# Numerical characterization of RNA secondary structure 

Jiaquan Zhan ${ }^{1}$, Bo Liao, ${ }^{2, *}$ Yusen Zhang ${ }^{3}$<br>${ }^{1}$ Management Dept Huangdao District Qingdao Institute of Architecture \& Engineering<br>Qingdao 266520,China<br>${ }^{2}$ Science 100, Graduate School of the Chinese Academy of Sciences<br>Beijing 100049,China<br>${ }^{3}$ School of information Engineer, Shandong University at weihai<br>Weihai 264209, China


#### Abstract

A secondary structure is a symbolic string composed of three kinds letters indicating the stack, external element and loop. A 2D graphical representation for this abstract symbolic sequence is proposed here. The curve is the unique representation for a given RNA secondary structure. Different geometrical properties of the curve are studies in details, which reflect the basic characteristics of the RNA secondary structure. Some characteristic matrices are derived from the definition of RNA secondary structure.


Key words: RNA secondary structure; 2D graphical representation; curve

## 1 INTRODUCTION

Ribonucleic acid(RNA) is an important molecule which performs a wide range of functions in the biological system. In particular, it is RNA(not DNA) that contains genetic information of virus such as HIV and therefore regulates the functions of such virus. RNA has recently become the center of much attention because of its catalytic properties, leading to an increased interest in obtaining structural information.

Almost all comparison of primary RNA structures are based on the comparison of strings. As is well-known, string comparisons are computer intensive, and despite the fact that practical schemes for sequence comparison have been outlined, there are a number of steeps in such approaches that involve arbitrary decisions e.g., decisions on the relative weights of different elementary string operations: deletion, insertions, substitution, and penalties for unacceptable alignments. The similarity between two structures have been formulated as problems of exact and approximate structure matching, finding a largest common substructure of the structures and computing optimal alignments under general scoring functions [1-8]. In order to find the numerical characterizations of structures, several author study the secondary structures using mathematical model approaches.[9-13]

In this paper, based on the special representation of three kinds of letters indicating the stack, external element and loop, we shall propose a 2-D graphical representation. Each RNA secondary structure corresponds to a unique curve representation and vice versa. In other words, each can be uniquely determined given the other. Therefore, the curve contains all the information that the secondary structure contains. It is found that the format of the curve can be of some advantages. Based on the mathematical definition of RNA secondary structure, some characteristic matrices are derived.

## 2 METHODS and RESULTS

[^0]
### 2.1 Characteristic Matrices and the connectivity index

Definition (Waterman [1]): A secondary structure is a vertex-labeled graph on $n$ vertices with an adjacency matrix $\mathbf{A}$ fulfilling
(i) $a_{i, i+1}=1 \quad$ for $1 \leq i \leq n-1$
(ii) For each $i$ there is at most a single $k \neq i-1, i+1$ such that $a_{i, k}=1$
(iii) If $a_{i, j}=a_{k, l}=1$ and $i<k<j$ then $i<l<j$

Let $\mathbf{M}=\mathbf{A D}^{-1}$, where $\mathbf{A}$ is the vertex-adjacency matrix, $\mathbf{D}$ is the diagonal matrix with the elements $\mathbf{D}=\left(d_{i i}=d_{i}\right)$ the number of vertex connecting i. Similar as D.J. Klein's approach[14], we introduce the following matrices:

$$
\begin{aligned}
& \mathbf{H}=\mathbf{D}^{-1 / 2} \mathbf{M} \mathbf{D}^{1 / 2} \\
& \mathbf{L}=\mathbf{D}-\mathbf{A}=\mathbf{D}^{1 / 2}(\mathbf{I}-\mathbf{H}) \mathbf{D}^{1 / 2}
\end{aligned}
$$

Where I-H is what sometimes called the normalized Laplacian matrix, $\mathbf{L}$ is call combinatorial Lapcian matrix. The wiener index $\mathbf{W}$ is also defined as $\mathbf{W}=\sum_{\lambda \neq 0} 1 / \lambda$, where $\lambda$ is the eigenvalues of
L. The connectivity index is defined as $\chi=\frac{1}{2} \sum_{i \neq j} H_{i j}$.

For example,(i) a secondary structure of RNA


Figure 1: Substructure of AlMV-3
(ii) The adjacency matrix $\mathbf{A}$ and the diagonal matrix $\mathbf{D}$ (from $3^{\prime}$ to $5^{\prime}$ )

$$
\mathbf{A}=\left(\begin{array}{lllllllll}
0 & 1 & 0 & 0 & 0 & 0 & 0 & 1 \\
1 & 0 & 1 & 0 & 0 & 0 & 0 & 1 & 0 \\
0 & 1 & 0 & 1 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 & 1 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 1 & 0 & 1 & 0 \\
0 & 1 & 0 & 0 & 0 & 0 & 1 & 0 & 1 \\
1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0
\end{array}\right), \mathbf{D}=\left(\begin{array}{lllllllll}
2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 3 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 2 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 2 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 2 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 3 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 3 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 2
\end{array}\right)
$$

(iii) Markov matrix $\mathbf{M}$

$$
\mathbf{M}=\left(\begin{array}{lcccccccr}
0 & 1 / 3 & 0 & 0 & 0 & 0 & 0 & 0 & 1 / 2 \\
1 / 2 & 0 & 1 / 3 & 0 & 0 & 0 & 0 & 1 / 3 & 0 \\
0 & 1 / 3 & 0 & 1 / 2 & 0 & 0 & 1 / 3 & 0 & 0 \\
0 & 0 & 1 / 3 & 0 & 1 / 2 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 / 2 & 0 & 1 / 2 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 / 2 & 0 & 1 / 3 & 0 & 0 \\
0 & 0 & 1 / 3 & 0 & 0 & 1 / 2 & 0 & 1 / 3 & 0 \\
0 & 1 / 3 & 0 & 0 & 0 & 0 & 1 / 3 & 0 & 1 / 2 \\
1 / 2 & 0 & 0 & 0 & 0 & 0 & 0 & 1 / 3 & 0
\end{array}\right)
$$

(iv) $\mathbf{H}$ matrix

$$
\mathbf{H}=\left(\begin{array}{lcccccccc}
0 & 1 / \sqrt{6} & 0 & 0 & 0 & 0 & 0 & 0 & 1 / 2 \\
1 / \sqrt{6} & 0 & 1 / 3 & 0 & 0 & 0 & 0 & 1 / 3 & 0 \\
0 & 1 / 3 & 0 & 1 / \sqrt{6} & 0 & 0 & 1 / 3 & 0 & 0 \\
0 & 0 & 1 / 3 & 0 & 1 / 2 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 / 2 & 0 & 1 / 2 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 / 2 & 0 & 1 / \sqrt{6} & 0 & 0 \\
0 & 0 & 1 / 3 & 0 & 0 & 1 / \sqrt{6} & 0 & 1 / 3 & 0 \\
0 & 1 / 3 & 0 & 0 & 0 & 0 & 1 / 3 & 0 & 1 / 2 \\
1 / 2 & 0 & 0 & 0 & 0 & 0 & 0 & 1 / \sqrt{6} & 0
\end{array}\right)
$$

(v) The connectivity index $\chi=\frac{1}{2} \sum_{i \neq j} H_{i j}=4.4663$
(vi) The normalized Laplacian matrix I-H

$$
\mathbf{I}-\mathbf{H}=\left(\begin{array}{lcccccccc}
1 & -1 / \sqrt{6} & 0 & 0 & 0 & 0 & 0 & 0 & -1 / 2 \\
-1 / \sqrt{6} & 1 & -1 / 3 & 0 & 0 & 0 & 0 & -1 / 3 & 0 \\
0 & -1 / 3 & 1 & -1 / \sqrt{6} & 0 & 0 & -1 / 3 & 0 & 0 \\
0 & 0 & -1 / 3 & 1 & -1 / 2 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & -1 / 2 & 1 & -1 / 2 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & -1 / 2 & 1 & -1 / \sqrt{6} & 0 & 0 \\
0 & 0 & -1 / 3 & 0 & 0 & -1 / \sqrt{6} & 1 & -1 / 3 & 0 \\
0 & -1 / 3 & 0 & 0 & 0 & 0 & -1 / 3 & 1 & -1 / 2 \\
-1 / 2 & 0 & 0 & 0 & 0 & 0 & 0 & -1 / \sqrt{6} & 1
\end{array}\right)
$$

(vii) The combinatorial Laplacian matrix $\mathbf{L}$

$$
\mathbf{L}=\left(\begin{array}{lrrrrrrrr}
2 & -1 & 0 & 0 & 0 & 0 & 0 & 0 & -1 \\
-1 & 3 & -1 & 0 & 0 & 0 & 0 & -1 & 0 \\
0 & -1 & 3 & -1 & 0 & 0 & -1 & 0 & 0 \\
0 & 0 & -1 & 2 & -1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & -1 & 2 & -1 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & -1 & 2 & -1 & 0 & 0 \\
0 & 0 & -1 & 0 & 0 & -1 & 3 & -1 & 0 \\
0 & -1 & 0 & 0 & 0 & 0 & -1 & 3 & -1 \\
-1 & 0 & 0 & 0 & 0 & 0 & 0 & -1 & 2
\end{array}\right)
$$

(viii) The Wiener number index $W=\sum_{\lambda \neq 0} \frac{1}{\lambda}=4.8827$

### 2.2 2-D graphical representation of RNA secondary structures

Lemma [10] Any secondary structure $\psi$ can be uniquely decomposed into stacks, loops, and external elements.
Consider the RNA secondary structure with n residues first. Usually the sequence has the form SEESLLSE $\cdots$, where S , L, and E denote the stacks, loops, and external elements, respectively. Suppose that the cumulative numbers of stacks, loops, and external elements occurring in this sequence from the first residue to the nth residue are denoted by $\alpha_{n}, \beta_{n}$ and $\gamma_{n}$, respectively. Obviously, $\alpha_{n}+\beta_{n}+\gamma_{n}=n$.


Figure 2
The three integers $\alpha_{n}, \beta_{n}$ and $\gamma_{n}$ can be mapped onto a point within the following regular triangle: considering the regular triangle $\triangle A B C$ with the height equal to n , as shown in Figure 2, we find that the sum of the three sides is equal exactly to n . The point P to the sides $\mathrm{BC}, \mathrm{AC}$, and AB be equal to $\alpha_{n}, \beta_{n}$ and $\gamma_{n}$, respectively, as shown in Figure 2. The point P constitutes a mapping of the secondary structure content of the RNA concerned. This is a mapping of the one-toone correspondence. A Cartesian coordinates system is set up as shown in Figure 2. The coordinates of the point $P_{n}(x, y)$ may be expressed in terms of $\alpha_{n}, \beta_{n}$ and $\gamma_{n}$ as follows:

$$
\left\{\begin{array}{l}
x_{n}=\left(\beta_{n}-\alpha_{n}\right) / \sqrt{3}  \tag{1}\\
y_{n}=\frac{2 n}{3}-\left(\alpha_{n}+\beta_{n}\right)=\gamma_{n}-\frac{n}{3}
\end{array}\right.
$$

There are $\mathrm{A}, \mathrm{B}$, and C vertices in the triangle $\triangle A B C$. For convenience, the vector pointing to the A vertex from the origin O is said to be of an A direction. Any vector parallel to the A direction is said to be of the A direction, too. The definition of the B and C directions are completely similar. The vector pointing to the point $P_{n}$ from the origin O is denoted by $\mathbf{r}_{n}$. The component of $\mathbf{r}_{i}$, i.e. $x_{n}$ and $y_{n}$ are calculated by Eq.(1). Let $\Delta \mathbf{r}_{n}=\mathbf{r}_{n}-\mathbf{r}_{n-1}$, then we have Property 1.
Property 1 For any $n=1,2, \cdots, N$, here N is the length of the studied DNA sequence, the vector $\Delta \mathbf{r}_{n}$ has only three possible direction, i.e., either the direction or the B or the C direction, depending on the n -th residue being either S or L or E , in the RNA secondary structure inspected. Furthermore, the length of $\Delta \mathbf{r}_{n}$, i.e., $\left|\Delta \mathbf{r}_{n}\right|$, is always equal to $m^{2}+n$, for any $n=1,2, \cdots, N$.
Proof: Actually, the components of $\Delta \mathbf{r}_{n}$, i.e., $\Delta x_{n}$ and $\Delta y_{n}$ can be calculated for each possible residue ( S L and E ) at the n -th position of the DNA sequence by using Eq.(1). For example, when the n -th residue is S , we find $\Delta x_{n}=-\frac{1}{\sqrt{3}}$ and $\Delta y_{n}=-\frac{1}{3}$. This result is independent of the conformation state of the (n-1)-th residue. The two numbers $\left(-\frac{1}{\sqrt{3}},-\frac{1}{3}\right)$ are called the direction of $\Delta \mathbf{r}_{n}$. The direction number and the length of $\Delta \mathbf{r}_{n}$ for each possible residue type at the n-th position are summarized as follows.

|  | $\Delta x_{n}$ | $\Delta y_{n}$ | $\left\|\Delta \mathbf{r}_{n}\right\|$ |
| :---: | :---: | :---: | :---: |
| S | $-\frac{1}{\sqrt{3}}$ | $-\frac{1}{3}$ | $\frac{2}{3}$ |
| L | $-\frac{1}{\sqrt{3}}$ | $-\frac{1}{3}$ | $\frac{2}{3}$ |
| E | 0 | $\frac{2}{3}$ | $\frac{2}{3}$ |

Property 2 For any positive integers $\mathrm{n}, \mathrm{m}$ and $\mathrm{n}>\mathrm{m}$, the vector equation $\mathbf{r}_{n}=\mathbf{r}_{m}$ is valid if only if

$$
\begin{equation*}
\alpha_{n-m}=\beta_{n-m}=\gamma_{n-m}=\frac{n-m}{3} . \cdot \tag{2}
\end{equation*}
$$

Where $\alpha_{n-m}, \beta_{n-m}$, and $\gamma_{n-m}$ are the cumulative numbers of the residues S,L, and E occurring in the subsequence from the m -th to the n th residue in the sequence inspected.
Proof: Obviously, $\mathbf{r}_{n}=\mathbf{r}_{m}$ implies $\mathbf{r}_{n}-\mathbf{r}_{m}=0$ that or

$$
\left\{\begin{array}{l}
x_{n}-x_{m}=\left(\beta_{n-m}-\alpha_{n-m}\right) / \sqrt{3}=0 \\
y_{n}-y_{m}=\frac{2(n-m)}{3}-\left(\alpha_{n-m}+\beta_{n-m}\right)=0
\end{array}\right.
$$

This leads to Eq.(2) immediately. Eq.(2) describes the loop property of the 2D graphical representation of RNA secondary structure.
Property 3 The 2D representation possesses the reflection symmetry.
Proof: Usually the sequence is expressed in the order from 5' to 3 '. Suppose that the 2D representation for DNA sequence is described by $\left(x_{n}, y_{n}\right), n=0,1,2, \cdots, N$. Suppose again
that the 2 D representation for the reverse sequence, i.e, the same sequence but from $3^{\prime}$ to $5^{\prime}$ is described by $\left(\hat{x}_{n}, \hat{y}_{n}\right)$, I find

$$
\left\{\begin{array}{l}
\hat{x}_{n}=x_{N}-x_{N-n} \\
\hat{y}_{n}=y_{N}-y_{N-n}
\end{array}\right.
$$

for $n=0,1,2, \cdots, N$.

## 3 CONCLUSIONS

We have presented a 2D graphical representation for the abstract symbolic sequence of RNA secondary structure. The curve is the unique representation for a given RNA secondary structure. Different geometrical properties of the curve are studies in details, which reflect the basic characteristics of the RNA secondary structure. Some characteristic matrices are derived from the definition of RNA secondary structure. Different structures have different characteristic matrices and different graphical representation. We also can apply these numerical characterizations to make comparisons between RNA secondary structures.

## 4 REFERENCES

[1] M. S. Waterman, Introduction to Computational Biology: Maps, Sequences and Genomes. Chapman \& Hall, London, 1995.
[2] Jason T. L. Wang, Kaizhong Zhang, Identifying approximately common substructures in tree based on a restricted edit distance, Information Science, 2000,126,165-189.
[3] D. Angluin ,Finding patterns common a set of strings, Journal of computer and system sciences ,1980, 21, 46-62.
[4] William J. Masek, A Faster Algorithm Computing string Edit Distances, Journal of computer and system sciences ,1980, 20 ,18-31.
[5] Chratal, V. and Sankoff, D. Longest Common subsequences of two random sequences. J.Appl.Probab, 1975, 12 306-315
[6] Hirschberg, D. S. A linear space algorithm for computing maximal common subsequences, Common, ACM ,18,341-343.
[7] Christian N. S. Pedersen Algorithms in Computational Biology , in: BRICS Dissertation Series 200
[8] Bo Liao, Tian-ming Wang, Largest common substructure of RNA structure, Internet Journal of Molecula Design, 3(2004),361-367.
[9] X. G Vienmt, M. v. de chaumont, Enumeration of RNA's secondary structures by complexity, in: V. Capasso, E. Grosso, S. L. Paver-Fontana(Eds),Mathematics in Medicine and Biology, Lect. Notes in Biomath, Vol. 57 Springer,Berlin,1985,360-365.
[10] Ivo .L. Hofacker, Peter Schuster, Peter F. Stadler, Combinatorics of RNA secondary structures. Discr. Appl. Math, 1998,88, 207-237.
[11] Bo Liao, Tian-ming Wang, General combinatorics of RNA hairpins and cloverleaves, J.Chem.Inf.Comput.Sci, 43(4)2003,1138-1142.
[12] Bo Liao, Tian-ming Wang, General combinatorics of RNA secondary structures, Mathematical Biosciences, 191(2004), 69-81.
[13] Bo Liao, Tianming Wang, A 3D Graphical Representation of RNA Secondary structures, Journal of Biomolecular Structure \& Dynamics, 21(6), 2004, 827-832.
[14] Douglas J. Klein, Jose Luis Palacios, Milan Randic, Nenad Trinajstic, Random Walks and Chemical Graph Theory, J.Chem.Inf.Comput.Sci, 44(2004), 1521-1525.


[^0]:    * Correspondence author; phone: 86-10-88256148; fax: 86-10-88256147; E-mail: dragonbw@163.com

