Classification of Helitron's Types in the C.elegans Genome based on Features Extracted from Wavelet Transform and SVM Methods

Rabeb Touati, Imen Messaoudi, Afef ElloumiOueslati and Zied Lachiri
Dept. Electrical Engineering, SITI Laboratory, University of Tunis el Manar, National Engineering School, Tunis, Tunisia

Keywords: Transposable Elements (TES), Helitrons, C.elegans, SVM, Kernel-tricks, FCGS, CWT, Energy-wavelet.

Abstract: Helitrons, a sub-class of the Transposable elements class 2, are considered as an important DNA type. In fact, they contribute in mechanism's evolution. Till now, these elements are not well studied using the automatic tools. In fact, the researches done in helitron's recognition are based only on biological experiments. In this paper, we propose an automatic method for characterizing helitrons by global signature and classifying the helitron's types in C.elegans genome. For this goal, we used the Complex Morlet Wavelet Transform to generate helitron's signatures (helitron's scalograms presentation) and to extract the features of each category. Then, we used the SVM-classifier to classify these 10 helitron's families. After testing different kernels and using the cross validation function, we present the best classification results given by the RBF-kernel with c=60, σ=0. 0000000015625 and OAO approach.

1 INTRODUCTION

The SVM classifier is proved to be effective supervised algorithm in solving recognition problems of the 2 classes and multi-class. It is applied to solve statistical learning problems (Shawe-Taylor, 1998; Poulter, 2005). The technique is based on structural risk minimization (SRM) problems (Shawe-Taylor, 1998; Vapnik, 1998). It has been widely used in different domains in data mining (NORINDER, 2003), bio-informatics studies (Mateos, 2002), DNA (ÖZ, 2013) and molecular genetics (Furey, 2000) due to its inherent discriminating learning and its generalization capabilities.

SVMs have a major advantage that is the ability to deal with samples of a very higher dimensionality. For these reason, we used the SVM classifier as classifier technique for the classification of particular transposable elements which are highly heterogeneous in size and which transpose by rolling circle replication; helitrons. Helitrons use a "cut-and paste" mechanism to transpose. These TEs are discovered in all eukaryotic genomes and the main challenges in cell biology is the location and identification of these elements. The first discovered of the helitrons in the plants (Arabidopsis Thaliana and Oryza sativa) and in the nematode (C.elegans). Now, they have been identified in a diverse range of species, protists to mammals (Kapitonov, 2001; Poulter, 2005; Hood, 2005, Du 2008). Helitrons sequences are widespread and highly heterogeneous. On a large scale, these sequences suggest that they are capable of duplicating and shuffling exon domains (Morgante, 2005; Lai, 2005; Du,2009; Schnable, 2009). Helitron's classification algorithms are based on the alignment theory which uses a comparison between the searched area and an helitron reference (Tempel, 2007; Sweredoski, 2008; Du, 2008; Edgar, 2004). The major problem encountered here is the lack of references (Xiong, 2014; Yang, 2009). On the other hand, Wicker et al. (Wicker, 2007) produced a system of classification for the eukaryotic transposable elements. Their objective was to have hierarchical classification system able to divide the transposable elements into two main classes: class 1 (retrotransposons) and class 2 (DNA transposon). Till now, the dynamic and structure of this helitron's sequence is not well studied. Besides, with the high variability of helitronic sequences, the systematic classification becomes an obstacle. In this work, we focus on helitron sequences to characterize and categorize these transposable elements. We show that when using statistical concept of coding technique, we are able to identify some helitrons. Meanwhile, we thought of a standard method which classifies helitrons, and that can help non-specialists to

Touati, R., Messaoudi, I., ElloumiOueslati, A. and Lachiri, Z.
Classification of Helitron's Types in the C.elegans Genome based on Features Extracted from Wavelet Transform and SVM Methods.
DOI: 10.5220/0006631001270134
In *Proceedings of the 11th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2018) - Volume 3: BIOINFORMATICS*, pages 127-134
ISBN: 978-989-758-280-6

annotate these elements. A key components of this system is the combination of three steps. First, coding the DNA with the Frequency Chaos Game Signal (FCGS); second, applying the Complex Morlet Wavelet Transform (CWT) to have the helitron features; third, using the Support Vector Machines (SVMs) as a classification technique. Following that, we divide this paper into four sections. The second section represents the materials and methods. The third section provides the experimental results and discusses the proposed methods. The last section is the conclusion.

2 MATERIALS AND METHODS

In this work, the Support vector machine have been used for the helitron sequences classification based on the CWT applied to FCGS2. In the figure 1 we illustrate the work steps: the first steps we extracted the genomique sequences database of helitron's types from NCBI for the Caenorhabditis elegans genome (a worm) (http://www.ncbi.nlm.nih.gov/Genbank).

The second step consists in coding the genomic sequence into a 1D signal by using the FCGS2 coding technique. Then, a signals database of eacg helitron is established. In the third step, the analysis window (CWT) is applied on the obtained signal. Therefore, we obtain a set of wavelet coefficients which we use to generate a helitron features database. In the fourth step, we extract the features relative of wavelet energy. This suitable wavelet-based features database are prepared for the classification of helitrons. Then, the feature extraction step has a direct impact on the performance of our classification systems. This database is divided into two sub-databases: training (70%) and testing (30%). In the final step, we have employed the energy features as an input of SVM classifier. Then, we apply the Support vector machine (SVM) that we use the cross-validation function to varied the kernels parameters and find the best accuracy rates.

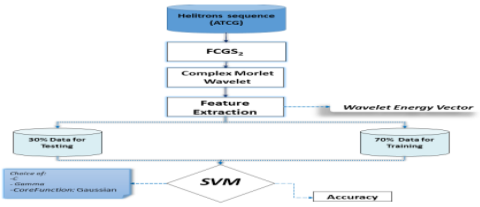


Figure 1: SVM-Helitrons recognizer Flowchart.

2.1 FCGS₂ Technique

The Frequency Chaos Game Signal order 2 is a new coding technique based on the apparition's frequencies (apparition's probabilities) of all 2 successive nucleotides groups in an entry genomic sequence (Fiser, 1994; Messaoudi, 2013; Messaoudi, 2014; Messaoudi, 2014, Messaoudi, 2014). The probability of a given dinucleotide ($\mathrm{P_{dinuc}}$) is calculated by the following equation:

$$\mathrm{P_{2nuc}} = \mathrm{N_{2nuc}}/\mathrm{N_{ch}} \tag{1}$$

With $\mathrm{N_{2nuc}}$ represents the apparition number of two nucleotides in the entire sequence

The $\mathrm{N_{ch}}$ represents the length of entry genomic sequence (in base pairs: bp).

As known,a sequence of DNA is the combination of 4 letters: A, T, C and G.

Then, the chromosomal sequences contains 42 possible dinucleotides: {AA, AC, AT, GG, GC … TT}. So, the dinucleotide's counting concern the occurrence number of each of all of these elements.

After that, to encode the genomic sequence regarding a dinucleotide (i), each element found in the position (k) on the chromosome is replaced by its occurrence's probability:

$$\mathrm{S_{2nuc}(k)} = \sum\nolimits_{\mathrm{i}} \mathrm{P_{2nuc}}\ (\mathrm{i,k}) \tag{2}$$

The FCGSignal order 2 is the sum of all of the dinucleotide indicators ($\mathrm{S_{2nuc}}$):

$$\mathrm{FCGS_2} = \sum\nolimits_{\mathrm{k}} \mathrm{S_{2nuc}} \tag{3}$$

The chromosome is represented by a signal that reflecting the dinucleotide's temporal evolution in the sequence.

2.2 Features Extraction

The DNA signal has a complex nature which requires a pertinent tool to analyze its content. In this work, the Continuous Wavelet Transform is applied on the obtained FCGS2 signal using a Complex Morlet wavelet as analysis window. The CWT decomposes a given signal into a sum of windows called wavelets. The latters are obtained by translating and expanding a mother wavelet ψ(t) (Grossmann, 1984; Merry, 2005; Tse, 2007; NAJMI, 1997; Oueslati, 2015). The set of wavelet windows is obtained by:

$$\psi_{s,u}(t) = \frac{1}{\sqrt{s}}\psi^{*}\left(\frac{t-u}{s}\right), \mathrm{s} > 0, \mathrm{u} \in \mathbb{R} \tag{4}$$

Here * is the complex conjugate. The mother wavelet is the Complex Morlet function which is expressed by:

$$\Psi_{cmor}(t) = \Pi^{-\frac{1}{4}}\left(e^{i\varpi_0 t} - e^{i\varpi_0{}^2}\right)e^{-\frac{t^2}{2}} \qquad (5)$$

Here ϖ_0 is the oscillation's number. The continuous wavelet transform is performed by applying this formula:

$$W_{(s,u)}[x(t)] = \frac{1}{\sqrt{s}}\int_{-\infty}^{+\infty} x(t)\,\psi^*\left(\frac{t-u}{s}\right)dt \qquad (6)$$

The final result is a matrix of coefficients which we use to generate the scalogram representation by considering the absolute value of these coefficients (Figure 2). Thus, we encode all chromosomes of C.elegans genome by $FCGS_2$. After that, we apply the CWT along 64 scales with the parameter (ϖ_0 = 5.4285). We established the wavelet coefficients database that represents helitron structures by particular behaviours (Messaoudi, 2014, Touati, 2016; Oueslati, 2015). These time-frequency representation can be used to our classification system. Besides the helitrons composition variability in the genome, these elements are also variable in size. Given this, the wavelet coefficients matrix leads to a set of features which is not balanced in size. However, the SVM method is limited when it is applied for imbalanced datasets. For this reason, the choice of the optimal dimensionality reduction method for the wavelet analysis is important since it keeps the computation cost very low and the classification accuracy very high. Here, we propose to calculate the energy-wavelet as a features for our classification system (Amin, 2015).

Therefore, we calculate the energy wavelet value for each matrix by frequency axis. This method can balance these features.

$$E(s) = \sum_{u=1}^{L}\left|W_{(s,u)}[x(t)]\right|^2 \qquad (7)$$

Where, L is the length of signal.

The final results of reduced features (energy-wavelet) are vector have size 64 (equal to scales). Each vector present one helitron. The figure 2 represents examples of the helitron's scalograms presentation and their corresponding energy vector.

2.3 Multi-class Support Vector Machines

Support Vector Machines (SVMs) were first proposed by Vladimir Vapnik in 1995 (Vapnik, 1995; Cortes, 1995). They are part of supervised learning methods based on the theory of Structural Risk Minimization (SRM). The Support Vector Machines (SVMs) are very effective supervised algorithm to solve recognition problems (Vapnik, 1995). SVMs have been the core of numerous domains such as bioinformatics studies, molecular genetics, DNA, data mining and psychiatry. In order to estimate the helitrons in DNA sequence, we use the SVM classification method which aims to find the optimal hyper-plane that separates two different classes. The SVM approach consists of constructing one or several hyper-planes in order to separate the different classes while maximizing margin. An optimal hyperplan was defined by Vapnik and Cortes (Vapnik, 1998) as the linear decision function with maximal margin between the vectors of the two classes. The hyper-plan can be described as:

$$f(x) = w^t \mathrm{x} + \mathrm{b} \qquad (8)$$

Where w is a dimensional vector and b is a scalar. The SVM determines a hyperplane that corresponds to f(x) =0 for linearly separable data. The support vectors, the samples closed to the hyper-plan boundaries, are used to decide which hyper-plan should be selected since this set of vectors is separated by the optimal hyper-plan. The input samples are mapped into a high dimensional feature space by a space φ function for non-linearly separable case:

$$f(x) = w^t \varphi(\mathrm{x}) + \mathrm{b} \qquad (9)$$

The decision function is described by:

$$D(x) = sign(w^t \varphi(\mathrm{x}) + \mathrm{b}) \qquad (10)$$

Practically, the real issue is often multi-classes. Multi-class SVM classifier aims to give labels to instances using SVMs, where the labels are drawn from a finite set of several elements. Multi-class problem can be taken as multiple binary classification problems. Three approaches exist to extend SVM linear classifiers to a multi-class classifiers are; One-Against-One (OAO) (Knerr, 1990; Hsu, 2002), One-Against-All (OAA) (Cristianini, 2000) and Directed Acyclic Graph (DAG) (Platt, 2000). In this work, a simple execution of a multi class SVM is supported by using the freely available LibSVM library and implementing it in MATLAB platform (Chang, 2011). One of the major tricks of SVM is the Kernel functions. In the case where non-linear separation is possible, these functions are used. In addition, the kernel function can be explained as a measure of similarity between the input samples xi and xj (Schölkopf, 2001), which allows SVM classifiers to meet the separation rule even with highly divergent and complex boundaries. Although several choices for the kernel function are available, including linear, polynomial, sigmoid, RBF we have focused in finding the best kernel. In this work RBF kernel give the best results. Below, we give the equation of the RBF (radial basis function) kernel:

$$k(x,y) = \exp\left(-\sigma\left\|x_i - x_j\right\|^2\right), \sigma > 0 \tag{11}$$

The accuracy of the classifier is highly sensitive on the choice of parameter gamma; it must be tuned to control the amount of smoothing. The behaviors of SVM change when σ becomes too small and when it becomes too large. We calculate, using cross-validation function, the kernel parameters: c and σ. This function consists in setting up a grid-search for σ and c (Hsu, 2009; Kuncheva, 2004).

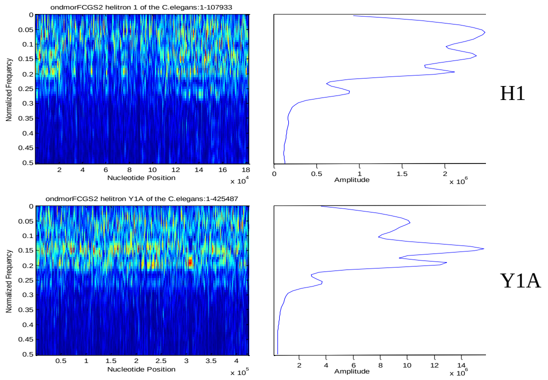
In this work, we use the following couples (c, σ):

$$c = \sigma = [2^{-6}, 2^{-5}, \ldots, 2^{9}, 2^{10}]$$

3 EXPERIMENTAL RESULTS

Helitrons are a families that have variable structures and their identification is a major topic.

Here, we can visually characterize the repetitive patterns in helitrons using the scalogram representation resulted from the CWT analysis of the FCGS2 coding. These specific periodic patterns can characterize helitrons independently of their nature. Note that the C.elegans organism contains 10 helitron families which are: {Helitron1 (H1), Helitron2 (H2), HelitronY1 (Y1), HelitronY1A (Y1A), HelitronY2 (Y2), HelitronY3 (Y3), HelitronY4 (Y4), NDNAX1, NDNAX2 and NDNAX3}.



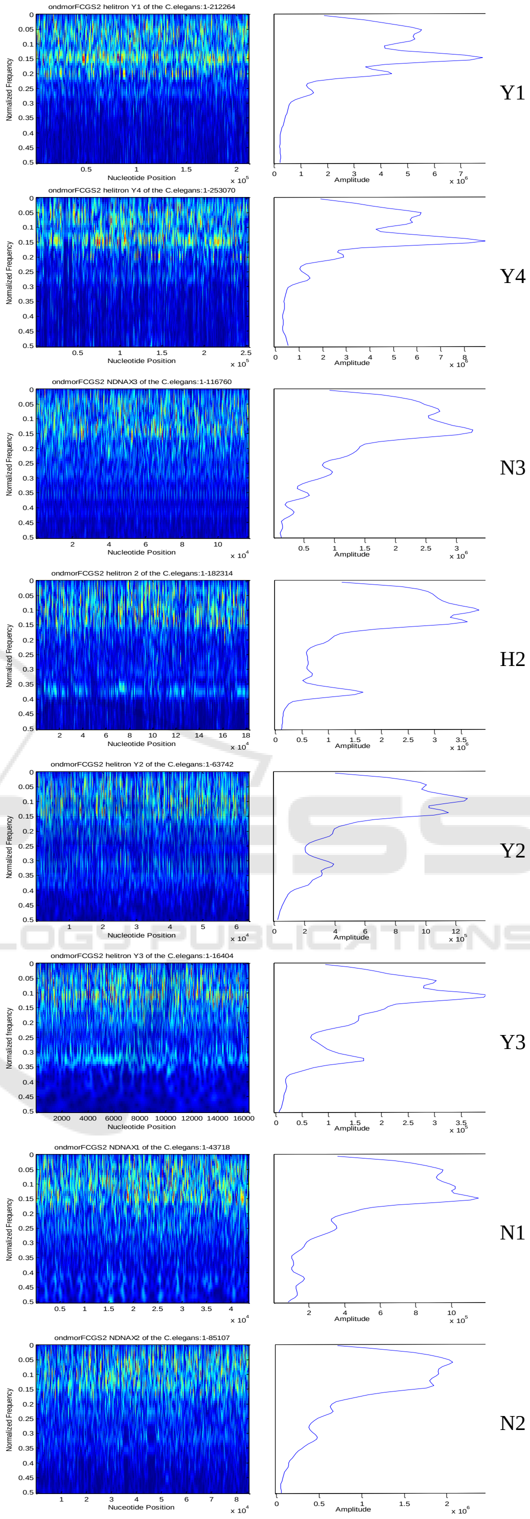


Figure 2: Helitron particular scalograms and energy-wavelet vector for each helitron's types.

3.1 Time Frequencies Signature of Each Helitron’s Types

For each helitron’s types we represent (figure 2) the helitrons scalograms and the corresponding energy-vector which are marked by sharp signatures and distinguished periodic structures. Here, for each helitron’s types our idea is to concatenate all signals and applied the CWT to these signals to visualize the globally signature. We can clearly see that for each helitron’s types have a specific signature around the specific frequency band. So, we can distinguish the periodic motifs for each helitron by a high level of energy around frequencies. The energy-wavelet vector reflect the power of the energy that correspond to the frequency bound.

More of this, we can see that we have similarities between some helitron’s types which are;

- Helitron1_CE and HelitronY1A_CE
- HelitronY1_CE and HelitronY1A_CE
- Helitron1_CE and Helitron4_CE
- Helitron2_CE and HelitronY2

Figure 2 represents the helitron’s scalograms that have a remarkable and repetitive motifs that have high energy around a frequency. Also, we have the specific, energy vector values for each helitron’s types.

3.2 SVM-Helitron’s Classification

A genomic sequence of DNA can be analyzed using digital signal processing techniques (Tsonis, 1996; Adorjan, 2002). In this work, we combined analysis technique (CWT) and classification technique (SVMs) to classify helitrons.

In the first step, we extracted the genomic helitron’s database and we applied the FCGS2 coding method. In the second step, we prepared our feature database which contains the frequencies features (energy-wavelet) of these sequences. These features have been extracted based on the CWT applied to the FCGS2 signal. After that, we calculate the energy correspond to each scales to balance the features extracted from the CWT. Then, we splitted the data into two sub-databases: 70% for training and 30% for testing (Table 1). Finally step, we made the classification accuracy of two approaches of multi-class SVM: OAO and OAA. A comparison between the four kernels-SVM based methods can be conducted; linear, Polynomial, RBF and sigmoid. Moreover, based on our experiments, the OAO approach given the best results when we used the RBF kernel. The experimental results of the multi-class SVM based method are shown in Table 2, Table 3 and Table 4 which represent the classification rates obtained with RBF-kernel with optimal parameters (c and gamma) and with the OAO approach.

Table 1: SVM-helitrons database.

	H1	H2	Y1	Y1A	Y2	Y3	Y4	N1	N2	N3
number	197	469	483	1093	337	117	523	77	188	134
training	137	328	338	765	236	83	368	54	131	94
testing	60	141	145	328	101	34	155	23	57	40

Table 2: Confusion matrix expose the classification results of all helitron’s types used RBF-SVM and OAO approach.

OAO and RBF-kernel with c= 60 and g= 0.0000000015625											
Helitron’s class	H1	H2	Y1	Y1A	Y2	Y3	Y4	N1	N2	N3	
H1	25,64	12,82	12,82	46,15	0	0	2,56	0	0	0	58.48 % (424/725)
H2	1,07	75,26	1,07	13,97	6,45	0	1,07	0	1,07	0	
Y1	2,06	9,27	36,08	39,17	1,03	0	10,30	1,03	1,03	0	
Y1A	5,50	5,50	8,71	74,31	1,37	0,45	3,21	0,45	0,45	0	
Y2	0	23,52	0	4,41	70,58	1,47	0	0	0	0	
Y3	0	21,73	0	17,39	0	60,86	0	0	0	0	
Y4	0	7,54	19,81	38,67	0,94	0	32,07	0	0,94	0	
NDNAX1	0	18,75	0	25	0	0	0	43,75	6,25	6,25	
NDNAX2	0	8,10	0	21,62	5,40	0	0	0	64,86	0	
NDNAX3	0	14,28	0	14,28	0	0	0	0	0	71,42	

Table 3: Confusion matrix expose the classification results of 7 helitron's types used RBF-SVM and OAO approach.

OAO approach and RBF-kernel with c= 60 and g= 0.0000000015625								
Helitron's class	H2	Y1A	Y2	Y3	Y4	N2	N3	71.20 % (408/573)
H2	76,34	13,97	6,45	0	2,15	1,075	0	
Y1A	6,88	85,32	1,37	0,45	5,96	0	0	
Y2	23,52	4,41	70,58	1,47	0	0	0	
Y3	16,73	12,39	0	70,86	0	0	0	
Y4	7,54	47,16	0,94	0	42,45	1,88	0	
N2	8,10	21,62	5,40	0	0	64,86	0	
N3	14,28	14,28	0	0	0	0	71,42	

Table 4: Confusion matrix expose the classification results of 6 helitron's types used RBF-SVM and OAO approach.

OAO and RBF-kernel with c= 60 and g= 0.0000000015625							
Helitron's class	H2	Y1A	Y2	Y3	N2	N3	80.2998% (375//467)
H2	86,36	6,12	6,45	0	1,07	0	
Y1A	6,88	90,82	1,37	0,45	0,45	0	
Y2	4,52	4,41	89,60	1,47	0	0	
Y3	10,73	17,39	0	71,88	0	0	
N2	8,1	19,62	5,4	0	67,86	0	
N3	10,28	9,28	0	0	0	80,44	

Here, using the Cross-Validation function we found the optimal value of 2 parameters: (σ) the kernel width and (c) the regularization parameter. Overall, the kernel width σ =0.0000000015625, the penalty c=60 and the SVM-RBF have given best accuracy rates of the classification system of all helitron's types (acc= 58.5%), the classification system of seven helitron's types (acc= 71.20 %) and the classification system of six helitron's types (acc= 80.29 %). The confusion matrix in the table 2 confirm the existence of the similarities between the helitrons cited in the first part of experimental results. The helitrons have a highest rates; Helitron2_CE (75%), HelitronY1A_CE (74%) and NDNAX3_CE (71%) and HelitronY2 (70%) were obtained using OAO approach of SVM-RBF(c =60 and σ =0. 0000000015625).

The confusion matrix in the table 3 represent the results of classification of 7 helitron's types (without HelitronY1, HelitronY1 and NDNAX1). The confusion matrix in the table 4 represent the results of classification of 6 helitron's types (without HelitronY1, HelitronY1, HelitronY4 and NDNAX1). By eliminating the helitrons which have a great similarity the classification rate increased.

4 CONCLUSIONS

In this paper, we characterized each helitron's types by a specific signatures. In fact, with the resulting the scalograms representation from the CWT analysis applied to FCGS2 coding technique. Then, we came to visually distinguish each helitron' families based on its specific time frequencies signature. Based on this, we have used the CWT analysis to extract the features (energy-wavelet) sets for the overall helitrons SVM-classification. Moreover, we investigated the optimal parameters of Kernel-SVM and features representations. Based on our experiments, the recognition system of all helitron's types was improved when we have chosen the best parameters of the RBF-kernel (c=60 and σ=0.0000000015625) which gave the best accuracy rates .For the classification of the not similar helitron's types, the best classification rate was obtained for the HelitronsY1A_CE class which value is 90% with c = 60, σ = 0.0000000015625 and using the OAO approach. Two other notable helitron's classes have shown high accuracy rate: HelitronsY2_CE and Helitron2_CE with the value of 89% and 86% respectively. The obtained results demonstrated the successfulness of the features (energy-wavelet) extracted from the CWT analysis applied to the FCGS2 signals to classify helitron's sequences in C.elegans. The novelty of this work resides in the fact of the all helitron’s classification using the energy of matrix contains the coefficient of wavelet (time-frequencies presentation). These energy-vector can characterize each helitrons by specific frequencies that have energy around the specific frequency.

REFERENCES

Amin, H. U., Malik, A. S., Ahmad, R. F., Badruddin, N., Kamel, N., Hussain, M., & Chooi, W. T. 2015. Feature extraction and classification for EEG signals using wavelet transform and machine learning techniques. *Australasian physical & engineering sciences in medicine*, 38(1), 139-149.

Chang, C. C., & Lin, C. J. 2011. LIBSVM: a library for support vector machines. *ACM transactions on intelligent systems and technology (TIST)*, 2(3), 27.

Du, C., Fefelova, N., Caronna, J., He, L., & Dooner, H. K. 2009. The polychromatic Helitron landscape of the maize genome. *Proceedings of the National Academy of Sciences*, 106(47), 19916-19921.

Du, C., Caronna, J., He, L., & Dooner, H. K. 2008. Computational prediction and molecular confirmation of Helitron transposons in the maize genome. Bmc *Genomics*, 9(1), 51.

Edgar, R. C. 2004. MUSCLE: multiple sequence alignment with high accuracy and high throughput. *Nucleic acids research*, 32(5), 1792-1797.

Norinder, U. 2003. Support vector machine models in drug design: applications to drug transport processes and QSAR using simplex optimisations and variable selection. *Neurocomputing*, 55(1), 337-346.

Mateos, A., Dopazo, J., Jansen, R., Tu, Y., Gerstein, M., & Stolovitzky, G. 2002. Systematic learning of gene functional classes from DNA array expression data by using multilayer perceptrons. In *Genome Research*, 12(11), 1703-1715.

Öz, E., & Kaya, H. 2013. Support vector machines for quality control of DNA sequencing. *Journal of Inequalities and Applications*, 2013(1), 85.

Furey, T. S., Cristianini, N., Duffy, N., Bednarski, D. W., Schummer, M., & Haussler, D. 2000. Support vector machine classification and validation of cancer tissue samples using microarray expression data. *Bioinformatics*, 16(10), 906-914.

Hsu, C. W., & Lin, C. J. 2002. A comparison of methods for multiclass support vector machines. *IEEE transactions on Neural Networks*, 13(2), 415-425.

Hsu,C.W., Chang, C.C. and Lin, C. J. 2009. A practical guide to support vector classification,” *Department of Computer Science and Information Engineering National Taiwan University, Taipei*, Taiwan, Available: www.csie.ntu.edu.tw/ cjlin/

Shawe-Taylor, J., Bartlett, P. L., Williamson, R. C., & Anthony, M. 1998. Structural risk minimization over data-dependent hierarchies. *IEEE transactions on Information Theory*, 44(5), 1926-1940.

Vapnik, V.N., Vapnik,V. 1998. “Statistical learning theory,” New York : Wiley,.

Vapnik, V., 1995. The nature of statistical learning theory,” *Springer Verlag New York*, Inc. New York,

Gutschoven, B., & Verlinde, P. 2000. Multi-modal identity verification using support vector machines (SVM). In Information Fusion, 2000. FUSION 2000. *Proceedings of the Third International Conference on* (Vol. 2, pp. THB3-3). IEEE.

Poulter, R. T. M., & Goodwin, T. J. D. 2005. DIRS-1 and the other tyrosine recombinase retrotransposons. *Cytogenetic and genome research*, 110(1-4), 575-588.

Hood, M. E. 2005. Repetitive DNA in the automictic fungus Microbotryum violaceum. *Genetica*, 124(1), 1-10.

Kapitonov, V. V., & Jurka, J. 2001. Rolling-circle transposons in eukaryotes. *Proceedings of the National Academy of Sciences*, 98(15), 8714-8719.

Lai, J., Li, Y., Messing, J., & Dooner, H. K. 2005. Gene movement by Helitron transposons contributes to the haplotype variability of maize. *Proceedings of the National Academy of Sciences of the United States of America*, 102(25), 9068-9073.

Schnable, P. S., Ware, D., Fulton, R. S., Stein, J. C., Wei, F., Pasternak, S., ... & Minx, P. 2009. The B73 maize genome: complexity, diversity, and dynamics. *Science*, 326(5956), 1112-1115.

Tempel, S. 2007. Dynamique des hélitrons dans le genome d'Arabidopsis thaliana: développement de nouvelles stratégies d'analyse des éléments transposables (Doctoral dissertation, Université Rennes 1).

Sweredoski, M., DeRose-Wilson, L., & Gaut, B. S. 2008. A comparative computational analysis of nonautonomous helitron elements between maize and rice. *BMC genomics*, 9(1), 467.

Xiong, W., He, L., Lai, J., Dooner, H. K., & Du, C. 2014. HelitronScanner uncovers a large overlooked cache of Helitron transposons in many plant genomes. *Proceedings of the National Academy of Sciences*, 111(28), 10263-10268.

Yang, L., & Bennetzen, J. L. 2009. Structure-based discovery and description of plant and animal Helitrons. *Proceedings of the National Academy of Sciences*, 106(31), 12832-12837.

Wicker, T., Sabot, F., Hua-Van, A., Bennetzen, J. L., Capy, P., Chalhoub, B., ... & Paux, E. 2007. A unified classification system for eukaryotic transposable elements. *Nature Reviews Genetics*, 8(12), 973-982.

Fiser, A., Tusnady, G. E., & Simon, I. 1994. Chaos game representation of protein structures. *Journal of molecular graphics*, 12(4), 302-304.

Merry, R. J. E., & Steinbuch, M. 2005. Wavelet theory and applications. *literature study, Eindhoven university of technology, Department of mechanical engineering, Control systems technology group*.

Morgante, M., Brunner, S., Pea, G., Fengler, K., Zuccolo, A., & Rafalski, A. 2005. Gene duplication and exon shuffling by helitron-like transposons generate intraspecies diversity in maize. *Nature genetics*, 37(9), 997.

Messaoudi, I., Oueslati, A. E., & Lachiri, Z. 2013. Complex Morlet wavelet analysis of the DNA frequency chaos game signal and revealing specific motifs of introns in C.elegans. *arXiv preprint arXiv:1306.5109.*

Messaoudi, I., Oueslati, A. E., & Lachiri, Z. 2014. Revealing Helitron signatures in Caenorhabditis elegans by the Complex Morlet Analysis based on the Frequency Chaos Game Signals. In I*WBBIO* (pp. 1434-1444).

Messaoudi, I., Oueslati, A. E., & Lachiri, Z. 2014. Wavelet analysis of frequency chaos game signal: a time-frequency signature of the C. elegans DNA. *EURASIP Journal on Bioinformatics and Systems Biology*, 2014(1), 16.

Messaoudi, I., Elloumi-Oueslati, A., & Lachiri, Z. (2014). Building specific signals from frequency chaos game and revealing periodicities using a smoothed Fourier analysis. *IEEE/ACM Transactions on Computational Biology and Bioinformatics*, 11(5), 863-877.

Touati, R., Massaoudi, I., Oueslati, A. E., Lachiri, Z., & Ellouze, N. 2016. Nucleosome location method based on morlet wavelet analysis scalograms investigation. In *Advanced Technologies for Signal and Image Processing (ATSIP), 2016 2nd International Conference on* (pp. 307-312). IEEE.

Grossmann, A., & Morlet, J. 1984. Decomposition of Hardy functions into square integrable wavelets of constant shape. *SIAM journal on mathematical analysis*, 15(4), 723-736.

Tse, N. C., & Lai, L. L. 2007. Wavelet-based algorithm for signal analysis. *EURASIP Journal on Applied Signal Processing*, 2007(1), 169-169.

Najmi, A. H., & Sadowsky, J. 1997. The continuous wavelet transform and variable resolution time-frequency analysis. J*ohns Hopkins APL Technical Digest*, 18(1), 134-140.

Oueslati, A. E., Messaoudi, I., Lachiri, Z., & Ellouze, N. 2015. A new way to visualize DNA's base succession: the Caenorhabditis elegans chromosome landscapes. *Medical & biological engineering & computing*, 53(11), 1165-1176.

Cortes, C., Vapnik, V.N. 1995. Support-Vector Networks, *Machine Learning, springer*, NewYork, vol. 20, no. 3, pp. 273-297,.

Schölkopf, B. 2001. The kernel trick for distances. In *Advances in neural information processing systems* (pp. 301-307).

Kuncheva, L. I. 2004. Combining pattern classifiers: methods and algorithms," *John Wiley & Sons*.

Knerr, S., Personnaz, L., & Dreyfus, G. 1990. Single-layer learning revisited: a stepwise procedure for building and training a neural network. *Neurocomputing: algorithms, architectures and applications*, 68(41-50), 71.

Cristianini, N. and Shawe-Taylor, J. 2000. An Introduction to Support Vector Machines and other Kernel-based Learning Methods," Cambridge, UK: Cambridge University Press.

Platt, J. C., Cristianini, N., & Shawe-Taylor, J. 2000. Large margin DAGs for multiclass classification. In *Advances in neural information processing systems* (pp. 547-553).

Tsonis, A. A., Kumar, P., Elsner, J. B. 1996. Wavelet analysis of DNA sequences," *Physical Review E*, vol. 53, no 2, p. 1828.

Adorján, P., Distler, J., Lipscher, E., Model, F., Müller, J., Pelet, C.,.. & Howe, A. 2002 Tumour class prediction and discovery by microarray-based DNA methylation analysis. *Nucleic acids research*, 30(5), e21-e21.