International Journal on Recent and Innovation Trends in Computing and Communication ISSN: 2321-8169
Volume: 5 Issue: 12 209 – 216

# Prediction of RNA 3D Structure using Parallel Algorithm

Mrs. Ujjwala H. Mandekar [a], Dr. S. Khandait[b]

[a]Department of Computer Science and Engineering,Priyadarshini J L College of Engineering, Nagpur,440009 India
[b]Professor & Head of Information Technology Department,KDK Engineering College, Nagpur,440009 India

***Abstract:-*** RNA structures are generally organized hierarchically organized. Prediction of RNA structure is a big challenge for the researchers. Many prediction algorithms have been develop for RNA secondary structure prediction. But prediction of tertiary structure is still a big area of research. Approaches for RNA tertiary structure prediction are broadly categorized into two methods viz. de novo methods and template-based prediction method. The De novo are useful only for the small sequences of the nucleotides. For the sequences with large number of nucleotides template based modelling technique is more useful. These template based method are very common in protein structure prediction but it is not explored in RNA tertiary structure prediction. This paper presents a novel methodology for prediction of RNA tertiary structure using the bank ok known structure (template). First, the RNA secondary structure is analysed on the basis of free nucleotides available region wise which may contribute in the prediction of tertiary structure. Next similar region structure templates are searched in PDB metadata. These templates are then used to for the tertiary structure. As all the templates stored in PDB are predicted structures with minimum negative energy, the resultant tertiary structure is also consequently has minimum negative energy. The proposed method is able to predict even large ribosomal RNA structures. The experimental results have shown for the predicted structures on the basis of percentage similarity as well as time required for prediction.

***Keywords:*** *RNA, Secondary structure, base pairs, tertiary structures.*

*****

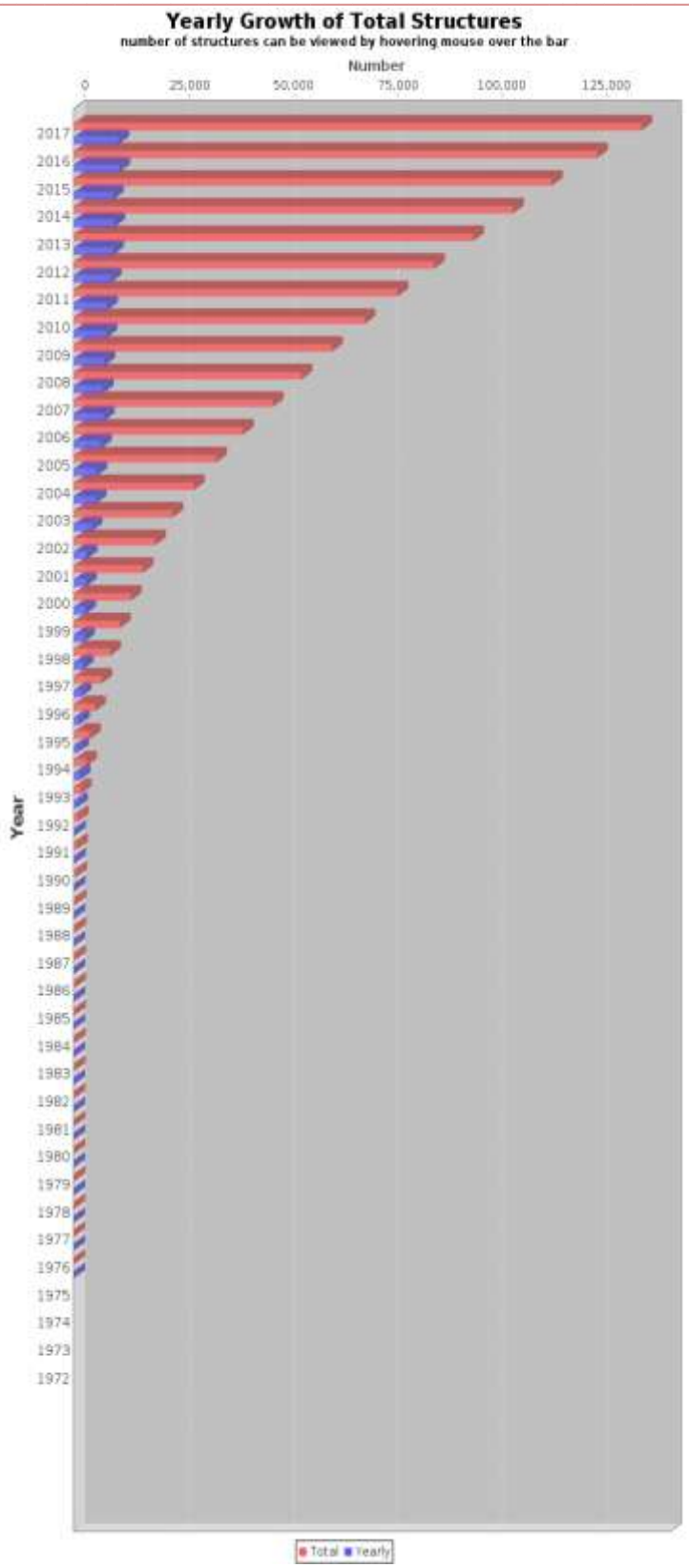
## 1. Introduction:

Traditionally RNA's bbiological role is transcription and translation. Beside this, RNA molecules play many important roles in many cellular processes, such as carrying genetic information, participating in the regulation of gene expression, acting as catalysts in many biological pathways [1]. The non-coding RNAs (ncRNAs) play important roles in many cellular activities e.g. Processing of messenger RNAs [5][6][7], control of protein stability [8] and RNA interference [9]. They are also concerned in number of human diseases like cancer [10][11], infectious and neurodegenerative diseases [12][13][14], and hence RNA structures are very important in disease detection as well as new remedial agents. Day by day, the number of RNA structures, deposited in the PDB and NDB databases [15][16], are increasing(graphical representation is as shown in graph below, hence it has been a vital task to develop the computational tools which are helpful in annotation of RNA structures and functions.

Using the primary sequence of RNA, it is possible to predict its secondary structure; consequently from the secondary structure tertiary structure of the molecule can be predicted [3]. Hence is it essential to analyze the secondary structure in order to know functional characterization of RNA as well as its tertiary structure prediction. For the prediction of the secondary structure Watson-Crick AU and GC base pairs, as well as wobbles pairs are important. These three canonical pairs are the key factors in the RNA folding process. But because of increasing number of known RNA 3D structures, it has become challenge to the researchers to study, in depth, RNA tertiary interactions as well as a variety of other base-base interactions. Generally these base-base interactions are known as non-canonical pairs. From the research study, it has been proved that almost 40 % of all bases in structured RNAs are eligible to take part in noncanonical interactions [4].

In this paper, we present an overview of RNA computational models for tertiary structures' predictions and then focus on a recently developed RNA tertiary model. As a lot of investigation has been carried out for secondary structure prediction, the more emphasize is given on the tertiary structure prediction; and hence as an input secondary structure produced be GT fold algorithm is chosen.

 ISSN: 2321-8169
209 – 216




## 2. Tertiary Structure prediction

Secondary structure consist of sequence of dots (.) and brackets (‘(’,’)’). Dots indicate free bases whereas brackets indicate paired bases. In kissing (tertiary structure) these dots (free bases) are more important. Secondary structure consists of hairpin loop bulge loop internal loop, multi loop, stack, single strand and free bases. Except stack all the loops are having free bases which further interact with each other to form kissing pairs. Hence it is important to know number of loops present in secondary structure.

ISSN: 2321-8169
209 – 216

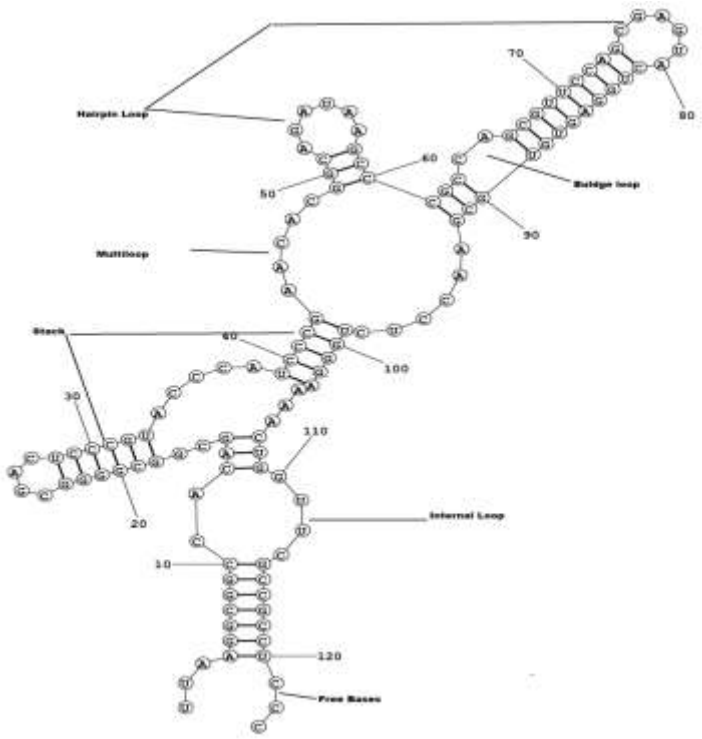



Figure 1: Different types of loop in secondary structure

After getting the information about number of loops present in secondary structure next step is to find out number of free bases present in each loop. In order to find the free bases present in secondary structure it is divided into different regions, as shown in figure below. The main purpose for splitting structure into regions is to avoid bonding of free bases of same loop. While formation of bonds, region number of free bases are checked. Free bases with different region numbers are allowed to form a pair.

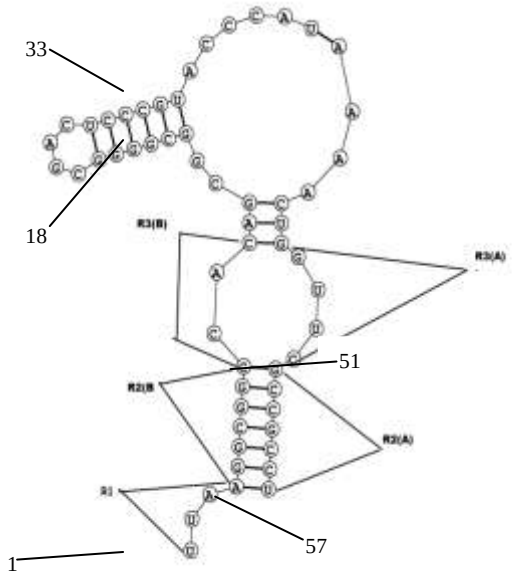



Figure 2: Secondary structure divided into different regions

As shown in figure 2 the secondary structure is divided into 7 region i.e. r1(nucleotides numbered from 1 to 4),r2(stem has two regions as r2(a) from 51 to 57 and r2(b) from 4 to 10) , r3( internal loop region from 10 to 13 and 46 to 51), r4(stem from 13 to 15 and 44 to 46) etc. From these regions free bases are extracted as volunteers to take part in kissing pair of 3D structure.

 ISSN: 2321-8169
209 – 216

### 3. Algorithm FreeBaseCount

These free bases can participate in kissing pair formation if they satisfy following conditions

a. Free bases of one loop will form the pairing with free bases of other loop i.e. pair formation within the free bases of the same regions are avoided.
b. Free bases can form Random match. In random match free bases of one loop are paired with free bases of two or more loop

### 4. Algorithm Kissing-Pair

If we consider the dot sequence of the following secondary structure we get the dot file as shown in figure 4.

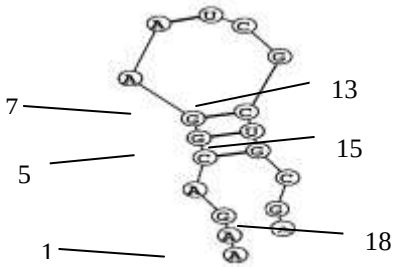



Figure 3: Sample secondary structure

If regions are formed for the structure as R1(1-5),R2(5-7,13-15),R3(7-13) and R4(15-18) , the dot file becomes

Figure 4: DOT file of structure

After applying the algorithm freeBaseSequence a vector is formed which consists of dots (free bases). Hence dot vector becomes

| • | • | • | • | • | • | • | • | • | • | • | • |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |

These free bases forms the data object as shown in table 1; which stores the information as index number, loop to which it belongs and pairable free base index as per Watson-Crick and wobbles pairs. But there is a possibility of formation of $n^{18}$ types of structure if 'n' is the total number of nucleotides present in the structure. It is very difficult to select the best structure amongst all possible kissing pair formation. Hence prediction is bases in similarity basis. Concept is to find out the sequence for kissing pair. This dot file sequence is searched in the PDB data bank. PDB data bank consists of more than 13600 sequences. If the dot files matches with any PDB sequence 100%, its corresponding nucleotide sequenced is checked. The sequence, that gives maximum similarity in nucleotides, is selected as most appropriate sequence. Hence algorithm Similarity calculates similarity using the concept of dynamic programming.

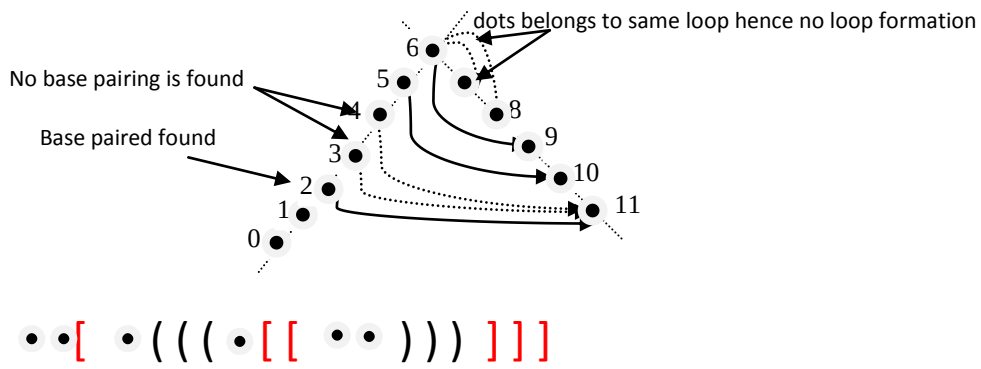
| 0 | -1 | ptr to SingleStrand |
|---|---|---|
| 1 | -1 | ptr to SingleStrand |
| 2 | -1 | ptr to SingleStrand |
| 3 | -1 | ptr to SingleStrand |
| 4 | -1 | ptr to hair pin loop |
| 5 | -1 | ptr to hair pin loop |
| 6 | -1 | ptr to hair pin loop |
| 7 | -1 | ptr to hair pin loop |
| 8 | -1 | ptr to hair pin loop |
| 9 | -1 | ptr to SingleStrand |
| 10 | -1 | ptr to SingleStrand |
| 11 | -1 | ptr to SingleStrand |

Table 1: Contents of data class object of free bases in secondary structure

 ISSN: 2321-8169
209 – 216

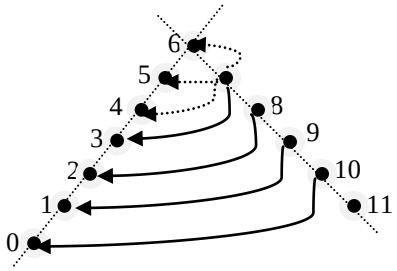
Algorithm : Similarity

1. Midpoint of this sequence is 6(=12/6). Hence there will be formation of two loops; loop1-> mid to 0 (outer) and loop2-> 7 to 11 (inner)






2. Next step is to find the similarity. Using algorithm SimilarityModel and PDBMetadata similarity is calculated.
3. Now revert the inner and outer loop
   loop1-> 7 to 11 (outer) loop1-> mid to 0 (inner)




4. Now shift mid from $6^{th}$ position to $5^{th}$,$4^{th}$ ,$3^{rd}$ ,$2^{nd}$ , $1^{st}$ ,$0^{th}$ position and repeat the same procedure.
5. In next set of iteration mid is shifted to $7^{th}$ ,$8^{th}$ ...up to last dot position and repeat the same procedure.
6. By the end of all iteration we get the sequence with highest similarity.

The main task of 3D structure is to form PDB file for tertiary structure. A PDB File is a textual file format describing the three-dimensional structures of molecules held in the Protein Data Bank. Protein Data Bank (PDB) format is a standard for files containing atomic coordinates. It is used for structures in the Protein Data Bank and is read and written by many programs. While this short description will suffice for many users, those in need of further details should consult the definitive description. The complete PDB file specification provides for a wealth of information, including authors, literature references, and the method of structure determination.

PDB format consists of lines of information in a text file. Each line of information in the file is called a record. A PDB file generally contains several different types of records, arranged in a specific order to describe a structure.

| **Selected Protein Data Bank Record Types** | |
|---|---|
| **Record Type** | **Data Provided by Record** |
| ATOM | atomic coordinate record containing the X,Y,Z orthogonal Å coordinates for atoms in standard residues (amino acids and nucleic acids). |
| HETATM | atomic coordinate record containing the X,Y,Z orthogonal Å coordinates for atoms in nonstandard residues. Nonstandard residues include inhibitors, cofactors, ions, and solvent. The only functional difference from ATOM records is that HETATM residues are by default not connected to other residues. Note that water residues should be in HETATM records. |
| TER | indicates the end of a chain of residues. For example, a hemoglobin molecule consists of four subunit chains that are not connected. TER indicates the end of a chain and prevents the display of a connection to the next chain. |
| HELIX | indicates the location and type (right-handed alpha, *etc.*) of helices. One record per helix. |

| | |
|---|---|
| SHEET | indicates the location, sense (anti-parallel, *etc.*) and registration with respect to the previous strand in the sheet (if any) of each strand in the model. One record per strand. |
| SSBOND | defines disulfide bond linkages between cysteine residues. |

Table 2: Contents of Protein data bank

The formats of these record types are given in the tables below.

| **Protein Data Bank Format: Coordinate Section** | | | | |
|---|---|---|---|---|
| **Record Type** | **Columns** | **Data** | **Justification** | **Data Type** |
| ATOM | 1-4 | "ATOM" | | character |
| | 7-11[#] | Atom serial number | right | integer |
| | 13-16 | Atom name | left[*] | character |
| | 17 | Alternate location indicator | | character |
| | 18-20[§] | Residue name | right | character |
| | 22 | Chain identifier | | character |
| | 23-26 | Residue sequence number | right | integer |
| | 27 | Code for insertions of residues | | character |
| | 31-38 | X orthogonal Å coordinate | right | real (8.3) |
| | 39-46 | Y orthogonal Å coordinate | right | real (8.3) |
| | 47-54 | Z orthogonal Å coordinate | right | real (8.3) |
| | 55-60 | Occupancy | right | real (6.2) |
| | 61-66 | Temperature factor | right | real (6.2) |
| | 73-76 | Segment identifier[¶] | left | character |
| | 77-78 | Element symbol | right | character |
| 79-80 | Charge | | character | |
| HETATM | 1-6 | "HETATM" | | character |
| | 7-80 | same as ATOM records | | |
| TER | 1-3 | "TER" | | character |
| | 7-11[#] | Serial number | right | integer |
| | 18-20[§] | Residue name | right | character |
| | 22 | Chain identifier | | character |
| | 23-26 | Residue sequence number | right | integer |
| | 27 | Code for insertions of residues | | Character |

Table 3: Protein Data Bank Format

Older PDB files may not adhere completely to the specifications. Some differences between older and newer files occur in the fields following the temperature factor in ATOM and HETATM records; these fields are omitted from the examples. Some fields are frequently blank, such as the alternate location indicator when an atom does not have alternate locations.

For example, PDB Format of Glucagon which is a small protein of 29 amino acids in a single chain is as given below. The first residue is the amino-terminal amino acid, histidine, which is followed by a serine residue and then a glutamine. The coordinate information (entry 1gcn) starts with:

```
ATOM      1  N   HIS A   1      49.668  24.248  10.436  1.00 25.00           N
ATOM      2  CA  HIS A   1      50.197  25.578  10.784  1.00 16.00           C
ATOM      3  C   HIS A   1      49.169  26.701  10.917  1.00 16.00           C
ATOM      4  O   HIS A   1      48.241  26.524  11.749  1.00 16.00           O
ATOM      5  CB  HIS A   1      51.312  26.048   9.843  1.00 16.00           C
ATOM      6  CG  HIS A   1      50.958  26.068   8.340  1.00 16.00           C
ATOM      7  ND1 HIS A   1      49.636  26.144   7.860  1.00 16.00           N
ATOM      8  CD2 HIS A   1      51.797  26.043   7.286  1.00 16.00           C
ATOM      9  CE1 HIS A   1      49.691  26.152   6.454  1.00 17.00           C
ATOM     10  NE2 HIS A   1      51.046  26.090   6.098  1.00 17.00           N
ATOM     11  N   SER A   2      49.788  27.850  10.784  1.00 16.00           N
ATOM     12  CA  SER A   2      49.138  29.147  10.620  1.00 15.00           C
ATOM     13  C   SER A   2      47.713  29.006  10.110  1.00 15.00           C
ATOM     14  O   SER A   2      46.740  29.251  10.864  1.00 15.00           O
ATOM     15  CB  SER A   2      49.875  29.930   9.569  1.00 16.00           C
ATOM     16  OG  SER A   2      49.145  31.057   9.176  1.00 19.00           O
ATOM     17  N   GLN A   3      47.620  28.367   8.973  1.00 15.00           N
ATOM     18  CA  GLN A   3      46.287  28.193   8.308  1.00 14.00           C
ATOM     19  C   GLN A   3      45.406  27.172   8.963  1.00 14.00           C
```

Notice that each line or record begins with the record type ATOM. The atom serial number is the next item in each record. The atom name is the third item in the record. Notice that the first one or two characters of the atom name consists of the chemical symbol for the atom type. All the atom names beginning with C are carbon atoms; N indicates nitrogen and O indicates oxygen. In amino acid residues, the next character is the remoteness indicator code, which is transliterated according to:

| | |
|---|---|
| α | A |
| β | B |
| γ | G |
| δ | D |
| ε | E |
| ζ | Z |
| η | H |

The next character of the atom name is a branch indicator. The next data field is the residue type. Notice that each record contains the residue type. In this example, the first residue in the chain is HIS (histidine) and the second residue is a SER (serine). The next data field contains the chain identifier. The next data field contains the residue sequence number. Notice that as the residue changes from histidine to serine, the residue number changes from 1 to 2. Two like residues may be adjacent to one another, so the residue number is important for distinguishing between them. The next three data fields contain the X, Y, and Z coordinate values, respectively. The last three fields shown are the occupancy, temperature factor (B-factor), and element symbol. The spacing of the data fields is crucial. If a data field does not apply, it should be left blank.

The exact time required for the execution for some sample RNA sequences is as given below.

| Sr. | File Name (dot) | File Size (KB) | Sequence Length | Execution Time (sec) | Similarity (%) |
|---|---|---|---|---|---|
| 1 | yeast_trna.dot | 0.178 | 75 | 21.49 | 85.69 |
| 2 | d.5.a.H.morrhuae.2.dot | 0.273 | 120 | 39.4 | 80.46 |
| 3 | d.5.a.H.marismortui.dot | 0.281 | 122 | 31.24 | 97.28 |
| 4 | d.5.a.H.saccharovorum.dot | 0.285 | 123 | 27.06 | 93.75 |
| 5 | d.5.a.H.morrhuae.1.dot | 0.281 | 123 | 39.51 | 81.44 |
| 6 | d.5.a.H.mediterranei.1.dot | 0.284 | 123 | 45.58 | 93.89 |
| 7 | d.5.a.D.mobilis.dot | 0.297 | 133 | 28.05 | 89.31 |
| 8 | X54252.dot | 1.4 | 697 | 190.79 | 84.34 |
| 9 | X54253.dot | 1.4 | 701 | 133.75 | 85.63 |
| 10 | Y00266.dot | 2.5 | 1244 | 186.47 | 85.06 |
| 11 | X98467.dot | 2.6 | 1295 | 227.96 | 87.12 |
| 12 | X65063.dot | 2.8 | 1432 | 462.85 | 86.34 |
| 13 | Z17210.dot | 2.8 | 1435 | 242.38 | 90 |
| 14 | X52949.dot | 2.9 | 1452 | 203.95 | 89.89 |
| 15 | K00421.dot | 2.9 | 1474 | 220.99 | 87.59 |
| 16 | Z17224.dot | 3.1 | 1550 | 257.10 | 86.98 |
| 17 | X59604.dot | 3.3 | 1701 | 458.64 | 86.36 |
| 18 | X00794.dot | 3.9 | 1962 | 298.29 | 87.53 |

Table 4: Results of 3D structure prediction algorithm based on similarity

## 5. CONCLUSIONS

As the tertiary structures are increasing consequently their interactions are also increasing it becomes a tedious job to treat free energy. Hence a better solution to this difficulty is to consider already predicted secondary structure to build tertiary structure using molecular dynamics arithmetic. V-fold algorithm[2] is a better choice for 2D as well as 3D structure prediction but the time required to treat large RNA is more. Every day new databases are added with increasing sizes; hence motif template based method gives better result when homologous conformations are to be extracted from the known databases. The main difficulty arises when a new structure is identified. It is necessary to take the backup of such structure if it represents a good structure as homologous conformations cannot be available in PDB database. Hence in this research a 2D structure is predicted using GT-fold algorithm

and a novel algorithm is developed using parallel techniques which can its corresponding 3D structure in faster and more accurate way. If the same algorithm is executed using parallel algorithm technique the result may be much better than as shown in table 4.

## REFERENCES

[1] Leontis NB, Westhof E, editors. RNA 3D Structure Analysis and Prediction. Volume 27. Berlin, Heidelberg: Springer Berlin Heidelberg; 2012 [Nucleic Acids and Molecular Biology].
[2] Gesteland RF. The RNA World, Third Edition. 3rd ed. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press; 2005.
[3] Saenger W. Principles of Nucleic Acid Structure. New York, NY: Springer New York; 1984 [Cantor CR (Series editor): Springer Advanced Texts in Chemistry].
[4] Leontis NB, Westhof E. Geometric nomenclature and classification of RNA base pairs. RNA. 2001;7:499–51
[5] Eddy,S.R. (2001) Non-coding RNA genes and the modern RNA world. Nat. Rev. Genet., 2, 919–929.
[6] Mattick,J.S. and Makunin,I.V. (2006) Non-coding RNA. Hum. Mol.Gen., 15(Suppl. 1), R17–R29.
[7] Mercer,T.R., Dinger,M.E. and Mattick,J.S. (2009) Long non-coding RNAs: insights into functions. Nat. Rev. Genet., 10, 155–159.
[8] Williams,K.P. (2002) The tmRNA Website: invasion by an intron. Nucleic Acids Res., 30, 179–182.
[9] Mello,C.C. and Conte,D. (2004) Revealing the world of RNA interference. Nature, 431, 338–342.
[10] Cheetham,S., Gruhl,F., Mattick,J. and Dinger,M. (2013) Long noncoding RNAs and the genetics of cancer. Br. J. Cancer, 108, 2419–2425.
[11] Huang,T., Alvarez,A., Hu,B. and Cheng,S.-Y. (2013) Noncoding RNAs in cancer and cancer stem cells. Chin. J. Cancer, 32, 582–593.
[12] Zamore,P.D. and Haley,B. (2005) Ribo-gnome: the big world of small RNAs. Science, 309, 1519–1524.
[13] Mehler,M.F. and Mattick,J.S. (2006) Non-coding RNAs in the nervous system. J. Physiol., 575, 333–341.
[14] Esteller,M. (2011) Non-coding RNAs in human disease. Nat. Rev.Genet., 12, 861–874.
[15] Berman,H.M.,Westbrook,J., Feng,Z., Gilliland,G., Bhat,T.N., Weissig,H., Shindyalov,I.N. and Bourne,P.E. (2000) The Protein Data Bank. Nucleic Acids Res., 28, 235–242.
[16] Berman,H.M., Battistuz,T., Bhat,T.N., Bluhm,W.F., Bourne,P.E., Burkhardt,K., Feng,Z., Gilliland,G.L., Iype,L., Jain,S. et al. (2002) The Protein Data Bank. Acta Crystallogr. D. Biol. Crystallogr., 58, 899–907.