An Experimental Comparison of PMSprune and Other Algorithms for Motif Search *

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Abstract

Extracting meaningful patterns from voluminous amount of biological data is a very big challenge. Motifs are biological patterns of great interest to biologists. Many different versions of the motif finding problem have been identified by researchers. Examples include the Planted \((l, d)\) Motif version, those based on position-specific score matrices, etc. A comparative study of the various motif search algorithms is very important for several reasons. For example, we could identify the strengths and weaknesses of each. As a result, we might be able to devise hybrids that will perform better than the individual components. In this paper we (either directly or indirectly) compare the performance of PMSprune (an algorithm based on the \((l, d)\) motif model) and several other algorithms in terms of seven measures and using well established benchmarks.

In this paper, we (directly or indirectly) compare the quality of motifs predicted by PMSprune and 14 other algorithms. We have employed several benchmark datasets including the one used by Tompa, et.al. These comparisons show that the performance of PMSprune is competitive when compared to the other 14 algorithms tested.

We have compared (directly or indirectly) the performance of PMSprune and 14 other algorithms using the Benchmark dataset provided by Tompa, et.al. It is observed that both PMSprune and DME (an algorithm based on position-specific score matrices) in general perform better than the 13 algorithms reported in Tompa et. al.. Subsequently we have compared PMSprune and DME on other benchmark data sets including ChIP-Chip, ChIP-seq, and ABS. Between PMSprune and DME, PMSprune performs better than DME on six measures. DME performs better than PMSprune on one measure (namely, specificity).

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1 Introduction

Genomic sequencing allows the identification of nearly all of the genes in an organism, from which the potential gene products can be inferred. However, genomic sequencing does not provide direct information on the function of the individual gene products, nor their interrelationships. Motifs provide clues on this function. Several computational approaches for identifying motifs can be found in the literature. These techniques differ in how motifs are defined and modeled. Each approach looks at a different facet of motifs. No single model or technique can identify all possible motifs. The final verification, as to whether a motif is functional or not, can only be assessed experimentally. Since experiments are expensive and time consuming, computational techniques that can select potential functional motifs with high accuracy are desirable.

Many versions of motif search have been identified in the literature. Examples include planted \((\ell, d)\) motif search (PMS), edit distance based motif search (EMS), and simple motif search (SMS). These algorithms have a common theme. In particular, they look for substrings that are common to many of the given input sequences. Algorithms based on these models have proven to be quite useful in practice for solving problems such as the identification of transcription factor binding sites. PMSprune \[DBR07\] is an algorithm based on the \((\ell, d)\)-motif model that is currently known to solve the largest challenging instances. Another important class of motif finding algorithms is based on position-specific score matrices. These algorithms are based on identifying the statistical difference between a substring and the background. Numerous papers have been written for motif search based on these two and other techniques. It will be highly desirable to compare the various motif search algorithms to identify the advantages and drawbacks of each technique. This comparative study could lead to the discovery of better algorithms. A study of this kind has been conducted by Tompa, et. al. \[TLB+\] who compared the performance of 13 different algorithms based on seven measures. In this paper we add the comparison of two more algorithms to this list. These two algorithms are PMSprune \[DBR07\] and DME \[ASZ05\] (an algorithm based on the position-specific score matrices).

The \((\ell, d)\)-motif Problem (LDMP): This problem takes as input \(n\) sequences each of length \(m\). Input also are integers \(\ell\) and \(d\). The problem is to find a motif \(M\) (a string of length \(\ell\)) that occurs in each input sequence up to hamming distance of \(d\).

Numerous algorithms have been developed to solve LDMP. LDMP algorithms can be categorized into two, namely, exact algorithms and approximation algorithms. An exact algorithm (also called an exhaustive enumeration algorithm) always finds the correct answer(s). On the other hand, an approximation algorithm (also known as a heuristic algorithm) may not always output the correct answer(s). Some examples of algorithms proposed for LDMP are Random Projection \[BT01\], MITRA \[LP02\], Winnow \[PS00\], Pattern Branching \[PRP03\], PMS1, PMS2, PMS3 \[RBH05\], PMSP \[DBR06\], CENSUS \[ES03\] and Voting \[CL05\]. Out of these algorithms, CENSUS, MITRA, PMS1, PMS2, PMS3, PMSP and Voting are exact algorithms.

Certain instances of LDMP have been identified to be challenging instances. In particular, an \((\ell, d)\)-motif instance is said to be challenging if the expected number of motifs that occur in the input by random chance is greater than or equal to one (when the input sequences themselves are generated randomly). For example, the instances \((9,2)\), \((11,3)\), \((13,4)\), and \((15,5)\) are examples of challenging instances. It is customary in the literature to show the performance of LDMP algorithms only on challenging instances. It is always a challenge to solve as large a challenging instance of LDMP as possible.

Pevzner and Sze \[PS00\] have proposed the WINNOWER algorithm. It generates a list of all
the \( l \)-mers present in the database and constructs a graph out of them. Each \( l \)-mer represents a node and there is an edge between two nodes if the hamming distance between these two nodes is at most \( 2d \) and they belong to different sequences. The problem of finding motifs is then reduced to finding large cliques in this graph. The problem of finding a maximum clique in a graph is known to be NP-hard. The authors use some novel pruning techniques to find large cliques. WINNOWER uses a technique to generate Extendable Cliques. It is an iterative algorithm. The run time of this algorithm is \( O(N^{2d+1}) \), where \( N = nm \). SP-STAR uses a technique which eliminates more edges than WINNOWER and hence is faster. It uses less memory as well.

PatternBranching \[PRP03\] performs a local search. It generates the neighbors of all \( l \)-mers present in the sequences and uses a scoring method to assign scores for these neighbors. There are \( n(m - l + 1) \) \( l \)-mers presenting in the sequences. Each \( l \)-mer has \( \binom{l}{d}3^d \) neighbors. The scores of all the neighbors of all the \( l \)-mers are computed and the best scoring neighbors are identified. Since it searches through only a selected set of \( l \)-mers, it is very efficient. This algorithm takes a \( u \), and then computes the best neighbor \( u_1 \) of \( u \). In the next step it identifies the best neighbor \( u_2 \) of \( u_1 \) and so on till it computes \( u_d \). The \( u_d \) values for all possible \( u \) are computed and then the best \( u_d \) value becomes the output. In every step it keeps only one value of the best neighbor but there could be a set of \( l \)-mers which could be the best neighbors for \( u \).

MITRA \[EP02\] is based on WINNOWER \[PS00\]. It uses pair wise similarity information. It uses a mismatch tree data structure and splits the space of patterns into subspaces which start with a given prefix. Pruning is applied to each of these subspaces. MITRA performs very well in practice and is one of the best performing algorithms designed for Planted Motif Search Problem.

AlignACE \[RHEC98\] uses the whole genome RNA quantitation to identify genes that are most responsive to environmental or genotypic change. Searching for mutually similar DNA elements among the upstream non-coding DNA sequences of these genes, the candidate regulatory motifs and corresponding candidate sets of co-regulated genes can be identified. This technique was applied to three regulatory systems in yeast accharomyces cerevisiae: galactose response, heat shock, and mating type. ANN-Spec \[WS00\] uses an Artificial Neural Network and a Gibbs Sampling Method to define the Specificity of a motif. It searches for parameters that will maximize the Specificity of the Binding sequence compared to the Background.

GLAM \[FHSW04\] adds some useful enhancements to the Gibbs Sampling alignment method like automatic detection of alignment width, calculation of statistical significance and optimization of alignment by Simulated Annealing. The Improbizer \[KLK+01\] searches for motifs in DNA or RNA sequences that occur with improbable frequency (to be just chance) using a variation of the expectation maximization (EM) algorithm. Oligo/dyad Analysis \[vHRCV00\] detects statistically significant motifs by counting the number of occurrences of each word or dyad and comparing these with expectation. The most crucial parameter is choosing the probabilistic model for the estimation of occurrence significance. In this study, a negative binomial distribution on word distributions was obtained from 1000 random promoter selections of the same size as the test sets.

QuickScore \[RD04\] uses an extended consensus method allowing well defined mismatches and uses mathematical expressions for computing \( z \)-scores and P values. SoSiMCMC \[ES03\] consists of two stages. In the first stage the weight matrix for a given motif and spacer length is optimized and in the second stage looks for the best motif and spacer lengths for obtained motif positions. It optimizes the common information of the motif and of distributions of motif occurrence positions.

Weeder \[PMM04\] is a consensus-based method where each motif is evaluated according to the number of sequences it appears in and also on how well-conserved they are in these sequences.
YMF \cite{ST03} performs an exhaustive search to find motifs with greatest z-scores. A $p$-value is used to assess significance of the motif.

Several algorithms for PMS have been proposed in \cite{RBH05}. These are exact algorithms based on radix sorting. The first algorithm proposed was PMS1. PMS1 simply generates neighbors of all the $\ell$-mers present in a sequence and saves it in an array $C_i$, where $i$ is the sequence number. It repeats this for all the sequences. The arrays are then sorted. The $\ell$-mers we get with the intersection of all $C_i$’s, where $1 \leq i \leq n$, is the list of motifs. However, PMS1 is not capable of solving challenging instances with large values of $\ell$. Some improvements have also been proposed on PMS1 in \cite{RBH05}. Another algorithm proposed is PMS2 \cite{RBH05}, which is capable of solving challenging instances up to $d = 4$. For instance, it could not solve the Challenging instance (15, 5). The third algorithm proposed in \cite{RBH05} was PMS3 which was later implemented and is capable of solving the challenging Instance (21, 8). Two new algorithms PMSP and PMSi were proposed in \cite{DBR07} which were built upon PMS1 and perform a lot better than PMS1.

PMSP \cite{DBR07} uses the idea of exploring the neighbors of all the $\ell$-mers that occur in the first sequence and then checking if these represent a motif or not. The worst case time bound of this algorithm is worse than that of PMS1 but in practice it performs much better. It is capable of solving the challenging instance (17, 6).

PMSPprune \cite{DBR07} is another algorithm based on PMS1 and is an improvement over PMSP. It uses a branch and bound approach. It shows significant improvements in terms of time taken and is also capable of solving the challenging instance (19, 7). In this paper we use qPMSprune, which is a special case of PMSPprune to perform our tests.

DME (Discriminating Matrix Enumerator) was proposed in \cite{ASZ05}. It uses an enumerative algorithm to exhaustively and efficiently search a discrete space of matrices. Each matrix is scored according to its relative over representation. A local search procedure is used to refine the highest-scoring matrices, which optimizes the relative over representation score. As soon as a motif is discovered, its occurrences are erased from the data and the procedure is repeated to discover additional motifs. In Tompa, et al. \cite{TLB+} 13 different motif finding algorithms have been tested with respect to 7 different statistical measures. We have tested the performance of PMSprune and DME over the benchmark datasets provided by Tompa, et.al. \cite{TLB+}. It is observed that the performances of PMS and DME are in general better than the 13 algorithms compared in \cite{TLB+}. On six of the seven measures, PMSprune did better than DME. DME did better than PMSprune on specificity. We have subsequently compared PMSprune and DME on additional datasets such as ChIP-Chip, ChIP-seq, and ABS.

\section{Methods}

Tompa, et al. \cite{TLB+} posted a challenge for Motif Search Problem where each participant was required to predict a single (or none) motif per dataset even though the 18 data sets have binding sites for multiple motifs. 13 different algorithms for Motif Search participated in this challenge.

The results were evaluated using the benchmark data sets available at http://bio.cs.washington.edu/asses. They have a collection of 56 datasets. In \cite{TLB+} they have tested 13 different programs using several statistical measures. These programs are AlignACE, ANN-Spec, Consensus, GLAM, The Improbizer, MEME, MITRA, MotifSampler, Oligo/dyad-analysis, QuickScore, SeSiMCMC, Weeder and YMF.

We need to define some terms, before the seven statistical measures for testing the programs
can be explained.

- **True Positives** (TP): Number of positions in both known sites as well as predicted sites.
- **False Positives** (FP): Number of positions in predicted sites which are not present in known sites.
- **True Negatives** (TN): Number of positions which are neither in known sites nor in predicted sites.
- **False Negatives** (FN): Number of positions that are in known sites but not in predicted sites.
- **Sensitivity** (Sn): It represents the fraction of sites that were correctly predicted.
- **Sensitivity** (Sp): It represents the fraction of non-sites that were correct.
- **Positive Predictive Value** (PPV): It represents the fraction of predicted sites that are known.

The Sn, Sp and PPV measures are computed as follows (x can either be n for nucleotide or s for site):

1. $xSn = \frac{xTP}{xTP + xFP}$
2. $xSp = \frac{xTN}{xTP + xFP}$
3. $xPPV = \frac{xTP}{xTP + xFP}$

To compute the value for $sSn$, we label a site to be a true positive if there is at least a 25% overlap between the predicted and the known sites.

Nucleotide level **Performance Coefficient** is defined as:

4. $nPC = \frac{nTP}{nTP + nFN + nFP}$

Nucleotide level **Correlation Coefficient** is defined as:

5. $NCC = \frac{nTPnTN - nFNnFP}{(nTP + nFN)(nTN + nFP)(nTP + nFP)(nTN + nFN)}$

In this paper we compare the performance of PMSprune with the above 13 algorithms (indirectly) and the DME algorithm on the Benchmark datasets in [TLB+]. Since a comparison of the above 13 algorithms are already available, a comparison of PMSprune with these 13 algorithms has been done using the results reported in [TLB+].

**Definition 2.1.** $d(x, S_i) = \min_{y \in S_i} d(x, y)$, where $y$ is an $\ell$-mer in $S_i$ and $d(x, y)$ is Hamming Distance between $x$ and $y$.

**Step 1** Find PMS Motifs.

Let $M$ be the list of predicted Motifs from PMS algorithm such that length of $M$, $|M| = m$. 
• PMSSumMin: For each motif $x$ in $M$, we compute the Score as follows. \( Score = \sum_{1 \leq i \leq n} d(x, S_i) \).

After the score is computed for each $x$, the motifs are sorted based on Score. We choose a subset $M'$ from PMS motifs using the following techniques.

Find MinScore = Minimum value of score out of Scores of all motifs $x$.

All motifs that have Score = MinScore are added to the list $M'$.

• PMSSumMin10: The top 10 motifs based on minimum Score is added to the list $M'$.

• PMSSumMin500: The top 500 motifs based on minimum Score is added to the list $M'$.

• PMSSumMinD: For each motif $x$ in $M$, we compute the Score as follows. If \( (d(x, S_i) \leq d) \), then \( ScoreD = ScoreD + d(x, S_i) \).

After the score is computed for each $x$, the motifs are sorted based on Score. We choose a subset $M'$ from PMS motifs using the following techniques.

Find MinScoreD = Minimum value of score out of ScoreD of all motifs $x$. All motifs that have ScoreD = MinScoreD are added to the list $M'$.

• PMSSumMinD10: The top 10 motifs based on minimum ScoreD are added to the list $M'$.

• PMSSumMinD500: The top 500 motifs based on minimum ScoreD are added to the list $M'$.

Step 2 Find DME Motifs

The output from DME are the motifs, corresponding PWMs and a Score for each PWM. Since, PMS outputs unique string motifs and DME motifs have some degenerate positions in them, we open the DME motifs to generate a list of unique motifs and then choose a subset $D'$ from all the DME motifs as follows:

• DMESumMin: Let $x_5, x_6, \ldots, x_{15}$ be the number of motifs of length 5 to 15 respectively in PMSSumMin. We generate the list of DME motifs where the list has $x_\ell$ motifs of length $\ell$, where $5 \leq \ell \leq 15$.

• DMESumMinD: Let $x_5, x_6, \ldots, x_{15}$ be the number of motifs of length 5 to 15 respectively in PMSSumMinD. We generate the list of DME motifs where the list has $x_\ell$ motifs of length $\ell$, where $5 \leq \ell \leq 15$.

• DMESumMin10: The top 10 motifs out of all the motifs from DME are put into $D'$.

• DMESumMin500: The top 500 motifs out of all the motifs from DME are put into $D'$.

• BestDMESumMin: The best $m$ motifs out of all the motifs from DME are included in $D'$, where $m$ is the number of motifs in PMSSumMin.

• BestDMESumMinD: The best $m$ motifs out of all the motifs from DME are included in $D'$, where $m$ is the number of motifs in PMSSumMinD.

Step 3 Compute Statistical Measures.

We compute the 7 statistical measures for each motif in all the 9 files generated. For each dataset the computation is done as follows. Plant all the motifs occurring in the dataset with a distance specified in Table 1 corresponding to the length of the motif. Pick one predicted motif at a time from the file and plant it in the dataset using the distance specified in Table 1 corresponding to the length of predicted motif. Find the values of nTP, nFP, nFN, nFP,
sTP, sTN, sFP, sFN. Use these values to compute the 7 Statistical measures nSn, nSp, sSn, nPPV, sPPV, nPC, and nCC.

| Length(s) | Hamming Distance |
|-----------|------------------|
| 5, 6      | 1                |
| 6, 8      | 2                |
| 9, 10, 11 | 3                |
| 12, 13, 14| 4                |
| 15        | 5                |

Table 1: The \((l, d)\) pairs used for testing

3 Results and Discussions

3.1 Result for Tompa’s dataset

We tested PMSprune and DME on ChIP-Chip, ChIP-Seq, ABS and Tompa’s datasets [TLB+]. Table 2 shows the results for 13 algorithms that were initially evaluated in [TLB+]. The data for the table was obtained from [http://bio.cs.washington.edu/assessment/assessment_result.html](http://bio.cs.washington.edu/assessment/assessment_result.html). The table shows the average values over all the datasets for all four species. It is observed that ANN-Spec shows the best result based on Sensitivity which is 0.087 followed by Weeder with Sensitivity as 0.086. Both PMSprune and DME perform better than these 13 algorithms on sensitivity and other measures. However, when it comes to specificity, many of the 13 algorithms perform better.

| Algorithm         | nSn   | nSp   | sSn   | nPPV  | sPPV  | nPC   | nCC   |
|-------------------|-------|-------|-------|-------|-------|-------|-------|
| AlignACE          | 0.0551| 0.9914| 0.0881| 0.1118| 0.1226| 0.0383| 0.0650|
| ANN-Spec          | 0.0870| 0.9822| 0.1551| 0.0881| 0.0848| 0.0458| nan   |
| Consensus         | 0.0205| 0.9968| 0.0402| 0.1132| 0.1329| 0.0176| 0.0404|
| GLAM              | 0.0257| 0.9872| 0.0459| 0.0381| 0.0482| 0.0156| nan   |
| The Improbizer    | 0.0685| 0.9819| 0.1226| 0.0695| 0.0836| 0.0357| nan   |
| MEME              | 0.0670| 0.9890| 0.1111| 0.1071| 0.1394| 0.0430| 0.0706|
| MEME3             | 0.0776| 0.9847| 0.1245| 0.0909| 0.1348| 0.0437| nan   |
| MITRA             | 0.0313| 0.9906| 0.0498| 0.0623| 0.0623| 0.0213| 0.0309|
| MotifSampler      | 0.0600| 0.9901| 0.0977| 0.1069| 0.1013| 0.0399| 0.0666|
| Oligo/dyad-analysis | 0.0398| 0.9957| 0.0727| 0.1542| 0.1214| 0.0326| 0.0694|
| QuickScore        | 0.0174| 0.9889| 0.0325| 0.0301| 0.0185| 0.0111| 0.0083|
| SeSiMCMC          | 0.0611| 0.9685| 0.0804| 0.0369| 0.0751| 0.0235| 0.0493|
| Weeder            | 0.0863| 0.9960| 0.1009| 0.2996| 0.2886| 0.0718| 0.1523|
| YMF               | 0.0639| 0.9920| 0.1206| 0.1369| 0.1200| 0.0455| 0.0815|

Table 2: Results for 13 algorithms evaluated in Tompa et. al. [12]
3.2 Results for Tompa’s Database for PMSprune and DME

There are 56 datasets in the database used in PMSprune and DME. Due to limitations of DME and PMS we could not test all the datasets. PMS does not work for datasets which have only one sequence in them. Tables 3 and Table 4 show the 7 Statistical Measures for all the 9 Scoring methods we used. The tables represent the values for the Best Motif that we found in Mus09r and Hm26r datasets, respectively. From Table 2 it is observed that although the sensitivity of DME algorithm is very good PMS performs better than DME in all the cases. The specificity for DME is better than PMS in most of the cases but the difference is 1.5% or less.

| Scoring Technique | nSn     | nSp     | sSn     | nPPV    | sPPV    | nPC     | nCC     |
|-------------------|---------|---------|---------|---------|---------|---------|---------|
| PMS SumMin        | 0.6139  | 0.9227  | 0.6149  | 0.3240  | 0.9988  | 0.2692  | 0.4009  |
| DME SumMin        | 0.4385  | 0.9354  | 0.5380  | 0.2907  | 0.9986  | 0.2118  | 0.3093  |
| BestDME SumMin    | 0.4385  | 0.9354  | 0.5380  | 0.2907  | 0.9986  | 0.2118  | 0.3093  |
| PMS SumMinD       | 0.7718  | 0.8910  | 0.7769  | 0.2993  | 0.9986  | 0.2750  | 0.4340  |
| DME SumMinD       | 0.5788  | 0.8899  | 0.6659  | 0.2409  | 0.9983  | 0.2050  | 0.3161  |
| BestDME SumMinD   | 0.4385  | 0.9354  | 0.5380  | 0.2907  | 0.9986  | 0.2118  | 0.3093  |
| PMS SumMin500     | 0.4386  | 0.9408  | 0.4167  | 0.3125  | 1.0000  | 0.2232  | 0.3251  |
| PMS SumMinD500    | 0.4386  | 0.9408  | 0.4167  | 0.3125  | 1.0000  | 0.2232  | 0.3251  |
| DME SumMin500     | 0.0877  | 0.9440  | 0.0833  | 0.0877  | 1.0000  | 0.0459  | 0.0327  |

Table 3: Result for Dataset Mus09r

| Scoring Technique | nSn     | nSp     | sSn     | nPPV    | sPPV    | nPC     | nCC     |
|-------------------|---------|---------|---------|---------|---------|---------|---------|
| PMS SumMin        | 0.3889  | 0.8745  | 0.4970  | 0.2516  | 0.9999  | 0.1803  | 0.2184  |
| DME SumMin        | 0.0658  | 0.9192  | 0.1265  | 0.0811  | 0.9995  | 0.0377  | -0.0166 |
| BestDME SumMin    | 0.1020  | 0.9646  | 0.1383  | 0.2381  | 0.9992  | 0.0769  | 0.0987  |
| PMS SumMinD       | 0.3889  | 0.8745  | 0.4970  | 0.2516  | 0.9999  | 0.1803  | 0.2184  |
| DME SumMinD       | 0.0658  | 0.9192  | 0.1265  | 0.0811  | 0.9995  | 0.0377  | -0.0166 |
| BestDME SumMinD   | 0.1020  | 0.9646  | 0.1383  | 0.2381  | 0.9992  | 0.0769  | 0.0987  |
| PMS SumMin500     | 0.3447  | 0.8695  | 0.4678  | 0.2229  | 1.0000  | 0.1565  | 0.1776  |
| PMS SumMinD500    | 0.3447  | 0.8695  | 0.4678  | 0.2229  | 1.0000  | 0.1565  | 0.1776  |
| DME SumMin500     | 0.0669  | 0.9663  | 0.0851  | 0.1777  | 1.0000  | 0.0511  | 0.0525  |

Table 4: Result for Dataset Hm26r

Table 5 compares the performance of results from all the 9 scoring techniques. We do the comparison in the following manner: For each dataset we compare the 7 Statistical Measures for all the 9 scoring techniques and find out which technique gave the best result for that measure. Then we count the total number of times the scoring technique gave the best result for that Statistical Measure. The numbers in Table 4 represent the count of best performance for each technique for each measure. The sum of each column is 45 which is the total number of datasets that we tested.

Table 6 shows the average values of each statistical measure over all the datasets for all the 9 scoring techniques. It is observed that the average value of nucleotide as well as site Sensitivity for PMS is better than DME. There is at least a difference of 8% or more for nSn and 10% or more
for sSn. DME is better with respect to Specificity. The difference is no more than 3.5%. PMS is better than DME based on the other 4 measures as well.

| Scoring Technique | nSn | nSp | sSn | nPPV | nPC | nCC |
|-------------------|-----|-----|-----|------|-----|-----|
| PMS SumMin        | 18  | 0   | 16  | 8    | 13  | 7   |
| DME SumMin        | 0   | 3   | 0   | 3    | 2   | 2   |
| BestDME SumMin    | 1   | 5   | 1   | 1    | 0   | 0   |
| PMS SumMinD       | 4   | 0   | 3   | 4    | 2   | 2   |
| DME SumMinD       | 0   | 7   | 0   | 0    | 1   | 1   |
| BestDME SumMinD   | 0   | 8   | 0   | 2    | 1   | 2   |
| PMS SumMin500     | 18  | 1   | 20  | 13   | 20  | 11  |
| PMS SumMinD500    | 4   | 0   | 5   | 6    | 3   | 7   |
| DME SumMin500     | 0   | 21  | 0   | 8    | 3   | 12  |

Table 5: Best performers

| Scoring Technique | nSn | nSp | sSn | nPPV | sPPV | nPC | nCC |
|-------------------|-----|-----|-----|------|------|-----|-----|
| PMS SumMin        | 0.2586 | 0.9164 | 0.3483 | 0.3752 | 0.9997 | 0.1561 | 0.1843 |
| DME SumMin        | 0.1638 | 0.9464 | 0.2332 | 0.3623 | 0.9994 | 0.1122 | 0.1385 |
| BestDME SumMin    | 0.1715 | 0.9377 | 0.2419 | 0.3366 | 0.9993 | 0.1122 | 0.1280 |
| PMS SumMinD       | 0.2880 | 0.9163 | 0.3695 | 0.3951 | 0.9996 | 0.1727 | 0.2100 |
| DME SumMinD       | 0.1936 | 0.9420 | 0.2696 | 0.3715 | 0.9995 | 0.1245 | 0.1566 |
| BestDME SumMinD   | 0.1863 | 0.9346 | 0.2626 | 0.3495 | 0.9993 | 0.1220 | 0.1409 |
| PMS SumMin500     | 0.2322 | 0.8961 | 0.3117 | 0.3809 | 0.9787 | 0.1476 | 0.1674 |
| PMS SumMinD500    | 0.2349 | 0.8959 | 0.3160 | 0.3842 | 1.0000 | 0.1487 | 0.1687 |
| DME SumMin500     | 0.1048 | 0.9302 | 0.1485 | 0.2802 | 0.8224 | 0.0747 | 0.0748 |

Table 6: Average of all datasets for Best Results

### 3.3 ChIP-Chip Results

We used the publicly available database for ChIP-Chip available at [http://bdtnp.lbl.gov/Fly-Net/browseChip](http://bdtnp.lbl.gov/Fly-Net/browseChip). Since some datasets are very large we only use the datasets which have less than 500 sequences and length of motifs are less than or equal to 15. A summary of the results can be found in Table 7.

### 3.4 ChIP-Seq Results

We used the Human database for the ChIP-Seq results. It consisted of 24 files (Chr1 - Chr22, ChrX, ChrY). Since the datasets were large, we just sampled a small subset of sequences. 20% of the total number of sequences were chosen at random and all motifs which occur in at least half the sequences are chosen by PMS. The motif and the locations in the sequences are available and we used that information to find where the truth occurred. The comparison results are summarized in Table 8.
| Scoring Technique | nSn  | nSp  | sSn  | nPPV | sPPV | nPC  | nCC  |
|-------------------|------|------|------|------|------|------|------|
| PMSSumMin         | 0.1464 | 0.8304 | 0.2254 | 0.3799 | 1.0000 | 0.1168 | 0.1463 |
| PMSSumMinD        | 0.1575 | 0.8148 | 0.2322 | 0.3603 | 1.0000 | 0.1058 | 0.1143 |
| PMSSumMin500      | 0.1441 | 0.8351 | 0.2253 | 0.3883 | 1.0000 | 0.1169 | 0.0762 |
| PMSSumMinD500     | 0.1181 | 0.8944 | 0.1848 | 0.4314 | 1.0000 | 0.1003 | 0.0277 |
| PMSSumMin10       | 0.1667 | 0.8342 | 0.2481 | 0.4181 | 1.0000 | 0.1364 | 0.112  |
| PMSSumMinD10      | 0.1278 | 0.8928 | 0.1890 | 0.4328 | 1.0000 | 0.1089 | 0.1275 |
| DMESumMin         | 0.1416 | 0.8717 | 0.2025 | 0.4118 | 1.0000 | 0.1193 | 0.0422 |
| DMESumMinD        | 0.1485 | 0.8741 | 0.2079 | 0.4300 | 1.0000 | 0.1265 | 0.0608 |
| DMESumMin500      | 0.1282 | 0.8833 | 0.1918 | 0.4232 | 0.9997 | 0.1077 | -0.0258 |
| DMESumMin10       | 0.1546 | 0.8855 | 0.2138 | 0.4553 | 1.0000 | 0.1339 | 0.0475 |

Table 7: Average Results for ChIP-Chip database

| Scoring Technique | nSn  | nSp  | sSn  | nPPV | sPPV | nPC  | nCC  |
|-------------------|------|------|------|------|------|------|------|
| PMSSumMin         | 0.1554 | 0.8613 | 0.2458 | 0.2086 | 0.9999 | 0.0977 | 0.1554 |
| PMSSumMinD        | 0.1339 | 0.8923 | 0.2142 | 0.2195 | 0.9999 | 0.0817 | 0.1793 |
| PMSSumMinD500     | 0.1135 | 0.9061 | 0.1555 | 0.1896 | 0.9998 | 0.0639 | 0.0935 |
| PMSSumMin500      | 0.1284 | 0.8802 | 0.2068 | 0.1879 | 0.9999 | 0.0776 | 0.1184 |
| DMESumMin         | 0.1128 | 0.9121 | 0.1687 | 0.1365 | 0.9989 | 0.0453 | 0.1769 |
| DMESumMinD        | 0.1043 | 0.8796 | 0.0618 | 0.1170 | 0.9999 | 0.0326 | 0.0429 |
| DMESumMin500      | 0.1189 | 0.9361 | 0.1963 | 0.1376 | 0.9998 | 0.0960 | 0.0891 |

Table 8: Average Results for ChIP-Seq database

3.5 ABS Results

ABS gives us an option to choose the number of sequences, length of sequences, the Motif to be planted along with the probability to plant the motif as an input. We generated datasets of 50 sequences with length 500 each and planted 1 motif with probability 1. Since, ABS plants the motif exactly in about 50% of the sequences, we generate the list M of PMS motifs by finding all motifs which occur exactly in 20 out of 50 sequences. Table 9 presents a summary of the comparison.

| Scoring Technique | nSn  | nSp  | sSn  | nPPV | sPPV | nPC  | nCC  |
|-------------------|------|------|------|------|------|------|------|
| PMS               | 0.1934 | 0.9104 | 0.2298 | 0.5275 | 1.0000 | 0.1783 | 0.2168 |
| DME               | 0.1485 | 0.9148 | 0.1650 | 0.3187 | 1.0000 | 0.1256 | 0.1797 |

Table 9: Average Results for ABS database

4 Conclusions

In this paper we have compared PMSprune, one of the best known exact algorithms based on the \((l, d)\) motif model, with 14 other algorithms. In particular, we have employed the 13 algorithms
reported in \[TLB^+\] and DME. These algorithms have been compared based on seven different statistical measures. This comparison shows that PMSprune is very competitive with the other 14 algorithms.

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