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Multivariate pattern analysis (MVPA) is a recently-developed approach for functional magnetic resonance imaging (fMRI) data analyses. Compared with the traditional univariate methods, MVPA is more sensitive to subtle changes in multivariate patterns in fMRI data. In this review, we introduce several significant advances in MVPA applications. We discuss the various combinations of algorithms and parameters in different problem settings. The limitations and the critical questions that need to be addressed in future research are also discussed.

fMRI; pattern recognition; computational biology

Unlike the traditional fMRI studies that mainly focus on mapping the magnitude of changes in the blood-oxygen-dependent level (BOLD) signal in various brain areas and during different task paradigms, a novel analytical approach to fMRI data, multivariate (or multi-voxel) pattern analysis (MVPA), aims to extract information from subtle voxel-wise activation patterns, and has attracted increasing attention^[1-7]

or decoding, because the activation of multiple voxels from fMRI data is treated as a pattern and this method aims to reveal information encoded in this pattern^[8,9].

Specifically, MVPA considers each pattern (referred to as a sample) consisting of n voxels as a vector in an n -

dimensional space. A set of samples (training-set) from different experimental conditions or brain states and then they are tested with another independent set of samples (test-set) to predict which conditions they are associated with. The accuracy of the prediction is referred to as the generalization performance.

Since the number of samples is usually less than the number of dimensions in fMRI data, certain algorithms featuring this case, such as supporting vector machine (SVM), are widely used.

Due to its multivariate nature, the MVPA approach is sensitive to differences in the voxel activation patterns between different brain states or representational contents^[9]. It takes account of the relative activation changes across the voxels in patterns. In this sense, traditional univariate

methods can be viewed as a special case that aims to detect voxels significantly changing (passing a statistical threshold)

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in the same direction^[8].

practice in univariate methods is to smooth and average the activation of the voxels, which may potentially cancel out the information encoded among the voxels. MVPA preserves more information in fMRI data by extracting information from patterns of activity across multiple voxels. One striking example is from Kamitani & Tong^[10], in which the authors demonstrated the capacity of MVPA to decode eight perceived orientations in early visual areas. Furthermore, they showed that attention strongly biased the orientation preference of the voxels. Such findings

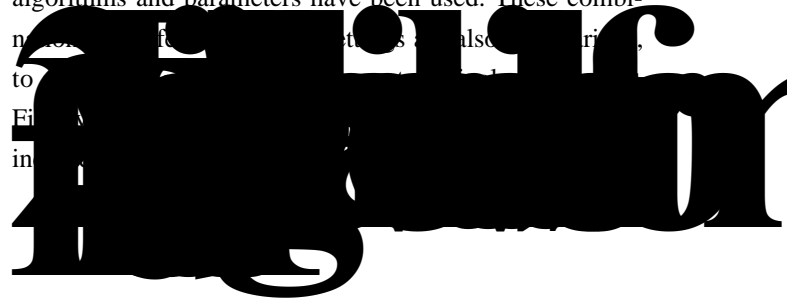
because the size of the voxel in fMRI data is usually much larger than the scale of the orientation-selective columns in early visual cortex, and thus the effects from neuronal populations with different orientation preferences are mixed together and hard to detect in a single voxel.

MVPA has been widely used to accurately predict (decode) behavioral variables encoded in a neuronal system^[2]. The term ‘MVPA’ is therefore interchangeable with ‘MVPA decoding’ in many circumstances. However, the concept of treating fMRI data as multivariate patterns has the same^[11]: “showing that one decode activity in the visual cortex to classify (above-chance) a subject’s percept is exactly the same as demonstrating significant visual cortex responses to perceptual changes”. Indeed, recent MVPA studies primarily aimed to recover multivariate patterns carrying information on behavioral variables, and several sophisticated methods (e.g., cross-condition classification and representational similarity analysis) have been proposed to achieve this end.

Applications of the MVPA have rapidly developed, covering studies of neuronal mechanisms in various domains, such as perception^[12–17], learning and memory^[18–21], language^[22], intention^[23], decision-making^[5,24–26], emotion^[27–30], and mental disorders^[31–33]. Instead of serving as

(see Pereira^[34], an excellent reference for this purpose), this review attempts to give a general introduction

to recent promising developments branching off from the original idea of treating fMRI data as multivariate patterns. We therefore classify the methods into two main categories according to their primary aims: methods that aim to accurately decode behavioral variables or identify/reconstruct stimuli (Sections 2 and 3), and those for identifying the brain activity patterns that encode the behavioral variables (Sections 4–6). Their features are illustrated with a few recent representative studies. Furthermore, with the rapid development of MVPA approaches, various combinations of algorithms and parameters have been used. These combinations have also been used to

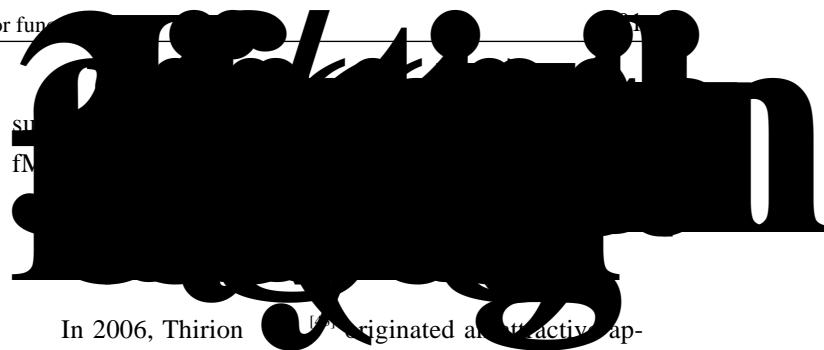


Besides its ability to detect spatially distributed effects, MVPA provides a quantitative way to infer the predictive power of the spatial patterns of brain activity in depth. Recent studies on decoding spatial^[35] and episodic^[18] memory in the human hippocampus have clearly demonstrated the applications of MVPA and provided promising results. In an interactive game that requires a subject to navigate between four arbitrarily chosen target positions, MVPA was applied to the voxels within the hippocampus and the wider medial temporal lobe (MTL) in a searchlight manner^[3] (see ‘Section 5 Searchlight MVPA’ for details) to search for local voxel activation patterns that carried predictive information about where the subjects were. The significance of the searchlight maps was assessed by nonparametric statistical tests based on permutations of the condition labels of the samples. As a result, the position of a subject within this virtual-reality environment was accurately decoded solely from the pattern of activity in the hippocampus, even when the visual input and the task were held constant. The authors also reported a dissociation of the responses in the

hippocampus from those in the parahippocampal gyrus, suggesting their different roles in navigation^[3].

The same group further extended that study by predicting which clip of episodic memory a person is recalling^[18]. Compared to the simple virtual-reality environment, human episodic memory is much richer in content. Intriguingly, different episodic memory clips were distinguishable merely from the activity patterns in some hippocampal regions, suggesting that the neuronal traces of episodic memories are stable (and thus predictable) even over many re-activations. These serial studies have important implications for understanding how information is represented within neuronal populations in the human hippocampus. Such findings were not observed using univariate approaches with fMRI data. Technically, the latter study is an excellent example of applying MVPA-searchlight feature selection to an fMRI dataset. Importantly, a three-split regime of the entire dataset is necessary in such applications. That is, one needs to first split the dataset into a training-set and a test-set, and perform the MVPA-searchlight feature selection only with the training-set to avoid circular reasoning issues^[36]. To do this, one needs to further split the training-set into a sublevel training-set and test-set.

Besides decoding the stimuli from the fMRI signal, MVPA has also been used to make accurate predictions about the behavioral characteristics of subjects. One typical example is by Dosenbach *et al.*, who predicted individual maturity from the connectivity pattern across multiple brain regions^[37]. In this study, supporting vector regression (SVR) was used to predict a continuous maturity index derived from the functional connectivity across 160 brain regions. The “importance” of each connection in the prediction was also reported, reflecting the key features related to brain maturity. Moreover, MVPA has been successfully used to distinguish patients with mental disorders from healthy control subjects^[38-42]. One typical study by Zeng *et al.*^[41] used the functional connectivity across 116 anatomical regions covering the entire brain to classify major depressive disorder (MDD) patients from healthy control subjects. With sophisticated techniques, the accuracy of identifying MDD patients reached 100%,



In 2006, Thirion *et al.*^[43] originated an “active” approach that developed MVPA towards “mind-reading”. In their study, the retinotopy of the visual cortex was used to infer the visual content of real or imagined scenes from the brain activation patterns elicited. They successfully reconstructed a pattern imagined by the subjects. Later, Kay *et al.*^[44] developed a more generalized decoding method based on quantitative receptive-field (RF) models that characterize the relationship between visual stimuli and

scale natural images were modeled with linear combinations of a set of elementary images (basis images) containing *N* pixels^[45,46]. By recording the activity in the early visual cortex with fMRI when the subject was viewing a large set of natural images, relationships (RF model) between the activation of each voxel and the basis images were computed (by solving linear equations). Combining the estimated RF models from all the voxels and their activation evoked by viewing natural images, the authors identified what the subject saw from a much larger image set. The clever connection of the RF model to the multi-voxel activation pattern allows this approach to “read out” images that have never been viewed by the subject. From a methodological perspective, this approach differs from multivariate pattern classification in that it requires an explicit model to connect the spatial patterns of the stimuli that are never used in the tuning parameters of the model.

With a similar strategy, Miyawaki *et al.*^[47] showed precisely reconstructed images from the early visual cortex, and suggested that if a perceptual state can be expressed by a combination of elemental features, a modular decoder can be trained for each feature with a small number of samples, but their combination can predict numerous states including those that have never been presented.

Meanwhile, Mitchell^[48] presented an approach to “read out” the words the subject was thinking of. They modeled the meaning of words with a set of intermediate semantic features (basis words), and determined the relationships from a large corpus of texts. After connecting this semantic model to the activation patterns of fMRI data, they were able to predict the words in the subject’s mind by linearly combining the fMRI signatures with each of the basis words. Following these studies, more sophisticated models have been proposed to better reconstruct the image^[49] or generalize the strategy to decode more complicated contents of the mind^[14,50].

4 Cross-condition pattern classification

Stepping forward from the classic MVPA approach that addresses whether the brain representations of different mental processes are separable, cross-condition pattern classification aims to verify whether the information encoded in spatial patterns is consistent across different con-

ditions. In this approach, subjects are asked to distinguish two or more mental states with spatial patterns obtained in one condition (or task), while their generalization performance is tested on spatial patterns observed in another condition (or task). An excellent example demon-

strates this approach is from Meyer^[51], who demonstrated that the subjective experience of sound, in the absence of auditory stimu-

lation, can be decoded from the activity of the primary auditory cortices in humans. In this study, subjects viewed nine sound-implicating, but silent, visual clips belonging to three conceptual categories, animals, musical instruments,

and objects. The authors showed that the classifiers trained using the spatial patterns for two videos per category could accurately classify a third video into the correct category and that the classifiers trained with the spatial patterns for the silent video clips were able to classify the corresponding sound into animal or object categories. These results provide

strong evidence for the role of the primary auditory cortex. More strikingly, using this method, Knops^[52] demonstrated a successful transfer of mul-

ti-variate patterns across completely different experimental conditions by showing that the MVPA classifiers trained to distinguish eye movement direction (left–right) could accurately classify arithmetic operations (subtraction–addition).

In the same vein, we used the cross-condition pattern classification approach to determine whether the spatial patterns in the visual word form area (VWFA) are consistent across different attention levels^[17] and different types of character (Chinese and Korean^[53]). The spatial patterns in category-selective visual areas such as the fusiform face area (FFA) and the para-hippocampal place area (PPA) were shown to be less consistent at a lower than a higher attention level^[54]. To further determine whether the attention level modulates the spatial representation of stimuli in these category-selective regions (FFA and VWFA), we

tested the spatial patterns in the low-attention condition and tested their performance with the spatial patterns in the high-attention condition. As a result, we found that the classification accuracy was higher than chance-level. More intriguingly, when increasing the contrast-to-noise ratio (CNR) of the spatial patterns in the low-attention condition, we found that the accuracy of the cross-condition classification kept increasing until it achieved

high accuracy both with the spatial patterns under the high-attention condition^[17]. This provided innovative evidence for stable category-selective spatial representations in the VWFA. With a slightly different implementation of the cross-condition pattern classification, we also demonstrated that the similarity of the spatial patterns in the VWFA representing Korean and Chinese characters was as high as that between Chinese characters^[53]. This means that Chinese and Korean characters may be processed as a single visual category in Chinese-Korean bilinguals.

The above examples demonstrate that cross-condition classification can determine whether the neuronal representations of different stimuli are highly similar. To answer this question in a conventional way, the only method is to compare the over-

all magnitude and the spatial location/extent of the activation. In this multi-classification, the CNR may be a better metric to help to further understand the performance of the multivariate

To detect brain regions that carry information about stimuli, researchers have developed a searchlight MVPA approach based on spatial filtering of the fMRI data^[3,55-57]. The basic idea is to apply MVPA to classify stimuli within the local neighborhood around each voxel on the image, and assign the performance metric of the MVPA to the center voxel. Exploiting its information-mapping nature, a number of studies have applied this approach to a vast range of research topics^[15,16,22,25,26,30,58-64]. On the other

most informative in distinguishing stimuli (see ‘Section 7 Summary of MVPA algorithms and parameters’). A recent novel application of searchlight MVPA to classify obsessive-compulsive disorder (OCD) patients and healthy control subjects was demonstrated by Weygandt^[64]

MVPA at the individual level to classify brain responses evoked by fear-eliciting and neutral pictures. Thus, the classifiers assigned a discrimination value to each voxel. The authors then applied searchlight MVPA to local patterns of discrimination values to classify OCD patients and healthy control subjects, yielding 100% accuracy in the experimental design. In this study, despite the complexity of the task, the searchlight MVPA was able to distinguish between the two groups with 100% accuracy^[64]. This result suggests that searchlight MVPA is a powerful tool for identifying brain regions that carry information about stimuli.

To generalize MVPA a broader scope, Kriegeskorte^[66] proposed an approach aiming to bridge the three branches of systems neuroscience: behavioral experimentation, brain-activity experimentation, and computational modeling, which is termed representation

similarity analysis (RSA). The core idea of this approach is generalizing the concept of voxel activation pattern to a more abstract similarity pattern that can be measured

are two levels of pattern analysis in this approach. At the first level, a representational dissimilarity matrix (RDM) is constructed to reveal the similarity (or dissimilarity) of the activity patterns evoked by different stimuli or predicted by computational models. At the second level, the relationships between the RDMs from multi-channel measures are tested with nonparametric statistics. The approach allowed the use of RDMs to quantitatively relate brain activity patterns to behavioral data. In this study, the RDMs from the cortex and the behavioral data were compared to identify the relationship between brain activity and behavior.

With the rapid development of MVPA, various techniques in the machine-learning field have been introduced into the analysis of fMRI data, yielding various combinations of algorithms and parameters used at stages of different analyses. In Table 1, we list different combinations of ‘features’, ‘feature selection methods’,

using MVPA (most published in 2011 and 2012). The term ‘features’ stands for the metrics that compose the patterns in the analysis. The most common features used in MVPA are either raw data volumes or regression coefficients

usually from studies using block or slow event-related studies^[17,60,64,67], while the latter choice can be found in fast event-related studies^[21,62,68,69]. Another alternative feature is

functions^[58,59]. In MVPA studies aiming to classify subjects into different groups, the choice of features is much wider, including but not limited to raw fMRI data^[40], grey matter density^[70], volumetric brain morphometry^[71], and functional connectivity measures^[37,41]. The ‘feature selection methods’ are used to reduce the number of variables (dimensionality)

		selection methods			
of stimuli	[67]	in block		cross-validation	-test
	[25, 58]		localizer	cross-validation	-test
	[60]			cross-validation	
	[15, 16, 22, 30, 59, 61, 72]				-test
	[68]				-test
	[62]				-test
	[21]				-test
behavior metrics					
of subjects	[73]	morphometry	multivariate		
			MRMR		
	[41]	across 116 brain regions	correlation	cross-validation	
	[37]	across 160 brain regions	out SVC		
	[40]				
	[70]			cross-validation	
Cross-task	[17]				-test
	[53]				-test
	[63]				-test
	[15]				-test
	[69]				-test

Most studies either used separate functional localizers to define features or directly applied searchlight MVPA to reveal the features. Much more sophisticated techniques from machine-learning theories have been applied in studies aiming to classify subjects (see Table 1 for details). For ‘classifiers’, the mainstream is the SVM,

a small number of samples. Besides the supporting vector classifier (SVC), some studies used supporting vector regression (SVR) to predict continuous scales in behavioral performance and demographic measures. Instead of the

can be a “predictor” of daily behavior that may contain up-to-infinite possibilities. A few studies simply used

patterns^[15,53]. The advantage of this method is that the relationships between patterns from each trial are clearly revealed. Therefore, this is more suitable for investigating

brain regions. The ‘validation schemes’ are used to assess the performance of the trained classifier. To train the classifiers with maximal samples, most studies chose to apply the ‘leave-one-out cross-validation’ scheme, which uses $n-1$ of the total

test it with the one sample left. Depending on the features used in the studies, ‘leave-one-run-out’ and ‘leave-one-block-out’ schemes have also been used. To evaluate the

significance of the MVPA accuracy, a permutation test is applied to the data. The null hypothesis is that the classifier is no better than random. The p-value is calculated as the proportion of times the classifier performs better than random in the permutation test.

MVPA has been deemed sensitive in detecting information encoded in multivariate patterns of brain activity. However, some recent studies have urged caution when interpreting MVPA results. For example, a study by Kamitani and Tong^[72] showed that MVPA is able to decode orientation performance in the early visual cortex even from neuronal structures smaller than the voxel size in

fMRI images. Conversely, a recent study showed evidence for a topographic map of orientation-preference in human V1 at a much coarser scale, suggesting that the successful MVPA decoding of orientation still depends on the information revealed in fMRI voxels^[73]. Another common

patterns of activation to infer the engagement of specific mental processes^[74,75]. For example, highly sensitive

house stimuli based on activation patterns in the primary visual cortex (V1), even though this region is not known to have category-preference. With knowledge about V1, researchers can attribute the results to the subtle differences in the basic physical properties in the stimuli.

However, this inference is risky when knowledge is unavailable^[76]. From a more substantial perspective, Logothetis^[77] stated that the presence of “voxels selective to two different stimuli attributes could be potentially detected by modern classifiers, yet the existence of two types of patterns does not necessarily imply the existence of two different types of neural populations”. Thereby, an important question for future methodology research is how to identify patterns that not only are informative but also are really used to process the stimuli.

of extracting information from data, an interesting ques-

formance^[8]. For example, different classifiers encode the feature covariance in different ways. Linear discrimination analysis and quadratic discriminant analysis explicitly model the covariance of the features, while the logistic

esting to see how this difference affects their performance in different problem settings. This is not merely a technical question, because performance differences between classifiers for our understanding of the organization of neuronal encoding.

In conclusion, we have summarized both the applica-

tion and technical aspects of recent advances in MVPA methodologies. Despite some unsolved problems and controversies, the development of MVPA has allowed us to better exploit the information in fMRI signals. The methodology will be developing rapidly, and we believe it will provide further insights into the understanding of the human brain.

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