

# Cloud Based Exon Prediction Methodology using Logarithmic Adaptive Algorithms for Genomic Signal Analysis

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## ABSTRACT

Cloud Computing provides healthcare companies with the major convenience in the research and economic aspects. Cloud services ensure that large quantities of such sensitive data will be stored and managed securely. The gene sequence labs send inferred data to various sequence libraries under traditional flow of gene information through the Internet. Cloud service use will reduce DNA sequencing storage costs to a minimum. In this work, we developed a novel genomic bioinformatics-based system, using Amazon Cloud Services, that stores and processes genomic sequence information. An important task in bio-informatics that is used for the recognition and implementation of disease drug, is the exact recognition of exon regions in deoxyribonucleic acid (DNA) sequence. All exon identification techniques are based on three basic periodicity (TBP) properties of exons. With the comparison of various existing methods, adaptive signal processing techniques have been promising. This paper uses the maximum normalized logarithmic mean least square (MNLMLS) algorithm also its signed variants to develop multiple adaptive exon predictor (AEPs) with less computational complexity. Eventually, a performance evaluation is performed for different AEPs using various standard gene data sequences derived from National Biotechnology Information Centre (NCBI) genomic sequence database, such as Sensitivity (Sn), Specificity (Sp) and Precision (Pr) measurements.

**Key words:** Adaptive exon predictor, cloud computing, computational complexity, DNA, health care.

## 1. INTRODUCTION

Genomics is the immense field in which areas that code for proteins are identified using smart AEP based system presented here. Exon areas have a role to play in the assessment of diseases and drug design. Intergenic and genic sections are included in DNA sequence [1]. The primary protein segments structure is studied to support both exon

sections tertiary also secondary structure. After determining this for overall exon segments, any malformations are likely to be identified, and heal diseases [2] [3]. All living things remain alienated aseukaryotes and prokaryotes. Protein coding sections are still referred to as exons in part of eukaryotes, whereas introns are known as non-protein coding sections. Just 3% of the eukaryotic human gene sequence has coding areas and rest remain non-coding areas. Consequently, it is an important task to detect coded sections in a DNA sequence [4] [5]. Therefore, several methodologies for the recognition of exon are proposed in literature [6]-[10].

Adaptive techniques using AEP based smart communication system in a number of iterations may process more lengthy sequences. Our current work presents a novel adaptive exon predictor (AEP) with MNLMLS adaptive algorithms. To obtain better efficiency than LMS, the signed variants of MNLMLS algorithms are considered. LMS drawbacks are resolved by NLMLS algorithm, thereby increases speed and ability of exon tracking. Excess mean square error (EMSE) is also decreased during exon identification [11]-[13]. Sign-based algorithms also reduce the sign function by quantity of multiplication calculations [14]-[16]. Several errors also do not meet the monitoring requirements due to the stationary step-size data-independent algorithms [17]. Lower EMSE and larger step size are necessary for the best convergence rate. Disadvantages of LMS are overcome by use of MNLMLS based techniques.

Based on the error signal generated in the iteration process shows instances changes of adaptive algorithm step sizes in [18]-[21] forbidden the step size. They exhibit better performance than the conventional Least mean squares (LMS) technique. To minimize the computational complexity, we combined MNLMLS algorithm with sign algorithms. The developed Hybrid AEP techniques are maximum normalized least mean logarithmic squares (MNLMLS), maximum normalized sign regressor NSRLMLS (MNSRLMLS), maximum normalized sign NLMLS (MNSLMLS), as well as maximum normalized sign sign LMLS (MNSLMLS)

algorithms. The evaluation of proposed AEPs is performed in terms of standard genomic database taken from NCBI gene database [22]-[26]. The performance of the several variants of proposed AEPs is measured in terms of convergence features, computational difficulty, Precision (Pr), Sensitivity (Sn) and

Specificity (Sp). Several procedures for the exon identification are described in [27]–[30]. The implementation of various types of AEPs based on adaptation methods is discussed in the following sections. The performance efficiency of developed AEPs is also described.

## 2. ADAPTIVE ALGORITHMS FOR EXON PREDICTION

The first step is gene sequence analysing it is considered based on densities of dimer nucleotide as NCBI sequence database. Then it is converted to numerical data in the proposed AEP. It remains a chief job of genomic processing because only digital or discrete signals can be used for signal processing. DNA sequence here is translated to binary information describing four binary streams with binary mapping. Converting the data into Digital information is the vital task in the processing of gene sequence while the signal processing techniques are used for the processing of such type of signal.

In the digital notation nucleotide presence is represented by 1 and nucleotide absence is represented by 0. Now the converted digital data is used as input of adaptive algorithm. By using signal processing adaptive filter algorithms generated an AEP. Let  $M(n)$  is mapped digital sequence,  $x(n)$  is data sequence of DNA,  $d(n)$  is TBP gene sequence,  $y(n)$  adaptive filter output and  $e(n)$  is the feedback signal that is used for updating weight coefficients obtained in feedback loop. Sequence length of LMS technique considered as 'T'. The current step size parameter 'P' is used to generate the next weight coefficient with current weight coefficient as  $h(n)$ , also at that instant the input binary mapped sequence is represented as  $M(n)$ . In [12] the mathematical analysis of LMS algorithm is described. Block diagram representation of AEP is shown in Fig. 1.

The LMS weight recursion is represented as

$$h(n + 1) = h(n) + P x(n) e(n) \quad (1)$$

The computation complexity should be minimum for Adaptive algorithms to identify exon recognition and it is used in applications like to attract Nano bioinformatics. Input Gene information is clipping; a feedback signal is possible with decreased values. In [18], for this purpose techniques are studied. The signed variants are implemented for these techniques.

The Signum function can be expressed as

$$C\{x(n)\} = \begin{cases} 1: x(n) > 0 \\ 0: x(n) = 0 \\ -1: x(n) < 0 \end{cases} \quad (2)$$

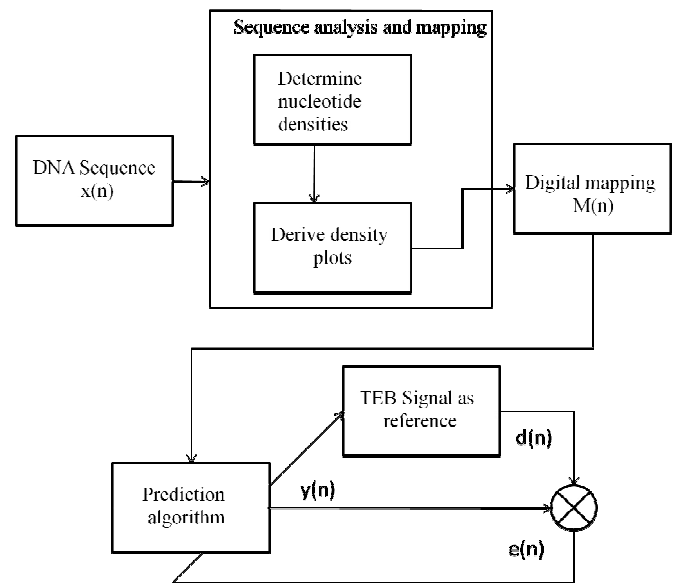


Figure 1: Proposed AEP block diagram

For reducing computational complexity of LMS these versions are used. Computational complexity is more for LMS compares to other three sign variants. Data Clipped LMS (DCLMS) technique can be expressed as LMS recursion by varying input data sequence. Input  $x(n)$  is replaced by averaged values of  $C\{x(n)\}$ , where signum function is used for removing  $x(n)$  on the basis of element by element.

The updated weight recursion expressions of DCLMS algorithm is represented as

$$h(n + 1) = h(n) + P C\{x(n)\} e(n) \quad (3)$$

Updated weight recursion expressions of ECLMS algorithm is obtained by applying signum function to the  $e(n)$

$$h(n + 1) = h(n) + P x(n) C\{e(n)\} \quad (4)$$

Also, the updated weight recursion expressions of DECLMS is obtained by applying signum function to both  $x(n)$ ,  $e(n)$  it is expressed as

$$h(n + 1) = h(n) + P C\{x(n)\} C\{e(n)\} \quad (5)$$

Due to its robustness as well as simplicity, the standard adaptive LMS technique is suitable for exon forecast. In order to choose parameter of step size for the convergence as well as stability, understanding of preceding input power level rate is required for LMS filter. As one of the statistical unknown levels is generally the input power level, it will normally be assessed through information prior start of adaptation process. The vector of the input information is proportionate to weight update process. Other one being its step size is fixed. Both these remain two setbacks of LMS.

Mathematical Modeling of NLMLS Algorithm

**Parameters:** T = number of taps (i.e. filter length),  $\mu$  = step size parameter

Let the tap input be  $x(n)$  and filter length T is moderate to large

**Initialization:** Set  $w(0) = 0$  as initial condition

**Data:** Given  $x(n) = T$ -by-1 tap input vector to filter  $n_2$  at time  $n = [x(n), x(n-1) \dots \dots x(n-T+1)]^T$

$w(n)$  is the tap weight vector of adaptive filter,  $d(n)$  is desired response at time  $n$ ,  $e(n)$  is the error signal,

$\omega_o$  is an unknown vector,  $\mu'$  is adaptation constant,  $(.)^T$  is the transpose of  $(.)$

**To be computed:**  $w(n+1)$  = estimate of tap-weight vector at time  $n+1$

**Computation:**

The FIR filter output is given by  $y(n) = x^T(n) w(n) = w^T(n) x(n)$

The conventional cost function of the error signal  $e(n)$  is  $F[e(n)] = E[(e(n))^2] = E[|e(n)|]$

Here, the normalized error cost function introduced using logarithmic function is given by

$$J(e(n)) = F(e(n)) - \frac{1}{\alpha} \ln(1 + \alpha F(e(n))) \quad (6)$$

where  $\alpha > 0$  is a design parameter and  $F(e(n))$  is a conventional cost function of error signal  $e(n)$ .

The overall steepest descent update is achieved according to the  $J(e(n))$  gradient as

$$w(n+1) = w(n) - \Delta_w \cdot F(e(n)) \left[ \frac{\alpha F(e(n))}{1 + \alpha F(e(n))} \right] \quad (7)$$

Thus, for  $F(e(n)) = E(e(n))^2$ , the weight update equation of the LMLS algorithm becomes

$$w(n+1) = w(n) + \mu \cdot x(n) e(n) \left[ \frac{\alpha (e(n))^2}{1 + \alpha (e(n))^2} \right] \quad (8)$$

$$\text{Setting the time varying size of step parameter as } \mu(n) = \frac{\mu'}{x^T(n)x(n)} = \frac{\mu'}{\|x(n)\|^2} \quad (9)$$

$$\text{A small positive constant } \varepsilon \text{ is added to prevent denominator is too low, } \mu(n) = \frac{\mu'}{\varepsilon + \|x(n)\|^2} \quad (10)$$

The alternate weight expression for NLMLS algorithm is written as

$$w(n+1) = w(n) + \frac{\mu'}{\varepsilon + \|x(n)\|^2} x(n) e(n) \left[ \frac{\alpha (e(n))^2}{1 + \alpha (e(n))^2} \right] \quad (11)$$

Thus, the weight update relation for maximum NLMLS for  $x_{Li} \neq 0$  and  $\varepsilon \neq 0$  becomes

$$w(n+1) = w(n) + \frac{\mu'}{\varepsilon + \max(\|x(n)\|)^2} x(n) e(n) \left[ \frac{\alpha (e(n))^2}{1 + \alpha (e(n))^2} \right] \quad (12)$$

**Figure 2:** Mathematical modeling of MNLMLS Algorithm.

An algorithm must be designed so that weak as well as strong signals can be handled in real time. Therefore, the tap coefficients must be adapted accordingly on the basis of filter changes in input as well as output. Thus, LMS algorithm is suffered with gradient noise amplification limitation for large input data sequences. Normalized LMLS algorithm is considered as a unique LMS algorithm application that takes into consideration signal level variation at the filter output also chooses a logarithmic normalized cost function which leads to a faster converging as well as stable adaptation algorithm. MNLMLS algorithm overwhelms LMS limitations and increases convergence speed and exon tracking ability. Here, we have used MNLMLS and its adaptive algorithm based on SRA to enhance AEP efficiency. The MNLMLS algorithm overcomes the LMS disadvantages and increases the ability of exon identification and quicker convergence when error is high. This also reduces the surplus EMSE in the exon identification process. These MNLMLS adaptive algorithms are used for developing AEPs in order to cope with computing difficulty of an AEP in practical applications.

Fig. 2 describes the mathematical modeling of MNLMLS algorithm. To reduce the computational burden of proposed algorithm we combined with various signum variants. With the combination of sign function the three simplified models of MNLMLS are MNSRLMLS, MNSLMLS, and MNSSLMLS algorithms are derived.

The weight recursion for MNSRLMLS, MNSLMLS, and MNSSLMLS models becomes

$$h(n+1) = h(n) + \frac{P'}{\varepsilon + \max(\|x(n)\|)^2} C[x(n)] e(n) \left[ \frac{\alpha (e(n))^2}{1 + \alpha (e(n))^2} \right] \quad (9)$$

$$h(n+1) = h(n) + \frac{P'}{\varepsilon + \max(\|x(n)\|)^2} x(n) C \left[ e(n) \left[ \frac{\alpha (e(n))^2}{1 + \alpha (e(n))^2} \right] \right] \quad (10)$$

$$\begin{aligned}
 &h(n+1) \\
 &= h(n) \\
 &+ \frac{P'}{\varepsilon + \max(|x(n)|)^2} C[x(n)]C \left[ e(n) \left[ \frac{\alpha(e(n))^2}{1 + \alpha(e(n))^2} \right] \right] \quad (11)
 \end{aligned}$$

At last, we implemented four AEPs by using these adaptive algorithms and compared their performance with AEP with LMS. Sensitivity, Specificity and Precision are taken for the performance measures. The performance measures proved that the MNSRLMLS shows better performance than the other variants. Computational difficulty is the performance metrics for the several techniques considered for the applications.

### 3. COMPUTATION COMPLEXITY AND CONVERGENCE ISSUES

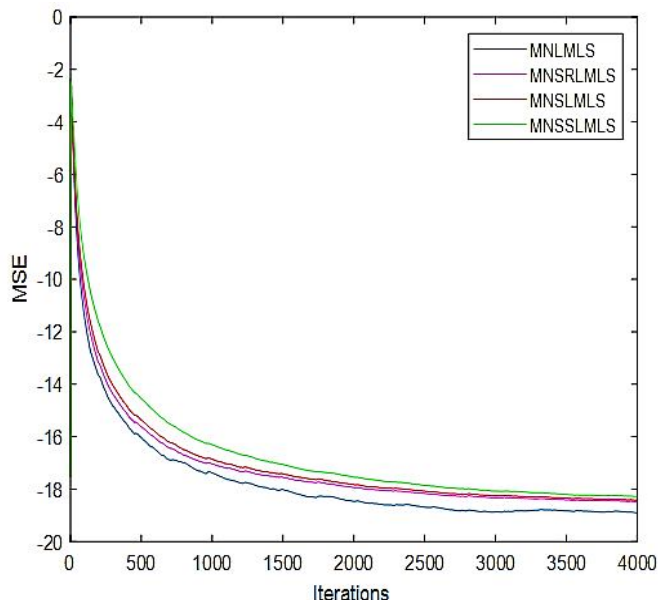
The number of multiplications required for the computations is taken as the performance metric. Main aim is not only to get computation complexity accurate analysis also for better convergence performance of various MNLMLS adaptive techniques. The sign based models are without complex multiplications which are necessary for prediction of exon regions. In the case of LMS, it requires T+1 complex multiplications and one addition in the computation of weight recursion. Whereas for the MNSRLMLS based adaptive technique requires T complex multiplications. The other two sign variants of MNLMLS algorithms require 2T+1 multiply computations. With MNSRLMLS, it needs fewer multiplications with less computing difficulty compared to other MNLMLS based techniques. Table I describes the computational complexities of conventional LMS and three sign variants of MNLMLS algorithms. The MNLMLS based developed AEPs exhibits a smaller number of computations for the location of the desired gene position in a genomic input sequence and can be used in nano bioinformatics applications [5].

**Table1: Computations required for LMS and various MNLMLS based AEPs**

S.No	Algorithm	Multiplications	Additions
1	LMS	T+1	T+1
2	MNLMLS	T+7	T+2
3	MNSRLMLS	T	T+2
4	MNSLMLS	T+5	T+2
5	MNSSLMLS	2	2

Fig.3 describes the convergence performance of MNLMLS and its three sig variants. All the recommended MNLMLS based techniques have obviously faster convergence than the LMS based AEP. Therefore, the MNSRLMLS adaptive algorithm is considered better, based on computing difficulty as well as convergence efficiency in contrast to LMS and its other signed algorithms, among the algorithms considered for AEP implementation. It was obvious that MNSRLMLS

converges quicker compared to MNSLMLS and MNSSLMLS based AEPs from convergence features.



**Figure 3:** MNLMLS algorithm and its signed versions convergence curves

### 4. RESULTS AND DISCUSSION

Performance analysis of several AEPs are discussed. AEP block diagram is described in Figure 1. Several AEP models are implemented based on MNMLS algorithm and its three sign variants. LMS-based AEP is implemented for comparison analysis. From NCBI database [19], Ten genomic datasets are considered for performance comparisons. The performance of the implemented models is measured through by taking the parameters such as Precision (Pr), Sensitivity (Sn), also Specificity (Sp). The detailed study of these specifications is mentioned in [13]. The numerical values of simulation results of various algorithms are mentioned in Table 3.

As part of the determination of exon segments by using DSP methods, there are few measures based on changes in the threshold level in the output spectrum used for comparison. Nucleotides amount situated like introns in exon locating phase remains expressed as True Negative (TN), whereas exon areas exactly predicted is stated for instance True positive (TP). Besides, all the amount of exon areas positioned as intron areas is indicated to be False negative (FN), then compares with number of introns for exact prediction like areas of false positive (FP) exon prediction. Ten gene datasets of NCBI remains regarded to analyze the performance efficiency of various algorithms. The accession for these sequences remains X59065.1, E15270.1, U01317.1, X77471.1, AF009962, X92412.1, AB035346.2, AJ223321.1, AJ225085.1, and X51502.1 respectively as shown in Table 2.

**Table 2:** Gene datasets from NCBI gene databank

Seq. No.	Accession No.	Sequence Definition
1	E15270.1	Human gene for osteoclastogenesis inhibitory factor (OCIF) gene
2	X77471.1	Homo sapiens human tyrosine aminotransferase(TAT) gene
3	AB035346.2	Homo sapiens T-cell leukemia/lymphoma 6(TCL6) gene
4	AJ225085.1	Homo sapiens Fanconi anemia group A(FAA) gene
5	AF009962	Homo sapiens CC-chemokine receptor (CCR-5) gene
6	X59065.1	Homo sapiens human acidic fibroblast growth factor(FGF) gene
7	AJ223321.1	Homo sapiens transcriptional repressor(RP58) gene
8	X92412.1	Homo sapiens titin (TTN) gene
9	U01317.1	Human beta globin sequence on chromosome 11
10	X51502.1	Homo sapiens gene for prolactin-inducible protein (GPII)

Expressions for performance metrics are

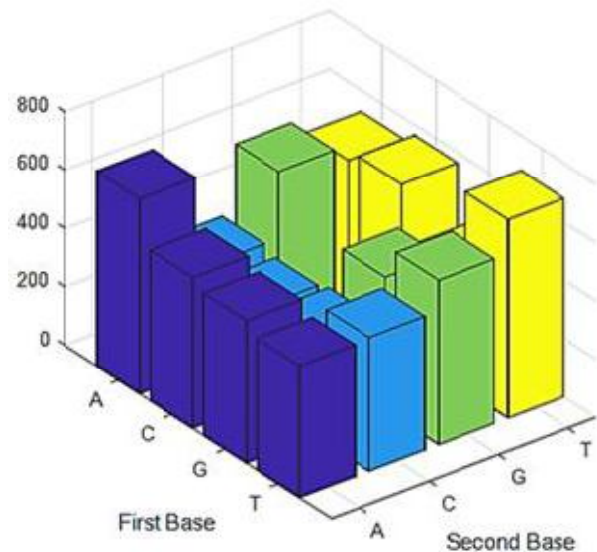
$$Pr = (TP + TN) / (TP + FP + TN + FN)$$

$$Sp = TP / (TP + FP)$$

$$Sn = TP / (TP + FN)$$

Specificity (Sp) is the amount of exon regions exactly found as a part of exons sections, while Sensitivity (Sn) is measured as the amount of exons quantity that remains adequately forecasted. The analysis results of Exon gene sequence 5 predictions with MNLMLS based methods are described in the Fig. 5. The threshold levels are taken from 0.4 to 0.9 with the interval of 0.05. The efficiency of metrics Pr, Sn, and Sp is evaluated by using these values. It is precise at the value of threshold equal to 0.8. Consequently, the measures for performance at threshold value 0.8 are depicted in Table III. The exons with greater A+T percentage nucleotides of a DNA sequence usually exhibit intergenic sequence components, whilst low A+T and greater G+C nucleotides show potential genes. Mostly, high CG dinucleotide content is often found ahead for a gene. Functions of statistics for a gene sequence remains beneficial for determining whether the input gene sequence has protein-coding segments. For DNA sequence having accession AF009962, Fig.4 shows a standard nucleotide density plot. Its dimer distribution is displayed in a bar illustration using MATLAB software.

It has been shown from Fig. 4 that T-T base pair dimers are more in this gene sequence 5 when contrasted to all its dimers. The gene sequence is incorporated with 680 T-T base pair dimers and it also contains 527 A-T and 70 G-C dimers. The G+C content is shown to be smaller than the A+T dimer content which demonstrates that it has less gene count.

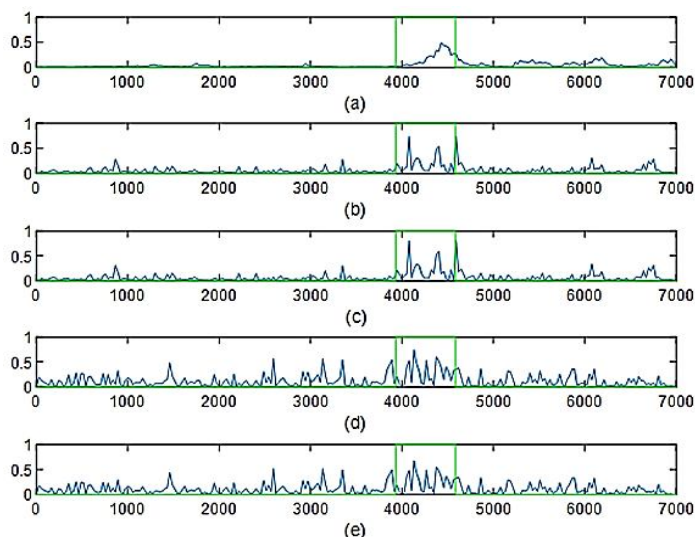


**Figure 4:** Plot for Nucleotide density of dimers for gene sequence 5 with accession AF009962.

The following steps represents step by step process of developed AEP.

- The gene data sets taken from NCBI database are analyzed to find out the existence of gene locations by using PSD plots and are shown in Fig. 5 for genes dependent upon nucleotide density base pairs for G+C also A+T dimers. Following the assessment, this sequence is then converted into digital notation after analysis using the digital mapping technique, while input of AEP remains to be binary information from Figure 1.
- This ensuing sequence is then given as input for the implemented AEP following assessment. TBP obedient biological information is used as a reference signal for developed MNLMLS dependent AEPs.
- For updating filter coefficients, derived e(n) feedback signal from Fig.1 has been used.
- Once this signal becomes minimal, the genes from DNA sequences are precisely located using PSD plots.
- Plots of desired exon areas are shown in PSD. Moreover, Sp, Pr and Sn are also taken for the comparison analysis.

For all sign versions of MNLMLS algorithms gene sequence 5 parameter measures with Accession AF009962 are simulated using MATLAB software. The performance measures of MNSRLMLS based AEP are superior than that of MNLMLS based AEP, with low computational burdens due to less number iterations. It is observed that this model can be able to locate exons sections accurately at 3934-4581 with high resolutions and a sharp spike in the plots of PSD.



**Figure 5:** PSD plots with position of exon (3934-4581) located for genomic data sequence using several developed AEPs, (a). LMS based AEP, (b). MNLMLS based AEP, (c). MNSRLMLS based AEP, (d). MNSLMLS based AEP, (e). MNSSLMLS based AEP. (For these plots the x-axis is Relative Base Location and y-axis is Power Spectrum)

In such cases, the MNSRLMLS algorithm becomes efficient due to low complexity in performing the computations and in terms of exon locating ability. The signum function present in all signed versions of MNLMLS reduces the computational complexity and thus all signed versions predict the exon locations more accurately.

Of all these algorithms, MNSRLMLS based AEP is effective in terms of accurate exon prediction when compared to LMS, MNLMLS and its other signed variants with Specificity Sp, 0.7890 (78.90%), Sensitivity Sn 0.7789(77.89 %), also Precision, Pr 0.7806 (78.06%) respectively. At 0.8 threshold value, the exon prediction appears to be better for MNSRLMLS based AEP. The PSD plots for three signed variants of MNLMLS algorithm are depicted in Fig. 5(b), (c), and (d) respectively. Finally, all proposed MNLMLS based AEPs are more effective to discover exon areas in genomic sequences compared with the prevailing LMS technique.

**Table 3:** Performance Measures of various Implemented AEPs in terms of Sn, Sp and Pr Parameters

Algorithm	Metric	Gene sequence serial number									
		1	2	3	4	5	6	7	8	9	10
LMS	Sn	0.6286	0.6384	0.6457	0.6273	0.6481	0.6162	0.6193	0.6241	0.6268	0.6202
	Sp	0.6435	0.6628	0.6587	0.6405	0.6518	0.6324	0.6529	0.6289	0.6452	0.5965
	Pr	0.5922	0.5894	0.5934	0.5858	0.5904	0.5786	0.5896	0.5856	0.5814	0.5761
MNLMLS	Sn	0.8081	0.7768	0.8072	0.8067	0.7987	0.8073	0.7962	0.8109	0.7981	0.8094
	Sp	0.8001	0.7893	0.7999	0.7987	0.8091	0.7984	0.8078	0.7963	0.8092	0.7966
	Pr	0.8098	0.7967	0.7991	0.8098	0.8001	0.8094	0.7998	0.8094	0.7989	0.8082
MNSRLMLS	Sn	0.7901	0.7553	0.7915	0.7891	0.7789	0.7899	0.7787	0.7890	0.7773	0.7894
	Sp	0.7799	0.7679	0.7778	0.7785	0.7890	0.7789	0.7872	0.7785	0.7869	0.7780
	Pr	0.7782	0.7792	0.7882	0.7890	0.7806	0.7887	0.7769	0.7887	0.7791	0.7897
MNSLMLS	Sn	0.7792	0.7486	0.7705	0.7679	0.7685	0.7693	0.7602	0.7701	0.7600	0.7656
	Sp	0.7687	0.7477	0.7715	0.7703	0.7707	0.7543	0.7682	0.7593	0.7599	0.7569
	Pr	0.7598	0.7665	0.7699	0.7684	0.7701	0.7711	0.7606	0.7665	0.7651	0.7723
MNSSLMLS	Sn	0.7579	0.7201	0.7524	0.7488	0.7476	0.7526	0.7400	0.7487	0.7417	0.7535
	Sp	0.7487	0.7312	0.7886	0.7410	0.7505	0.7479	0.7489	0.7407	0.7403	0.7348
	Pr	0.7509	0.7382	0.7516	0.7511	0.7499	0.7484	0.7381	0.7495	0.7385	0.7509

#### 4. CONCLUSION

In this work we presented the process for the detection of exons in gene sequence. For the adaptive exon identification, a modern approach using smart communication-based system is described here. For this MNLMLS-based adaptation techniques are used to process multiple DNA sequences. The PSD plots of developed MNLMLS algorithm and its three variants techniques are depicted in Fig. 5. Performance measures of exon prediction are mentioned in Table III. The implemented AEP model can exactly locate exon position at 3934-4581 with

greater resolution in PSD plots. MNSRLMLS variant shows better performance in terms of computational complexity, the performance measures are measured for gene sequence 5 having accession AF009962 at the threshold value of 0.8. The computation complexity of the MNSRLMLS based AEP is less compared to MNLMLS based AEP. Also, the MNSRLMLS based AEP provides faster convergence in the identification of exact exon locations. Hence the MNSRLMLS based AEP is the best choice and can be used in system on chip nano-bioinformatics applications and cloud-based exon prediction applications.

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