CUN.L
	CRBL6.L	PCUN.R	CRBL8.L	CRBL6.R	MOG.L
Accuracy [%]	86.7	93.3	90.0	90.0	86.7



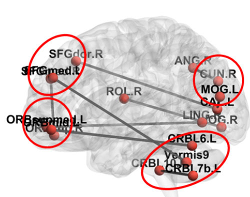
(a) trial 1



(b) trial 2



(c) trial 3

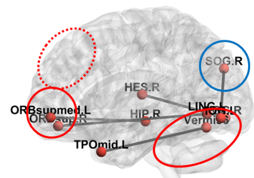


(d) trial 10

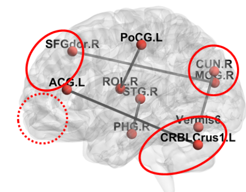
Fig. 6. Functional brain networks and ROIs ($M = 10$; accuracy 100%)

Therefore, it is reasonable that ORBsup and ORBmed were extracted by the proposed method because they are associated with emotional response.

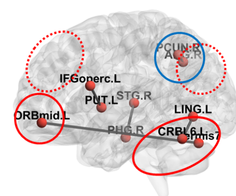
CUN receives and processes visual information and plays a key role in primary visual processing. Moreover, it is associated with inhibitory control in bipolar depression patients [24]. In Fig.7(a), SOG replaces CUN; however, it has been reported that SOG activation is observed more in patients suffering depression than healthy subjects [25]. Thus, both CUN and SOG are extracted as ROIs because they are associated with emotion control.



(a) trial 3



(b) trial 4



(c) trial 7

Fig. 7. Functional brain networks and ROIs ($M = 5$; accuracy 93.3%)

It is assumed that CRBL and Vermis were extracted because they are associated with emotion control and awareness of negative emotion [26] [27]. Moreover, in Fig.6(b), we assume that the highest classification accuracy was obtained by choosing many regions around the cerebellum in addition to three important regions.

On the other hand, in Fig.7(c), only two important regions were selected. However, precuneus (PCUN), which integrates emotion and awareness and generates pleasant emotions [28], was extracted. As a result, high classification accuracy of 93.3% was obtained.

From these observations, the effectiveness of the proposed method has been demonstrated.

VI. CONCLUSION AND FUTURE WORK

In this study, we have proposed an automatic ROI extraction method for functional brain networks measured by fMRI. The proposed method explores the best brain regions in order to classify predefined brain states, such as pleasant and unpleasant emotions, using a GA. Through GA optimization, the binary value, which indicates whether each feature vector (correlation coefficient between the time series MRI signals of two brain regions) is used for classification, is used as a design variable. Combinations of brain regions were optimized to maximize the classification accuracy of the brain states in the feature space constructed by the selected feature vectors. The number of feature vectors was constrained to a predefined value. To verify the effectiveness of the proposed method, fMRI data measured during pleasant and unpleasant emotions were used. Two brain states were classified, and the ROIs for their classification were extracted. Through the experiments we could find the five important ROIs: the superior frontal gyrus (SFGmed and SFGdor), orbitofrontal cortex (ORBsup, ORBmed), cuneus (CUN), cerebellum (CRBL), and cerebellar vermis (Vermis). We found that these five regions were associated with emotional functions, and the classification accuracy obtained using these only five ROIs was high (93.3%). These findings indicate the effectiveness of the proposed method for ROI determination of the functional brain networks. Further studies focused on improvement of optimization by GA (e.g., regarding constraint handling, crossover method, parameter configuration of GA, and multi-objective optimization for classification accuracy and number of features), deviations of optimized results with more than 10 runs, validations in other brain activities, and a comparative study with other feature extraction methods are necessary to ensure the effectiveness of the proposed method. They will be investigated in our future work.

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