AN EVOLUTIONARY APPROACH TO MULTIVARIATE FEATURE SELECTION FOR FMRI PATTERN ANALYSIS

Malin Åberg, Line Löken and Johan Wessberg
Institute of Neuroscience and Physiology, Göteborg University, Box 432, SE-40530 Goteborg, Sweden

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Abstract: Multivariate pattern recognition has recently gained in popularity as an alternative to univariate fMRI analyis, although the exceedingly high spatial dimensionality has proven problematic. Addressing this issue, we have explored the effectiveness of evolutionary algorithms in determining a limited number of voxels that, in combination, optimally discriminate between single volumes of fMRI. Using a simple multiple linear regression classifier in conjunction with as few as five evolutionarily selected voxels, a subject mean single trial binary prediction rate of 74.3% was achieved on data generated by tactile stimulation of the arm compared to rest. On the same data, feature selection based on statistical parametric mapping resulted in 63.8% correct classification. Our evolutionary feature selection approach thus illustrates how, using appropriate multivariate feature selection, surprising amounts of information can be extracted from very few voxels in single volumes of fMRI. Moreover, the resulting voxel discrimination relevance maps (VDRMs) showed considerable overlap with traditional statistical activation maps, providing a model-free alternative to statistical voxel activation detection.

1 INTRODUCTION

We recently showed that the evolutionary algorithm is an effective tool for classifier and feature subset optimization for single-trial discrimination of electroencephalography (EEG) (Åberg and Wessberg, 2007). In this study, we extend our approach to functional magnetic resonance imaging (fMRI).

Similar to the EEG, fMRI data is non-stationary, multivariate, noisy and very high-dimensional. These properties are typically dealt with by applying statistical parametric mapping (SPM) methods, where the average level of voxel activity is computed offline in a univariate, model-based fashion (Friston et al., 1994).

However, by being univariate, the SPM-based method is not appropriately sensitive to cognitive information that is encoded in the combined effect of numerous voxels. Pattern recognition approaches, on the other hand, provide tools that are multivariate, that is, based on the combined effect of several voxels. Moreover, trained pattern classifiers can be used in situations that demand real-time results, including online detection and identification of brain patterns. Several recent studies have established the feasibility of multivariate methods (Norman et al., 2006; Haynes and Rees, 2006).

Due to the vast spatial dimensionality (in the order of tens to hundreds of thousands of voxels), efficient feature selection has been identified as a major challenge in the development of pattern classification algorithms for fMRI (Norman et al., 2006). In this study we therefore present an algorithm based on evolutionary techniques, proven effective in numerous optimization areas, including feature subset selection (Hussein, 2001; Reeves and Rowe, 2002), that detects which number and combination of individual voxels that optimally carry information relevant to a stimulus. These voxels are used as features in a classifier, and we have chosen to use rudimentary multiple linear regression (MLR) to show that even a very simple classification scheme can detect and distinguish relevant cortical information in noisy fMRI data given proper feature selection.

Our algorithm also generates a voxel selection

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frequency ranking, illustrating how relevant each voxel is in discriminating between given patterns. This ranking can be presented slicewise as a two-dimensional image, or what we propose to call a voxel discrimination relevance map (VDRM), showing the anatomical location of brain regions involved in the stimulus.

In this study we thus aim to evaluate the effectiveness of the evolutionary approach in automatic voxel subset selection, aspiring to improve single-volume discrimination of cortical patterns. We also explore how the results compare with established statistical methods for detecting activated areas of the brain. The data is acquired from a tactile stimulation experiment where the physiology of brain activation is reasonably well understood (Olausson et al., 2002). Part of the findings have been previously presented in abstract format (Åberg et al., 2006).

2 METHODS

Data Acquisition and Paradigm

A 1.5 T fMRI scanner (Philips Intera, Eindhoven, Netherlands) with a sense head coil (acceleration factor 1) and a BOLD (blood oxygenation level dependent) protocol with a T2*-weighted gradient echo-planar imaging sequence (TR 3.5 s; TE 51 ms; flip angle 90°) was used to acquire brain scans in six healthy human volunteers. The scanning planes (6 mm thickness, 2.3 x 2.3 mm in-plane resolution) were oriented parallel to the line between the anterior and posterior commissure and covered the brain from the top of the cortex to the base of the cerebellum. Each scan volume contained 25 slices at a spatial resolution of 128 x 128 voxels.

Following cues from the scanner, an experimenter stroked a 7 cm wide soft brush over a 16 cm distance in the distal direction on the right arm. Each brushing, lasting 3.5 seconds (one single scan volume), was repeated three times and rest periods of equal duration were interleaved. The Regional Ethical Review Board at Goteborg University approved the study, and the experiments were performed in accordance with the Declaration of Helsinki.

Data Pre-processing

Data pre-processing was carried out with software developed at the Montreal Neurological Institute (Montreal, Canada; available at http://www.bic.mni.mcgill.ca/software/). Functional data were motion corrected and low-pass filtered with a 6 mm full-width half-maximum Gaussian kernel.

Slices and voxels not containing brain matter were discarded. To correct for hemodynamic delay, the remaining data (slices 2-20) was shifted by one volume. An arm/rest data set containing 456 3.5 second patterns of each class was formed per subject and slice, and the samples were linearly normalized to the range [0 1]. The first 80% of the patterns were randomized and used in the evolutionary process (training data). The remaining volumes were exclusively used in estimating the prediction accuracy on already optimized classifiers (validation data).

Feature Selection using Evolutionary Algorithms

An evolutionary algorithm is an optimization scheme inspired by Darwinian evolution (Reeves and Rowe, 2002). The aim of the algorithm in this study is to select a limited number of voxels that, in combination with a classifier, are maximally optimal in discriminating between the brain states induced by brushing on the skin compared to rest.

Tournament selection is used here, where, for each parent, a subset of individuals is randomly chosen from the population and the fittest of these is selected. The tournament size is set to a third of the total population size. Reproduction is asexual, meaning that the offspring is identical copies of the parents.

The fitness is computed as the proportion of correctly classified patterns using multiple linear regression. In order to avoid overfitting, the classifier parameters are established on the training data, whereas a designated 25% of the training data (termed testing data) is used for fitness computation.

The only mutation operation is substitution of a voxel in the individual voxel subset with another, unused voxel. The frequency of mutation is regulated by a constant mutation rate parameter.

Due to the stochastic nature of evolutionary algorithms and the low signal-to-noise levels in the data, the algorithm is unlikely to evolve the same voxel subset at every attempt. To achieve robust results, the algorithm is thus run numerous times.

The algorithm was implemented in Matlab (The Mathworks, Massachusetts, USA) and C on a standard PC by one of the authors (M. Åberg).

Brain State Discrimination Performance

The prediction accuracy was evaluated on the validation data using the classifier and voxels from the run that achieved best results on the training and testing data. A discrimination accuracy of 50% corresponds to chance.

For comparison, the prediction accuracy using the voxels with highest activation according to a statistical parametric mapping (SPM) method was also determined. To this end, a statistical reference analysis was performed on the training data (Worsley et al., 2002).

Voxel Discrimination Relevance Maps

By aggregating the best feature subsets from each algorithm run a voxel discrimination relevance ranking, specifying the number of times each voxel has been selected, can be obtained. This can be presented as a slicewise two-dimensional voxel discrimination relevance map (VDRM).

In order to mimic a classic block-design study for comparison with the univariate SPM approach, all data were used in the training process and there was no prediction involved when generating the VDRMs.

3 RESULTS

Brain State Prediction Performance

The classification algorithm was applied to all subjects individually using five voxels and 500 runs. The prediction accuracies are well above chance (figure 1); a subject mean maximum prediction accuracy of 74.34% (range 65.79%-81.58%) was achieved. Using the five most active voxels as judged by the SPM analysis, the subject mean maximum prediction accuracy was significantly lower at 63.81% (Wilcoxon, p=0.031; range 59.21-73.68%). Random classification results in a prediction rate of 50%. Measuring the prediction success in terms of information bits (Krippendorf, 1986; Laubach et al., 2000), the difference between methods is even more apparent: the SPMt-based subject mean result is 0.094 bits (range 0.025-0.22 bits), whereas the EA-based approach achieves more than the double at 0.21 bits (range 0.077-0.32 bits).

The primary and secondary sensory cortices (SI and SII), expected to be activated by tactile stimuli, are approximately found in slices 4-7 and 11-12 (slice numbers in the dorsal-ventral direction). As shown in the bar chart in figure 2, the subject mean prediction accuracies obtained in these slices are markedly higher than in less relevant slices. Interestingly, the prediction trend is clearly similar to the behavior of the highest $|SPMt|$-value, a measure of brain activation (figure 2). It should be noted, however, that all data is analyzed individually in native space rather than at group level and that any anatomical congruence between subjects is approximate at best.

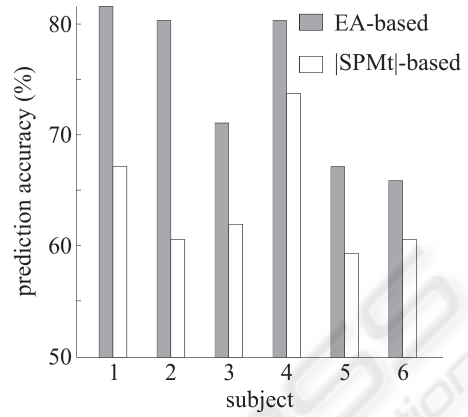

Figure 1: Brain state prediction accuracies for all subjects, as evaluated on the validation data set using the five best voxels and corresponding classifiers obtained after 500 training runs. The prediction accuracy using the five most activated voxels according to SPMt computations of the training data is also shown. The level of chance is 50%.

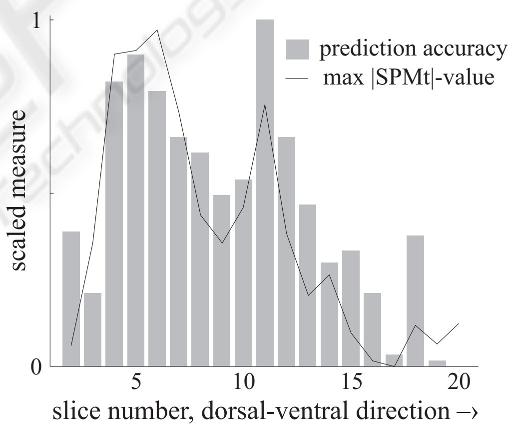

Figure 2: The subject mean brain state prediction performance and maximum $|SPMt|$-values per slice. The two variables show high correlation, and slices with voxels where a BOLD response was expected (SI: slices 4-7, SII: slices 11-12) show consistently higher values. The measures have been scaled to the range [0 1] within subjects to emphasize trends.

Voxel Discrimination Relevance Maps

The VDRMs also show striking visual similarity to the SPMt (figure 3), although the VDRMs appear less noisy overall. SI (slices 5-6), for example, is detected in the SPMt as well as in the VDRM. Similarly, the location of SII (slices 11-12) and also the insular cortex (slices 11), to which unmyelinated tactile afferents project (Olausson et al., 2002), is clear from either

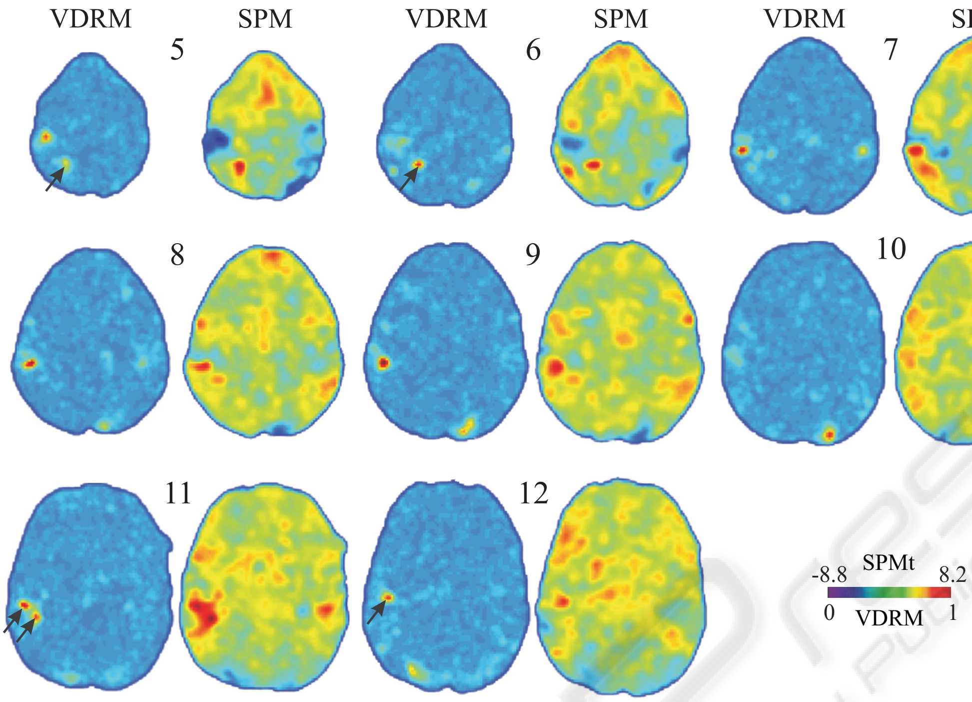

Figure 3: Voxel discrimination relevance maps for subject one, generated using five voxels over 500 runs, with corresponding SPMts. The VDRMs and SPMts are clearly correlated. The right side of the images corresponds to the right side of the brain.

map. The SPMt also suggests several activated areas that are not found in the VDRM. It should be noted, however, that the SPMt maps are not thresholded, and that all voxels with a $|t|$-value of less than 5.2 are below the required significance levels. The VDRM appears to detect highly activated negative and positive BOLD responses equally well, but does not distinguish between them (e.g. slice 5).

The Rffect of Voxel Subset Size

Including as few as two evolutionarily selected voxels yields voxel discrimination relevance maps where some visual correlation with the SPM is clear (figure 4A). Further addition of voxels results in more pronounced clustering at relevant sites, but also adds noise. At 30 voxels the noise levels render the map barely interpretable. Similarly, the subject mean evolution-based prediction accuracy (figure 4B), increases rapidly with the addition of up to three voxels, after which it levels out. Addition of more than 11 voxels decreases the performance drastically. SPMt-based voxel selection behaves differently: the performance for low numbers of voxels is poor, and increases linearly with addition of voxels. Note that the maximum number of available voxels is in the order of thousands.

4 DISCUSSION

This study demonstrates the effectiveness of evolutionary algorithms in selecting an optimal combination of voxels for highly accurate discrimination between single volumes of brain patterns — even in conjunction with an exceedingly simple classifier. Using as few as five evolutionarily selected voxels and a standard multiple linear regression classifier, a subject mean single-trial brain state prediction accuracy of over 74% was achieved. Moreover, the voxel discrimination relevance maps correlate clearly with statistical parametric maps, and the expected patterns of brain activation were detected. Not surprisingly, evolutionary feature selection achieved higher classification accuracy than voxel selection using SPM ranking. The latter approach merely selects voxels that show the largest individual average difference between brain states, whereas the evolutionary method determines a combination of voxels that is tailored for brain pattern discrimination. The feasibility of the multivariate approach is further established by the fact that the contribution of so little temporal and spatial information — 3.5 seconds worth of data from only five voxels — allows for accurate brain state prediction. The maximum prediction accuracy using evolutionary feature selection is achieved at drastically less

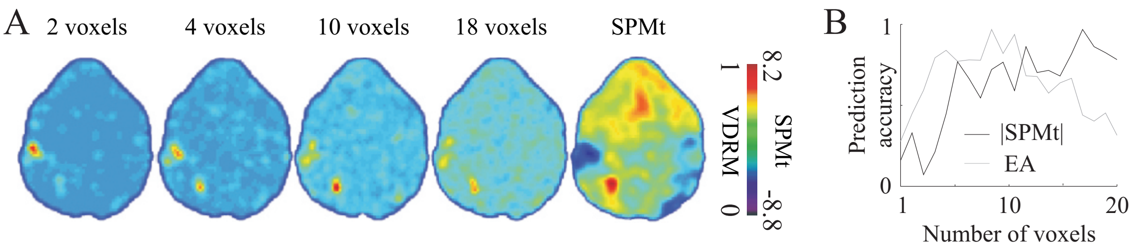

Figure 4: A: The effect of number of included voxels on the voxel discrimination relevance maps for subject one, slice five. The maximum number of possible voxels is in the order of thousands. B: Subject mean evolutionary and SPMt-based prediction accuracy as a function of voxels subset size. The SPMt-based feature selection peaks at 65 voxels. The data has been scaled within subjects to the range [0 1] to emphasize trends.

voxels than the SPMt approach (figure 4), indicating that a large number of SPMt voxels are irrelevant for the discrimination task. In addition, univariate fMRI-analysis requires averaging over time to overcome the inherently low signal quality, and lacks any prediction qualities.

Our approach is not limited to brain state identification, but also provides two distinct approaches to information localization. The fact that the slicewise prediction accuracy correlates very well with the corresponding maximum $|SPMt|$-value — the classical method of detecting activation — is a clear indication that the information revealed by the prediction performance is physiologically related to the stimulus (figure 2). The algorithm can be applied to voxel clusters of any size and shape, defined either beforehand or through evolution, thus optimizing the classification-based information localization. Alternatively, the voxel discrimination relevance maps serve as relative activation detection charts, visually showing which voxels are highly related to the stimulus. Significance levels akin to SPMt values can be computed using boot-strap statistical methods, involving data permutations, allowing for proper VDRM thresholding (Efron and Tibshirani, 1993). Although not done here, the algorithm can be applied to a whole head volume, resulting in a global rather than slicewise VDRM.

In combination with excessive amounts of data, typical for fMRI studies, the time taken to run an evolutionary algorithm can be staggering. However, in our design the number of included voxels is very small, and using a standard PC (3.20GHz processor, 3GB RAM) one five-voxel training run on one individual (20 slices) takes only approximately 1.5 minutes, whereas the validation is done in (biological) real-time. Furthermore, several refinements can be added to make the algorithm considerably more efficient.

The multiple linear regression method used for classification in this study is sensitive to noise and limited to linearly separable problems. In its simplicity, however, the MLR effectively illustrates the power of evolutionary algorithms in extracting relevant information buried in substantial amounts of noise. Pattern analysis using advanced non-linear algorithms, such as artificial neural networks, have been attempted and show promising results. Additional discrimination algorithms, such as support vector machines and other state-of-the-art classifiers, can easily be incorporated into the evolutionary scheme as required.

5 CONCLUSIONS

We have shown that evolutionary based multivoxel feature selection is effective in extracting relevant characterizing information from single volumes by utilizing the multivariate properties of fMRI. Moreover, our approach provides a data-driven alternative to voxel activation detection based on statistical methods.

ACKNOWLEDGEMENTS

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