CHARACTERIZATION OF CEREBRAL BLOOD FLOW OSCILLATIONS USING DIFFERENT CLASSIFICATION METHODS

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Abstract: Oscillation of the cerebral blood flow (CBF) is a common feature in several physiological or pathophysiological states of the brain. It is a promising opportunity to identify the disorders of the cerebral circulation based on the classification of CBF signals. Three classification models are developed with different heuristic in order to carry out the systematic classification based on a problem specific feature extraction. The efficiency of the selected classification methods are evaluated and compared.

Keywords: Biomedical systems, Classification, Neural-network models, Radial base function networks, Support vector machine.

1. INTRODUCTION

Oscillation of the cerebral blood flow (CBF) is a common feature in several physiological or pathophysiological states and may significantly influence the metabolic state of the brain. Inhibition of nitric oxide (NO) synthesis reportedly evokes CBF oscillations although the mechanism of this action has not been clarified yet. In isolated rat middle cerebral arteries, it has been recently demonstrated that the induction of vasomotion after blockade of the NO synthesis is mediated mainly by the thromboxane-pathway (Lacza *et al*., 2001).

In a subsequent in vivo study the vulnerability of the cerebral circulation to thromboxane-induced CBF-oscillations has been reported in the absence of NO (Lenzsér *et al*., 2003). The aim of the present study was to characterize the temporal pattern of the CBF oscillations induced by the stimulation of thromboxane-receptor in case of diminished NO synthesis.

In an earlier paper Fourier transform (FFT) was successfully applied for the signal pattern recognition (Lenzsér *et al*., 2003). However, this method was not able to provide a general formula for the classification of the signals.

An alternative method for CBF signal classifications is to use the coefficients of the Wavelet spectrum as a feature vector. This feature extraction method allows systematic classification but the selectivity of the resulted procedure was limited because of the information loss resulted by the applied feature extraction (Benyó *et al.,* 2004).

The goal of the work presented in this study was to develop a systematic classification method with appropriate selectivity. In order to reduce information loss, a problem specific feature extraction method is used. For the signal classification different methods are developed. The first two methods are Artificial Neural Network (ANN) model based classifiers, the third one is based on Support Vector Machine algorithms. The teaching of the first model was unsupervised, and it was supervised in the other two cases.

1.1 Experimetnal Method

The experiments were carried out on anesthetized (urethan, 1.3 g/kg ip.), spontaneously breathing adult male Wistar rats. The head of the animals was fixed in a stereotaxic head holder, the skull was thinned over the parietal cortex on both sides where two laser Doppler (LD) probes were placed in predefined positions as described previously (Lacza *et al*., 2000). A 5-min segment of the LD flux (LDF) recording was evaluated before the administration of the NO synthase (NOS) inhibitor NG-nitro-L-arginine methyl ester (L-NAME, 100 mg/kg iv.).

After 75 minutes the thromboxane receptor-agonist U-46619 was applied intravenously in a dose of 1 μg/kg. The pattern of the LDF recording was evaluated before and 25 minutes after the administration of U-46619.

Medical experts defined three classes of CBF signals based on their qualitative features:

- Class A:
  Normal blood flow signals before applying any drugs, without any oscillation.
- Class B:
  Blood flow signals, after the administration of L-NAME, before the administration of U-46619. Oscillation can be seen in these signals.
- Class C:
  Blood flow signals, after the administration of U-46619. Strong oscillation can be seen in these signals.

For the computations *Mathematica 5.* and its Neural Networks Application were used.

2. FEATURE EXTRACTION

It has been shown that an adequate feature extraction method is to use the maximal amplitude of the Discrete Fourier Spectrum of the time signals and the corresponding frequency. The typical time signal is shown in Fig. 1, and the corresponding Fourier Spectrum in Fig. 2. This feature extraction method is first suggested in Lenzsér *et al*., 2003.

The points representing the experiments on the two dimensional plane using the selected feature extraction is shown in Fig. 3. Triangles represent the normal blood flow signals (class A), boxes represent the signals after the administration of L-NAME (class B), and stars represent the signals after the administration of U-46619 (class C).

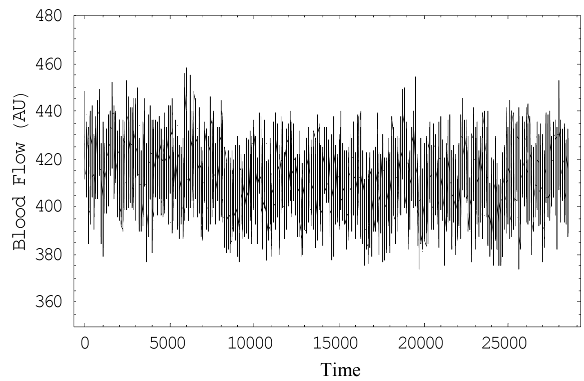

Fig. 1. A typical time signal

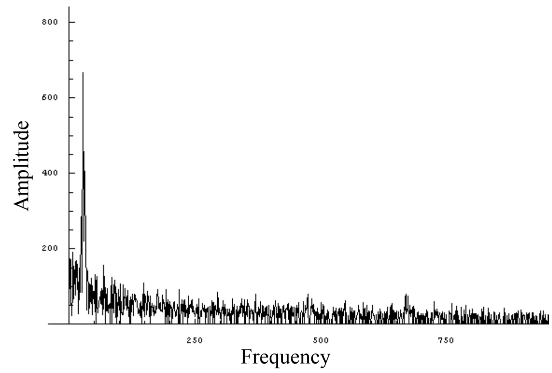

Fig. 2. Discrete Fourier Spectrum of a typical time signal (Class B)

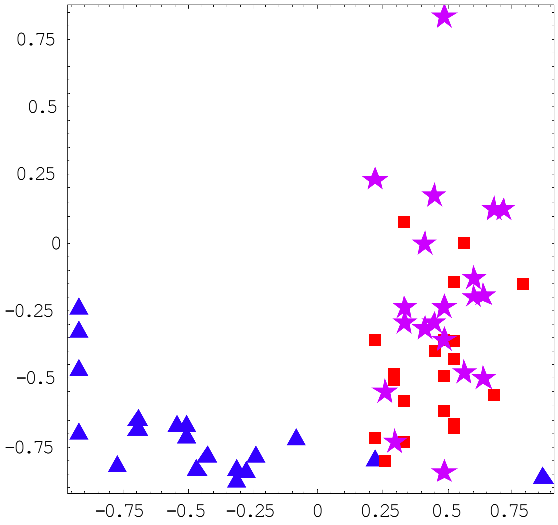

Fig. 3. Normalized feature map of cerebral blood flow: normal blood flow, class A (triangle), before administration of U-46619, class B (box) and after administration of U-46619, class C (star)

3. CLASSIFICATION

Considering N patterns of measured CBF signals representing three different states of blood flow, which have $x_i \in R^2$, $i = 1,\ldots,N$ as feature vectors. These labeled patterns $\{x_i, y_i\}, y_i \in [1,2,3]$ corresponding to class A, B, and C, should be classified. This means, that we are looking for a decision function $f(x)$, which satisfies the following expression:

$$y_i = f(x_i)$$

for every i. In our case the number of the measurements were $N = 60$.

To carry out the systematic classification of CBF signals, three methods are developed. All of them use different heuristic. The first method uses Kohonen Neural Network with unsupervised learning phase. The second method uses Radial Basis Function (RBF) Neural Network. The third classification method is a Support Vector Machines (SVM) algorithm based classifier. These computations were carried out with Mathematica and its Neural Networks application.

3.1 Unsupervised Neural Network

First, unsupervised learning with three codebook vectors has been applied.

The result of the classification using Kohonen Neural Network is shown on Fig. 4. The classes are separated by straight lines reflecting the linear nature of the Kohonen network. The points in the middle of the region of Voronoi Cells indicate the positions of the codebook vectors representing the given class. To find the positions of these codebook vectors, the standard unsupervised learning was used (Kohonen, 2001).

The points in the middle of the ranges are the codebook vectors belonging to the given class.

This classification method could efficiently separate the signals of class A from the signals of other two classes. Since the learning phase of the classification was unsupervised this result validates the use of the selected feature extraction method.

This classification method could not make difference between the class B and class C signals. Based on the number of misclassified signals these two classes seems to be overlapping in this classification scheme.

3.2 Supervised RBF Neural Network

The RBF network consists of two input nodes in the input layer, five nodes in the hidden layer, and one node in the output layer. The activation functions in the hidden nodes were Gaussian, radial basis function. The result of classification is shown in Fig. 5. This method gave significantly better result in classification of the signals after the administration of L-NAME, i.e. the separation of signals in class B and class C were significantly better. This is the benefit of the non-linear nature of the RBF Neural Networks.

The number of misclassified signals is significantly less than in the previous case; however the classification is not perfect.

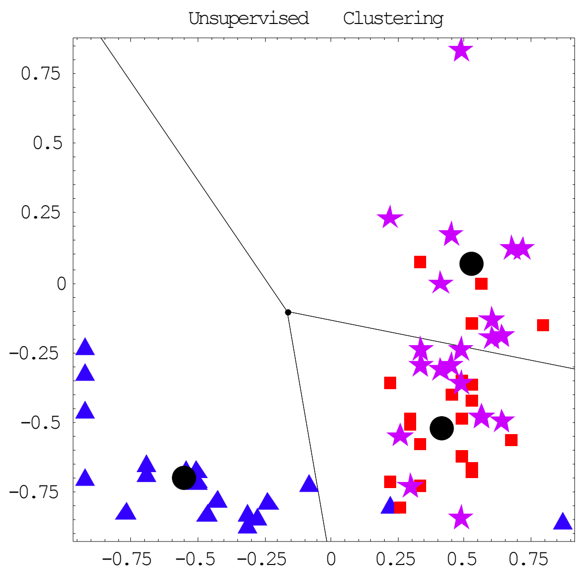

Fig. 4. Classes generated by Kohonen Neural Network using unsupervised learning. The points

are the codebook vectors belonging to the given class.

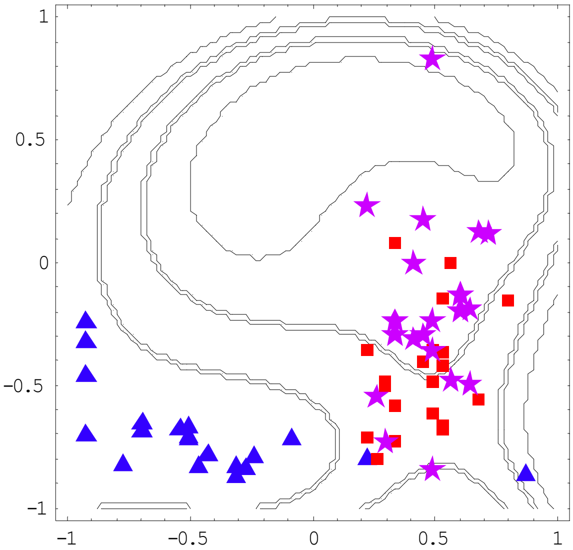

Fig. 5. Result of Radial Basis Function Neural Network classification. The learning phase was supervised.

3.3 Support Vector Machine

In the last few years, there have been very significant developments in the theoretical understanding of a relatively new family of algorithms, the Support Vector Machines (SVM) algorithms. They present a series of useful features for classification as well as generalization of datasets (Berthold and Hand 2003).

SVM algorithms combine the simplicity and computational efficiency of linear algorithms, such as the perceptron algorithm or ridge regression, with the flexibility of nonlinear systems, like neural networks, and rigour of statistical approaches, as regularization methods in multivariate statistics (Burgers 1998).

As a result of the special way they represent functions, these algorithms typically reduce the learning step to a convex optimization problem, that can always be solved in polynomial time, avoiding the problem of local minima typical of neural networks, decision trees and other nonlinear approaches (Hearst 1998).

Their foundation in the principles of statistical learning theory makes them remarkably resistant to overfitting especially in regimes where other methods are effected by the curse of dimensionality. Therefore, they have become popular in bioinformatics.

The SVM algorithm based classification (SVC) methods can distinguish only two classes. Therefore, two binary classifications were carried out in two subsequent steps:

- Making difference between signals in class A and classes B and C;
- Making difference between signals in class B and class C.

For computations, an SVM classification algorithm implemented in *Mathematica* (Paláncz, 2004) was employed, using the following wavelet kernel:

$$K(u,v)=\prod_{i=1}^{n}\cos\left(1.75\frac{u_i-v_i}{a}\right)\exp\left(-\frac{(u_i-v_i)^2}{2a^2}\right)$$

with the following parameters:

$$n=2, a=0.4.$$

(Zhang L. *et al*., 2004).

The result of the first level classification is shown in Fig. 6.

The SVC method was very precise in the separation of the signals before the administration of U-46619, i.e. distinguishing the class A signals from the signals belonging to classes B and C. It is important to outline, that the class domains containing the class B and class C signals are not continuous.

The result of the second level classification is shown in Fig. 7.

The separation of class B and class C signals required the definition of multiple inconsequential domains. The classification was much more accurate than in the other two cases.

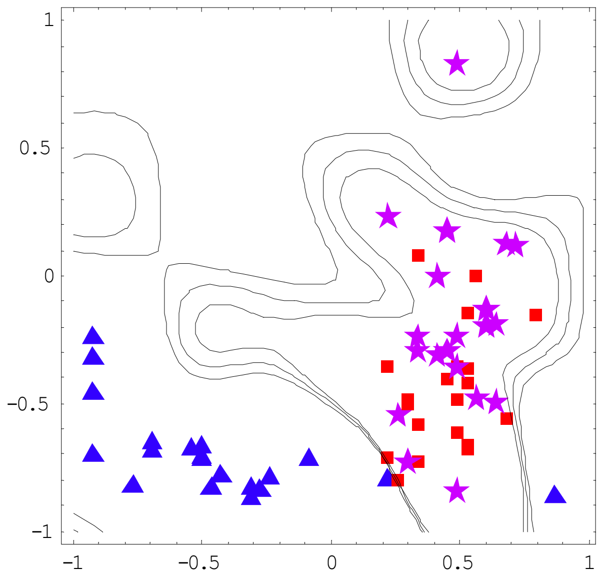

Fig. 6. Result of the first phase of the Support Vector Machine algorithm based classification.

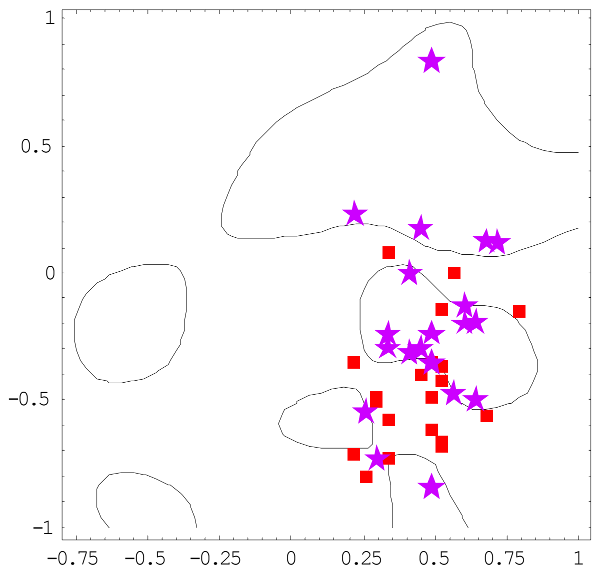

Fig. 7. Result of the second phase of the Support Vector Machine algorithm based classification.

4. DISCUSSION

The number of misclassified experiences is shown in Table 1. It can be clearly seen that the number of misclassified class A signals was much less by using all the three classification method. This shows that the separation of class A signals from the other signals is much more easier based on the selected feature extraction method than making difference between the class B and class C signals.

It is likely that the separation of class B and class C signals requires the improvement of the feature extraction method. These two classes appear to be overlapping in the case of the applied feature extraction.

Based on the results in Table 1, the selectivity of the SVC algorithm was the best according to our preliminary expectations. The price of this high selectivity was the definition of small inconsequential class domains. The biological interpretation of this result is difficult.

Table 1 Misclassification rate

	Class A (triangle)	Class B (square)	Class C (star)
Kohonen ANN	2/20=10%	4/20=20%	11/20=55%
RBF ANN	1/20=5%	6/20=30%	4/20=20%
SVC	0/20=0%	2/20=10%	1/20=5%

The punctuality of the Kohonen NN bases classification was relatively low, especially regarding the class B and C signals. But the robustness of the method could be advantageous in the case of noisy signals. The Kohonen NN classification shows relative high tolerance towards the signal uncertainty.

The results of the RBF Network based classification look like to be easy to interpret, since the class domains are continuous. Based on these experiments the RBF Neural Network based classification proved to be the best candidate to apply in the practice. However more measurements are required for the absolutely punctual general classification model.

5. CONCLUSION

In this study three CBF signal classification methods are introduced. All the three methods gave the opportunity of the systematic classification of the given time signals. The misclassification rate was steadily decreasing when using more advanced classification algorithms.

The medical interpretation of the results is an ongoing process. Although the physiological mechanism of the spontaneous oscillation of the vascular tone (called vasomotion) is studied intensively (Nilsson H 2003) the biophysical model of the vasomotion is not yet known. In the subsequent phase of this research we are going to use our results to develop such a model. For example the parameters of the classification models can help to identify the parameters of the biophysical model of the vasomotion.

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REFERENCES

Benyó, B., G. Lenzsér, B. Paláncz (2004). Characterization of the Temporal Pattern of Cerebral Blood Flow Oscillations, *Proc. of 2004 International Joint Conference on Neural Networks, July 25-29, 2004*, 468-471.

Berthold, M. and Hand D.J. (2003). *Intelligent Data Analysis, An Introduction*, Springer, Berlin.

Burgers, C.J.C (1998). A tutorial on support vector machines for pattern recognition, *Data Mining and Knowledge Discovery,* **2**, 121-167.

Hearst, M. A. (1998). Support Vector Machines, *IEEE Intelligent Systems*, **35**, 18 -28.

Kohonen T. (2001). *Self-Organizing Maps*, Springer, Berlin, Germany, ISBN 3-540-67921-9

Lacza, Z., P. Hermán, C. Görlach, T. Hortobágyi, P. Sándor, M. Wahl and Z. Benyó (2001). NO synthase blockade induces chaotic cerebral vasomotion via activation of thromboxane receptors. *Stroke*, **32**, 2609-2614.

Lacza, Z., B. Erdös, C. Görlach, M. Wahl, P. Sándor and Z. Benyó (2000). The cerebrocortical microcirculatory effect of nitric oxide synthase blockade is dependent upon baseline red blood cell flow in the rat. *Neuroscience Letters,* **291,** 65-68.

Lenzsér, G., P Hermán, K. Komjáti, P. Sándor and Z. Benyó (2003). Nitric oxide synthase blockade sensitizes the cerebrocortical circulation to thromboxane-induced CBF oscillations. *Journal of Cerebral Blood Flow and Metabolism*, **23,** 88.

Nilsson. H., Aalkjær, C. (2003). Vasomotion: mechanisms and physiological importance. *Molecular Interventions*, **3**, 79-89.

Paláncz, B. (2004). Support Vector Classifier, e-publication, Wolfram Research Inc. http://library.wolfram.com/infocenter/MathSource/5293

Zhang L, Zhov W. and Jiao L (2004). Wavelet Support Vector Machine, IEEE Trans. System, Man and Cybernetics-Part B: Cybernetics, **4**, No. 1., 34-39.