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# DISCRIMINATION OF OUTER MEMBRANE PROTEINS USING REFORMULATED SUPPORT VECTOR MACHINE BASED ON NEUTROSOPHIC SET

**Wen Ju and H. D. Cheng**

wen.ju@aggiemail.usu.edu, hengda.cheng@usu.edu

Department of Computer Science, Utah State University, Logan, UT 84311-4205, U.S.A

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## Abstract.

Neutrosophic logic is introduced in 1995 as a generalization of fuzzy logic.

It includes a new component as neutralities.

In this presentation, we propose a novel neutrosophic set for SVM inputs and combine it with the reformulated SVM which treats samples differently according to the weighting function.

The proposed classifier helps reducing the effects of outliers.

The authors test it on discriminating outer membrane proteins (OMPs) from globular proteins and  $\alpha$ -helical membrane proteins using amino acid composition and residue pair information.

The experiment results show that the proposed method outperforms the traditional SVM in both classification accuracy and MCC.

# I. INTRODUCTION.

Neutrosophic logic was introduced by Florentin Smarandache in 1995 as a generalization of fuzzy logic.

It studies the neutrosophic logical values of the propositions.

Each proposition is estimated to have three components: the percentage of truth in a subset  $T$ , the percentage of indeterminacy in a subset  $I$ , and the percentage of falsity in a subset  $F$  [1].

[1] F. Smarandache, J. Dezert, A. Buller, M. Khoshnevisan, S. Bhattacharya, S. Singh, F. Liu, Gh. C. Dinulescu-Campina, C. Lucas, C. Gershenson, Proceedings of the First International Conference on Neutrosophy, Neutrosophic Logic, Neutrosophic Set, Neutrosophic Probability and Statistics, 2001.

Compared with all other logics, neutrosophic logic introduces a percentage of "indeterminacy" due to unexpected parameters hidden in some propositions.

The main distinction between neutrosophic logic (NL) and fuzzy logic (FL) is that the sum of neutrosophic components in NL is not necessarily 1 as in FL but any number from  $-0$  and  $3+$  [2].

[2] F. Smarandache, "A unifying Field in Logics: Neutrosophic Logic. Neutrosophy, Neutrosophic Set, Neutrosophic Probability and Statistics," third edition, Xiquan, Phoenix, 2003.

## I. INTRODUCTION – cont.

Support Vector Machine (SVM) developed by Vapnik and Cortes has superior features such as avoiding over-fitting and obtaining global optimal [3].

[3] V. Vapnik and C. Cortes, “Support vector networks”, Machine learning, vol. 20, pp. 273-293, 1995.

It has been applied to many problems in bioinformatics.

Kim and Park [4] used it to predict protein relative solvent accessibility.

[4] H. Kim and H. Park, “Prediction of protein relative solvent accessibility with support vector machines and long-range interaction 2D local descriptor”, Proteins, vol. 54, pp. 557562, 2004.

Nguyen and Rajapakse [5] applied SVM to predict protein secondary structures.

[5] M. N. Nguyen and J. C. Rajapakse, “Two-stage multi-class support vector machines to protein secondary structure prediction”, Pac, Symp. Biocomput., pp. 346-357, 2005.

## I. INTRODUCTION – cont.

It has also been applied to protein domains identification (Vlahovicek et al., [6]), protein-protein binding sites prediction (Brandford and Westhead [7]), remote protein homology detection (Busuttil et al. [8]) and protein subcellular localization (Nair and Rost [9]).

[6] K. Vlahovicek, et al., “Prediction of protein domain-architecture using support vector machine”, *Nucleic Acids, Res.*, vol. 33, pp. 223-225, 2005.

[7] J. R. Bradford and D. R. Westhead, “Improved prediction of proteinprotein binding sites using a support vector machines approach”, *Bioinformatics*, vol. 21, pp. 1487-1494, 2005.

[8] S. Busuttil, et al., “Support vector machines with profile-based kernels for remote protein homology detection”, *Genome Inform. Ser. Workshop Genome Inform.*, vol. 15, pp. 191-200, 2004.

[9] R. Nair and B. Rost, “Mimicking cellular sorting improves prediction of sub-cellular localization”, *J. Mol. Biol.*, vol. 348, pp. 85-100, 2005.

Outer membrane proteins (OMPs) perform a variety of functions, such as selectively allowing the passage of molecules, mediating non-specific, passive transport of ions and small molecules [10].

[10] K. Park, M. M. Gromiha, P. Horton and M. Suwa, “Discrimination of outer membrane proteins using support vector machines”, *Bioinformatics*, vol. 21, pp. 4223-4229, 2005.

## I. INTRODUCTION – cont.

Discriminating OMPs from globular proteins and  $\alpha$ -helical membrane proteins is an important task both for dissecting OMPs from genomic sequences and for the successful prediction of their secondary and tertiary structures.

Park et al used SVM to discriminate OMPs based on amino acid composition and residue pair information in [10].

[10] K. Park, M. M. Gromiha, P. Horton and M. Suwa, “Discrimination of outer membrane proteins using support vector machines”, *Bioinformatics*, vol. 21, pp. 4223-4229, 2005.

In this presentation, the authors propose a novel neutrosophic set for the input samples of SVM.

Combining the neutrosophic set with the reformulated SVM, authors discriminate OMPs from globular proteins and  $\alpha$ -helical membrane proteins.

They use the same dataset in [10], which is composed of 208 OMPs, 673 globular proteins and 206  $\alpha$ -helical membrane proteins.

[10] K. Park, M. M. Gromiha, P. Horton and M. Suwa, “Discrimination of outer membrane proteins using support vector machines”, *Bioinformatics*, vol. 21, pp. 4223-4229, 2005.

The experimental results show that the proposed method outperforms the traditional SVM in both accuracy and MCC.

## II. REFORMULATED SUPPORT VECTOR MACHINE.

SVM uses hypothesis space of linear functions in a high-dimensional feature space, and it is trained with a learning algorithm based on optimization theory [11].

[11] N. Cristianini and J. Shawe-Taylor, An Introduction to Support Vector Machines. Cambridge, U.K. Cambridge Univ. Press, 2000.

Suppose we are given a training set  $S$  containing  $n$  labeled points  $(x_1, y_1), \dots, (x_n, y_n)$ , where  $x_i \in \mathbb{R}^N$  and  $y_i \in \{-1, 1\}$ ,  $i=1, \dots, n$ .  $\Phi(x)$  denotes the mapping from  $\mathbb{R}^N$  to a feature space  $Z$ . We want to find the hyperplane with maximum margin as:

$$w \cdot z + b = 0 \quad (1)$$

such that for each point  $(z_i, y_i)$ , where  $z_i = \Phi(x_i)$ ,

$$y_i(w \cdot z_i + b) \geq 1, \quad i = 1, \dots, n. \quad (2)$$

When the data set is not linearly separable, the soft margin is allowed by introduction of  $n$  non-negative variables, denoted by  $\xi = (\xi_1, \xi_2, \dots, \xi_n)$ , such that the constraint for each sample in Eq. (2) is rewritten as:

$$y_i(w \cdot z_i + b) \geq 1 - \xi_i, \quad i = 1, \dots, n. \quad (3)$$

The optimal hyperplane problem is the solution to the problem

$$\text{minimize } \frac{1}{2} w \cdot w + C \sum_{i=1}^n \xi_i \quad (4)$$

subject to

$$y_i(w \cdot z_i + b) \geq 1 - \xi_i, \quad i = 1, \dots, n. \quad (5)$$

## II. REFORMULATED SUPPORT VECTOR MACHINE – cont.

The first term in equation (4) measures the margin between support vectors and the second term measures the amount of misclassifications.

$C$  is a constant parameter that tunes the balance between the maximum margin and the minimum classification error.

Lin and Wang proposed fuzzy support vector machine in [12].

[12] C. F. Lin and S. D. Wang, "Fuzzy Support Vector Machines", IEEE transactions on Neural Networks, vol. 13, pp.464-471, 2002.

A membership  $s_i$  is assigned for each input sample  $(x_i, y_i)$ , where  $0 < s_i < 1$ .

Since the membership  $s_i$  is the attitude of the corresponding point  $x_i$  toward one class and the parameter  $s_i \xi_i$  is a measure of error in the SVM, the term  $s_i \xi_i$  is a measure of error with different weighting.

The optimal hyperplane problem is then regarded as the solution to minimize  $\frac{1}{2} w \cdot w + C \sum_{i=1}^k s_i \xi_i$  (6)  
subject to  $y_i(w \cdot z_i + b) \geq 1 - \xi_i, \quad i = 1, \dots, n.$  (7)



## II. REFORMULATED SUPPORT VECTOR MACHINE – cont.

The authors use the similar idea in the reformulated SVM.

The difference is that the membership  $s_i$  is substituted by weighting function  $g_i$  where  $g_i > 0$ .

Different inputs contribute differently to the training procedure, and we use weighting function  $g_i$  to evaluate the degree of importance for each input.

The value of  $g_i$  is a positive number and is unnecessary to be smaller than 1.

Now the optimal hyperplane problem in the reformulated SVM is the solution to

$$\text{minimize } \frac{1}{2} w \cdot w + C \sum_{i=1}^k g_i \xi_i \quad (8)$$

subject to

$$y_i(w \cdot z_i + b) \geq 1 - \xi_i, \quad i = 1, \dots, n. \quad (9)$$

## III. INTEGRATING NEUTROSOPHIC SET WITH REFORMULATED SVM.

### III. 1. Neutrosophic Set

Neutrosophic set is a generalization of the intuitionistic set, classical set, fuzzy set, paraconsistent set, dialetheist set, paradoxist set and tautological set [2].

[2] F. Smarandache, "A unifying Field in Logics: Neutrosophic Logic. Neutrosophy, Neutrosophic Set, Neutrosophic Probability and Statistics," third edition, Xiquan, Phoenix, 2003.

In classical theory, there are only  $\langle A \rangle$  and  $\langle \text{Non-}A \rangle$ .

The degree of neutralities  $\langle \text{Neut-}A \rangle$  is introduced and added in neutrosophic theory.

Generally a neutrosophic set is denoted as  $\langle T, I, F \rangle$ .

An element  $x$   $(t, i, f)$  belongs to the set in the following way: it is  $t$  true in the set,  $i$  indeterminate in the set, and  $f$  false, where  $t, i,$  and  $f$  are real numbers taken from the sets  $T, I,$  and  $F$  with no restriction on  $T, I, F,$  nor on their sum  $m=t+i+f$ .

The major difference between neutrosophic set (NS) and fuzzy set (FS) is that there is no limit on the sum  $m$  in NS while in FS  $m$  must be equal to 1.

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## III. INTEGRATING NEUTROSOPHIC SET WITH REFORMULATED SVM.

### III. 2. Proposed Neutrosophic Set for SVM input

Many research results have shown that the SVM is very sensitive to noises and outliers.

Here the authors propose a neutrosophic set for the input samples of SVM based on the distances between the sample and the class centers.

The reformulated SVM integrated with the proposed neutrosophic set can help solving the problems of noise and outliers.

Using the same notations, the neutrosophic set for input samples are denoted as a sequence of points:

$$(x_j, y_j, t_j, i_j, f_j), \quad j = 1, \dots, n.$$

### III. 2. Proposed Neutrosophic Set for SVM input - cont.

Here for a sample  $x_j$  belongs to class  $y_j$ , it is  $t_j$  true,  $i_j$  indeterminate and  $f_j$  false. We define the center of positive samples  $C_+$ , the center of negative samples  $C_-$  and the center of all samples  $C_{all}$  as following:

$$C_+ = \sum_{k=1}^{n_+} x_k, C_- = \sum_{k=1}^{n_-} x_k, \quad (10)$$

$$C_{all} = \sum_{k=1}^n x_k$$

where  $n_+$  is the number of positive samples and  $n_-$  is the number of negative samples.

We denote  $U$  as the whole input samples set,  $P$  as the positive samples subset and  $N$  as the negative samples subset. For positive samples where  $y_j = 1$ , the neutrosophic components are defined as:

$$\begin{aligned} t_j &= 1 - \frac{\|x_j - C_+\|}{\max_{x_k \in P} \|x_k - C_+\|} \\ i_j &= 1 - \frac{\|x_j - C_{all}\|}{\max_{x_k \in U} \|x_k - C_{all}\|} \\ f_j &= 1 - \frac{\|x_j - C_-\|}{\max_{x_k \in P} \|x_k - C_-\|} \end{aligned} \quad (11)$$

where  $\|x\|$  denotes the Euclidean distance of variable  $x$ .

### III. 2. Proposed Neutrosophic Set for SVM input - cont.

For negative samples where  $y_j = -1$ , the neutrosophic components are defined as:

$$\begin{aligned} t_j &= 1 - \frac{\|x_j - C_-\|}{\max_{x_k \in N} \|x_k - C_-\|} \\ i_j &= 1 - \frac{\|x_j - C_{all}\|}{\max_{x_k \in U} \|x_k - C_{all}\|} \\ f_j &= 1 - \frac{\|x_j - C_+\|}{\max_{x_k \in N} \|x_k - C_+\|} \end{aligned} \quad (12)$$

With the above definition, every input sample is associated with a triple  $\langle t_j, i_j, f_j \rangle$  as its neutrosophic components. The larger  $t_j$  it has, the more probability it belongs to the labeled class. The larger  $i_j$  it has, the more probability it is indeterminate. The larger  $f_j$  it has, the more probability it belongs to the opposite of the labeled class.

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## III. INTEGRATING NEUTROSOPHIC SET WITH REFORMULATED SVM.

### III. 3. Integrating Neutrosophic Set with Reformulated SVM

In order to use the reformulated SVM, we should define a weighting function for input samples.

Following the steps in section III.2, every sample has been associated with a triple  $\langle t_j, i_j, f_j \rangle$  as its neutrosophic components.

Larger  $t_j$  means the sample is nearer to the center of the labeled class and is less likely an outlier.

So  $t_j$  should be emphasized in the weighting function.

Larger  $i_j$  means the sample is harder to be discriminated between two classes.

This factor should also be emphasized in the weighting function in order to classify the indeterminate samples more accurately.

Larger  $f_j$  means the sample is more likely an outlier.

### III. 3. Integrating Neutrosophic Set with Reformulated SVM – cont.

This sample should be treated less importantly in the training procedure. Based on these analyses, we define the weighting function  $g_j$  as:

$$g_j = t_j + i_j - f_j \quad (13)$$

The reformulated SVM combined with the proposed weighting function treats samples differently in the training procedure and can help reducing the effects of outliers in the training samples.

## IV. EXPERIMENTAL RESULTS.

The same four measures in [10] are used to evaluate the classification performance.

[10] K. Park, M. M. Gromiha, P. Horton and M. Suwa, “Discrimination of outer membrane proteins using support vector machines”, *Bioinformatics*, vol. 21, pp. 4223-4229, 2005.

Sensitivity, specificity, overall accuracy and MCC are defined as

$$\text{sensitivity} = \frac{TP}{TP + FN} \quad (14)$$

$$\text{specificity} = \frac{TN}{TN + FP} \quad (15)$$

$$\text{overall accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \quad (16)$$

$$\text{MCC} = \frac{TP \times TN - FP \times FN}{\sqrt{(TP + FP)(TP + FN)(TN + FP)(TN + FN)}} \quad (17)$$

where TP, FP, TN and FN refer to the number of true positives, false positives, true negatives and false negatives proteins, respectively.



## IV. EXPERIMENTAL RESULTS – cont.

The authors use the same dataset and repeat all the experiments with the same parameter  $\gamma$  as stated in [10].

[10] K. Park, M. M. Gromiha, P. Horton and M. Suwa, “Discrimination of outer membrane proteins using support vector machines”, *Bioinformatics*, vol. 21, pp. 4223-4229, 2005.

There are three categories of experiments: discrimination of OMPs and globular proteins, discrimination of OMPs and  $\alpha$ -helical membrane proteins and discrimination of OMPs and non-OMPs.

All of the experiments are results of 5-fold cross-validation test as in [10].

[10] K. Park, M. M. Gromiha, P. Horton and M. Suwa, “Discrimination of outer membrane proteins using support vector machines”, *Bioinformatics*, vol. 21, pp. 4223-4229, 2005.

The results are listed in Tables 1, 2 and 3 respectively.

The original results of [10] are listed in normal font while our results using FSVM are listed in *Italic* and **Bold** font with ‘F’ as postfix.

[10] K. Park, M. M. Gromiha, P. Horton and M. Suwa, “Discrimination of outer membrane proteins using support vector machines”, *Bioinformatics*, vol. 21, pp. 4223-4229, 2005.

#### IV. EXPERIMENTAL RESULTS – cont.

Table 1. Discrimination of OMPs and globular proteins.

Input	Sen (%)	Spe (%)	Overall (%)	MCC
20D	82.7	93.8	91.1	0.757
<b>20DF</b>	<b>82.9</b>	<b>95.4</b>	<b>92.5</b>	<b>0.793</b>
400D	83.2	97.3	94.0	0.830
<b>400DF</b>	<b>85.1</b>	<b>97.7</b>	<b>95.2</b>	<b>0.863</b>
420D	63.5	100	91.4	0.755
<b>420DF</b>	<b>70.6</b>	<b>98.8</b>	<b>93.4</b>	<b>0.805</b>
17D	87.5	94.1	92.5	0.798
<b>17DF</b>	<b>91.6</b>	<b>95.3</b>	<b>92.9</b>	<b>0.829</b>

Table 2. Discrimination of OMPs and  $\alpha$ -helical membrane proteins.

Input	Sen (%)	Spe (%)	Overall (%)	MCC
20D	98.6	91.3	94.9	0.901
<b>20DF</b>	<b>98.8</b>	<b>92.9</b>	<b>95.7</b>	<b>0.913</b>
400D	99.0	90.3	94.7	0.897
<b>400DF</b>	<b>98.7</b>	<b>92.6</b>	<b>95.6</b>	<b>0.918</b>
420D	95.7	89.8	92.8	0.856
<b>420DF</b>	<b>95.1</b>	<b>92.9</b>	<b>93.8</b>	<b>0.881</b>
15D	99.0	92.7	95.9	0.920
<b>15DF</b>	<b>99.1</b>	<b>93.4</b>	<b>96.6</b>	<b>0.928</b>

#### IV. EXPERIMENTAL RESULTS – cont.

Table 3. Discrimination of OMPs and nonOMPs.

Input	Sen (%)	Spe (%)	Overall (%)	MCC
20D	87.5	92.6	91.6	0.752
<b>20DF</b>	<b>87.8</b>	<b>93.7</b>	<b>93.1</b>	<b>0.792</b>
400D	86.5	96.4	94.5	0.823
<b>400DF</b>	<b>86.8</b>	<b>97.2</b>	<b>94.9</b>	<b>0.848</b>
18D	89.9	92.5	92.0	0.767
<b>18DF</b>	<b>90.3</b>	<b>94.9</b>	<b>94.1</b>	<b>0.821</b>
28D	90.9	94.7	93.9	0.816
<b>28DF</b>	<b>89.7</b>	<b>96.3</b>	<b>94.8</b>	<b>0.831</b>

Due to the page settings, some notations are abbreviated in the tables.

Sensitivity is truncated as *sen* while specificity is denoted by *spe*.

The results show that the proposed method outperforms the traditional SVM in both overall classification accuracy and MCC.

The increase of overall accuracy is 1%-2% and the MCC is increased by 3%-4% in most cases.

The improvement is significant and adequately validates the correctness and effectiveness of the proposed method.



## CONCLUSION.

SVM is sensitive to outliers and noises in the input samples.

In order to eliminate the effects of outliers, we integrate reformulated SVM with neutrosophic set derived from input samples.

The reformulated SVM treats samples differently according to the weighting function in the training procedure.

The weighting function is based on the neutrosophic set.

We apply the proposed method to the discrimination of outer membrane proteins and compare the results with that of the traditional SVM.

The experimental results have shown that the proposed classifier achieves higher accuracy and MCC than the traditional SVM method does.

## REFERENCES

- [1] F. Smarandache, J. Dezert, A. Buller, M. Khoshnevisan, S. Bhattacharya, S. Singh, F. Liu, Gh. C. Dinulescu-Campina, C. Lucas, C. Gershenson, Proceedings of the First International Conference on Neutrosophy, Neutrosophic Logic, Neutrosophic Set, Neutrosophic Probability and Statistics, 2001.
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