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TN curve: A novel 3D graphical representation of DNA sequence based on trinucleotides and its applications

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1. Introduction

Developments of sequencing technologies cause the number of biological sequences increasing exponentially in databases. However, it is difficult to obtain information directly from the primary sequences. Then mathematical analysis of the large volume of sequences data becomes one of the challenges for bio-scientists. Using graphical approaches to study biological problems can provide intuitive picture or useful insights for helping analyzing complicated relations in these systems, as demonstrated by many previous studies on a series of important biological topics, such as enzyme-catalyzed reactions (Andraos, 2008; Chou, 1981, 1989; Chou and Forsen, 1980; Chou and Liu, 1981; Myers and Palmer, 1985), protein folding kinetics (Chou, 1990), inhibition kinetics of processive nucleic acid polymerases and nucleases (Althaus et al., 1993a, 1993b, 1993c), analysis of codon usage (Chou and Zhang, 1992; Zhang and Chou, 1993, 1994), base frequencies in the antisense strands (Chou et al., 1996). Moreover, graphical methods have been introduced for QSAR study (Gonzalez-Diaz et al., 2006, 2007b; Prado-Prado et al., 2008) and for dealing with complicated network systems (Diao et al., 2007; Gonzalez-Diaz et al., 2007a, 2008). Recently, the images of cellular automata (Wolfram, 1984) were also used to represent biological sequences (Xiao et al., 2005a) for predicting protein structural classes (Xiao et al., 2008) and subcellular location (Xiao et al., 2006b), identifying G-protein-coupled receptor functional classes (Xiao et al., 2009), investigating HBV virus gene missense mutation (Xiao et al., 2005b) and HBV viral infections (Xiao et al., 2006a), as well as visually analyzing SARS-CoV (Gao et al., 2006; Wang et al., 2005). In this study, we attempted to propose a different 3D graphical representation for DNA sequences in hopes to provide a useful tool for the relevant areas.

Since Hamori and Ruskin (1983) first proposed a 3D graphical representation, some different graphical approaches have been reported for DNA sequences. Zhang and Zhang (1991, 1994) create Z curve to represent DNA sequences in a 3D space. It demonstrates that Z curve does not lose any biological information of the sequence, because it especially uses the classifications of chemical structure on purines–pyrimidines, amino–keto groups and strong–weak hydrogen bonds. Nandy (1994) proposes a 2D graphical representation by arbitrarily assigning A, G, T, and C to four directions of Cartesian coordinate axes, but such a representation of DNA is accompanied by some loss of visual information associated with crossing and overlapping of the resulting curve by itself. Randic et al. (2000) presents a 3-D graphical representation based on four mutually equivalent tetrahedral directions, which has an important advantage in that the assignment of the four bases to the four tetrahedral directions does not involve arbitrary decisions. Nevertheless, this model is also accompanied by the limitations associated with crossing and overlapping of the spatial curve representing a DNA sequence. Since 2000, researchers have outlined different representations of DNA sequences based on 2D (Guo et al., 2001; Huang et al., 2008;
Liu et al., 2006; Randic et al., 2003a, 2003b; Randic, 2004; Song and Tang, 2005; Yao et al., 2006). 3D (Cao et al., 2008; Liao and Wang, 2004a; Liao and Ding, 2006; Qi and Fan, 2007; Qi et al., 2007), 4D (Chi and Ding, 2005), 5D (Liao et al., 2007) and 6D (Liao and Wang, 2004b) spaces. However, some representations still cannot avoid loss of information due to overlapping and crossing of the curve with itself (Guo and Nandy, 2003; Wu et al., 2003; Nandy and Nandy, 2003). Moreover, some mathematical models are based on complex distance matrices and equations, their computations are so complicated, which may also ignore biology information hidden between the neighboring nucleotides (Liao and Wang, 2004c).

Motivated by these aforementioned works, we propose a novel 3D graphical representation based on trinucleotides (TN curve). Consideration of trinucleotides instead of individual and dual nucleotides has superior reasons and advantages. For example, the genetic code consists of trinucleotides of DNA and one can easily find the ORF as the longest sequence of trinucleotides that contains no stop codons when read in a single reading frame. Comparing with other models, TN curve is the first model that can display the information of trinucleotides within 3D space, which helps in visual inspections of sequence features such as composition and distribution of trinucleotides in DNA sequences, recognizing similarities/dissimilarities among different DNA sequences, and allows one to construct considerable numerical characterizations. With two vectors composed of 64 and 6 components, we outline two methods to compare similarities of different DNA sequences, respectively, which may provide convenient tools in sequences alignment.

2. Construction of TN curve

As we know, the four nucleic bases A, G, T, and C can build up 64 kinds of trinucleotides; the second base of a trinucleotide is associated with the hydrophobic/hydrophilic property of the translated amino acid. According to the property of the second base of a trinucleotide, we can classify the 64 kinds of trinucleotides into four categories as presented in Table 1.

To numerically represent the trinucleotides in Table 1, we assign the first and third base of a trinucleotide as A, G, C, and T, while the second base is determined by positive sign “+” and negative sign “−” of the first and third base, i.e., {+,+}→A, {−,−}→G, {+,−}→C, {+,+}→T. In this way, each trinucleotide can be represented by using a set of coordinate (x, y), then the 64 kinds of trinucleotides are divided into four quadrants of a Cartesian 2D coordinates as shown in Fig. 1.

In Fig. 1, taking (3,−2) for example, pure number 3 and 2 denote that the first and the third bases of corresponding trinucleotide are C and G, respectively, and integration of “+” and “−” denotes the second base is T, therefore (3,−2) represents trinucleotide CTG. Similarly, (3,2) represents CAG, (−3,2) represents CGG and (−3,−2) represents CCG.

Table 1

| Category | Triplets |
|----------|----------|
| I        | AAA GAG CAC TAT AAG GAA CAT TAC GAC CAG AAT TAA AAC CAA GAT TAG |
| II       | AGA GGG CCG TCT AGG GCA CTT TGC GGC CGG AGT TGA AGC CCA GGT TGG |
| III      | ACA GCG CCC TCT ACG GCA CTT GCC CCG ACT TCA ACC CCA GCT TCG |
| VI       | ATA GTG CTC TTT ATG GTC CTT GTC GTC ATT TTA ATC CTA GTC TGG |

Fig. 1. Distributions of the 64 kinds of trinucleotides in Cartesian 2D coordinates.
Now we consider all possible trinucleotides of an arbitrary DNA primary sequence. In detail, supposing $S = s_1 s_2 s_3 \ldots$ is a DNA sequence, we have a map $\phi$, which can map $S$ into a plot set $\phi(S) = \phi(s_1 s_2 s_3) \phi(s_2 s_3 s_4) \phi(s_3 s_4 s_5) \ldots$, where, according to Fig. 1, $\phi(s_i s_{i+1} s_{i+2}) = \{k_i, y_i, i\}$

\[
\begin{align*}
(1, 1, i) &\rightarrow s_i s_{i+1} s_{i+2} = AAA \\
(2, 2, i) &\rightarrow s_i s_{i+1} s_{i+2} = GAG \\
(3, 3, i) &\rightarrow s_i s_{i+1} s_{i+2} = CAC \\
(4, 4, i) &\rightarrow s_i s_{i+1} s_{i+2} = TAT \\
\ldots & \\
(1, -3, i) &\rightarrow s_i s_{i+1} s_{i+2} = ATC \\
(2, -1, i) &\rightarrow s_i s_{i+1} s_{i+2} = CTA \\
(2, -4, i) &\rightarrow s_i s_{i+1} s_{i+2} = GGT \\
(4, -2, i) &\rightarrow s_i s_{i+1} s_{i+2} = TCG \\
& \quad (i = 1, 2, 3, \ldots, L - 2, L \text{ is the length of } S)
\end{align*}
\]

The corresponding plot set is called as characteristic plot set of the second base of corresponding trinucleotide, which links the second and third bases of a trinucleotide, $y > 0$ represents that the second base is A or G, otherwise C or T. An intact trinucleotide is represented by integration of $x$ and $y$. Therefore, one can obtain more information from these parameters. Letting $x' = \sum_{m=1}^{n} x_m$ and $y' = \sum_{m=1}^{n} y_m$, we can obtain the cumulative effect of given sequence and inspect both the local and overall information of DNA sequence. Table 2 and Fig. 2B show the corresponding results based on $(x', y', i)$.

**Discussion 1.** According to the definition, $x$ links the first and second bases of a trinucleotide, this can be used as an approximate descriptor of dinucleotide. If $x > 0$, the second base of given trinucleotide must be A or T, otherwise G or C. Similar results can be obtained for $y$ which links the second and third bases of a trinucleotide, $y > 0$ represents that the second base is A or G, otherwise C or T. An intact trinucleotide is represented by integration of $x$ and $y$. Therefore, one can obtain more information from these parameters.

**Table 2**

| Triplets  | $x$ | $y$ | $i$ | $x'$ | $y'$ |
|-----------|-----|-----|-----|------|------|
| ATG       | 1   | -2  | 1   | 1    | -2   |
| TGG       | -4  | 2   | 2   | -3   | 0    |
| GGT       | -2  | 4   | 3   | -5   | 4    |
| GTG       | 2   | -2  | 4   | -3   | 2    |
| TGC       | -4  | 3   | 5   | -7   | 5    |
| GCA       | -2  | -1  | 6   | -9   | 4    |
| CAC       | 3   | 3   | 7   | -6   | 7    |
| ACC       | -1  | -3  | 8   | -7   | 4    |

(A, C), or else (G, T), which just correspond to amino(A, C)/keto(G, T) groups. Thus, we have six descriptors $x, y, x', y', z$ and $z'$ to numerically represent a given DNA sequence, where, $z = x + y$, $z' = \sum_{m=1}^{n} z_m$.

**Discussion 3.** From the construction of TN curve, we know that the initial assignments are not unique. According to statistics theory, we have, that is to say, various 3D curves for the same primary DNA sequence based on different assignments. Nevertheless, we can only obtain a unique primary DNA sequence by translating any TN curve to DNA sequence according to the designations in Fig. 1. Since the zigzag curve does not represent the genuine molecular geometry, we are not interested in the unique relationship between the initial assignments and the possible number of TN curve, but are interested in them as numerical parameters that may facilitate analysis of DNA sequences.

### 3. Application

#### 3.1. Utility in providing visual information

A random DNA sequence can be represented by its 3D representation, as is introduced in the construction of TN curve. Based on trinucleotides, TN curve can provide more information that is intuitionistic. Fig. 3 shows the projections of the TN curves of the coding sequences of the first exon of $\beta$-globin gene of four different species Human, Gorilla, Opossum and Gallus in Cartesian.
2D x–y coordinates, different colors denote the trinucleotides’ densities which can be inferred from the colorbar. Furthermore, the numbers of the line linking the trinucleotides can also display the corresponding trinucleotides usage frequency and correlations between neighboring trinucleotides, the more lines linked, the higher frequency occurring in the DNA sequence (the numbers of the lines observed may be less than practical situation because of overlapping). We can likewise find out whether specific trinucleotides, such as start and stop codons, consist in the DNA sequence directly. It is well known that any sequences have six possible reading frames. The specific codons such as start and stop codons only in a corresponding reading frame are significant. If we calculate the TN curves of each possible reading frame and repeat the steps of Fig. 3, it is conceivable that one can find out the ORF candidates easily.

From Fig. 3, we can recognize directly the differences of the trinucleotides’ compositions and distributions in the four sequences. As can be seen, Human and Gorilla are similar in compositions of trinucleotides, which is accordant with actual evolution evidence, while Opossum and Gallus are the most dissimilar, this result is also coincident with the fact that Gallus is non-mammal and Opossum is the most remote species from the remaining mammals. In Fig. 4, we give the 2D plots of x’ and y’ vs. i of the four species, respectively, from which the same results can be obtained. Besides, we can also inspect detailed features such as composition of bases of corresponding sequence from Fig. 4. Therefore, TN curve provides a practical tool for us to have a deeper insight into DNA sequence with visual information.

3.2. Discrimination of conserved genes through numerical characterization of DNA sequences

The rapid growth of data in the DNA sequence databases has led to intensive research to develop different ways to identify new gene sequences and functions. In this section, we will illustrate an application of the DNA descriptors arising out of TN curve in differentiating various conserved gene sequences. Here, we take the mean values of \( x \) and \( y \) as the numerical descriptors of gene sequence.

Table 3 presents the mean values of \( x \) and \( y \) for ten histone H4 DNA sequences, column 1 lists the species common name, column 2 lists the EMBL ID of the corresponding DNA sequence, and the mean values of \( x \) and \( y \) is given in columns 3 and 4. For our purpose, only the CDS sequences are used in order to relate closely to the conserved sequences. Accordingly, we show the mean value values of \( x \) and \( y \) in Fig. 5.

Seen from Fig. 5, the ten sequences are efficiently clustered according to species, the results show the descriptors we adopt do well in representing the DNA sequence. To provide a broader basis.
for our hypothesis of gene discrimination through numerical characteristics parameters of DNA sequences, we also test this method by discriminating conserve sequences of different gene types. In Table 4, we compute the mean values of $x$ and $y$ of the coding sequences of the first exon of $\beta$-globin gene of human, gorilla, opossum and gallus.

![Fig. 4. 2D plots of $x'$ and $y'$ of the coding sequences of the first exon of $\beta$-globin gene of human, gorilla, opossum and gallus.](image)

Table 3
Mean values of $x$ and $y$ of the coding regions for 10 histone H4 genes.

| Species     | EMBL ID  | Mean value |
|-------------|----------|------------|
|             |          | $x$        | $y$        |
| Maize       | ZMH4C7   | -0.85484   | 0.21613    |
| Maize       | ZMH4C14  | -0.87742   | 0.20645    |
| Maize       | ZMH4A    | -0.85161   | 0.2129     |
| Chicken     | GGHIST4A | -0.87742   | 0.23548    |
| Chicken     | GGHIST4B | -0.89355   | 0.23871    |
| Wheat       | TAH4091  | -0.92258   | 0.090323   |
| Mouse       | MMHIST4  | -0.69677   | 0.16774    |
| Rat         | BB4H5    | -0.66129   | 0.2        |
| Human       | HSHIS4   | -0.43548   | 0.24194    |
| Human       | HSHISAD  | -0.37742   | 0.2871     |

Fig. 5. Numerically representing the ten histone H4 DNA sequences by mean values of $x$ and $y$. 
coding sequences for three gene types \(\alpha\) globin, \(\beta\) globin and histone H4 of different mammalian species.

In Fig. 6A, a 2D plot of the mean value of \(x\) and \(y\) shows three distinct regions for the three gene types based on Table 4. As is expected from the fact that similar gene sequences from different species bear close homologies and are distinctly different from other genes by virtue of the base composition and distribution patterns, Nandy (2003) obtained the similar results except for the mouse gene of \(\alpha\) globin by using his 2D graphical representation system for DNA sequences to calculate the normalized mean moments for the coding segments of the three gene types, as shown in Fig. 6B. Obviously, these gene types are clustered into three groups correctly in our work, while the mouse gene of \(\alpha\) globin is intermingled by histone genes in Nandy’s work. Then, the resolution of TN curve is much better.

3.3. Similarities/dissimilarities analysis of the coding sequences of \(\beta\)-globin gene among different species

Comparing similarities/dissimilarities among different DNA sequences is one of the essential motivations of graphical representation, which is reflected in recently researches (Chi and Ding, 2005; Chen et al., 2008; Cao et al., 2008; Liu et al., 2006; Liao and Wang, 2004a, 2004b, 2004c; Liao and Ding, 2006; Liao et al., 2006, 2008; Qi and Fan, 2007; Qi et al., 2007; Randic et al., 2006; Wang and Zhang, 2006; Yao et al., 2006; Zhang et al., 2007; Zhu et al., 2007). In these works, most researchers emphasize their approaches on the coding sequences of the first exon of \(\beta\)-globin gene of different species. Nandy and his partners (2006) suggest that researchers should apply their graphical techniques to complete genes, or at least to the complete coding sequence, so that an unambiguous point of contact is available for comparing to the real world. In this section, we illustrate the utilities of TN curve with the examination of similarities analysis among the coding sequences of the first exon of \(\beta\)-globin gene of 11 species. For comparison, we also do similarities analysis among the complete coding sequences of \(\beta\)-globin gene of the 11 species, and the detailed information of related DNA sequences is presented in Table 5.

| Table 4 |
|-----------------|------------------|
| **Mean values of** | **EMBL ID** | **Species** | **x** | **y** |
|-----------------|------------------|
| Histone H4 | | Mouse | MMHIST4 | –0.69677 | 0.16774 |
| | | Rat | RR4HE5 | –0.68129 | 0.2 |
| | | Human | HSHIS4 | –0.43548 | 0.24194 |
| | | Human | HSHISAD | –0.37742 | 0.2871 |
| Alpha globins—exons | | Horse | ECHBA22 | –0.6815 | –0.31382 |
| | | Goat | CHHBAI | –0.68852 | –0.30679 |
| | | Rh. monkey | MMHBA | –0.79157 | –0.27869 |
| | | Mouse | MMAGL1 | –0.49883 | –0.29508 |
| | | Rabbit | OCHBAPT | –0.65574 | –0.25527 |
| | | Orangutan | PPHBA02 | –0.77518 | –0.31382 |
| Beta globins—exons | | Human beta globin | HSHBB | –0.19457 | –0.19457 |
| | | Mouse | MMAGL1 | –0.3552 | –0.14932 |
| | | Rat | RNGLB | –0.22624 | –0.10633 |
| | | Goat | CHHBAIA | –0.31193 | –0.05734 |
| | | Opossum | DWHBBB | –0.1267 | –0.16216 |
| | | Lemur | LMHBB | –0.34842 | –0.11765 |
| | | Chimp | OCBGLO | –0.3371 | –0.20236 |

Sequence descriptors comparison is one of the main methods to do similarity analysis. It is based on the quantitative characterization of DNA sequences by ordered sets of descriptors derived from the sequences, such as the normalized eigenvalues of all kinds of matrices. For example, Randic et al. (2003a) proposed E matrix, M/M matrix, L/L matrix and L\(^2\)/L\(^2\) matrix, then used their eigenvalues as descriptors. These methods were proved to be useful and used by many authors. However, these matrices become too large to calculate the eigenvalues when DNA sequence is very long, and the computations are very complex. Furthermore, there is some loss of information associated with these matrices (Liao and Wang, 2004c). Then, how to create a simple and convenient method has been a considerable challenge. Here, we propose two methods by constructing two kinds of vectors composed of different numerical descriptors, and both methods do not relate to complex calculations. The underlying assumption is that if two vectors point to a similar direction, two DNA sequences represented by the descriptor vectors are similar. Using Euclidean distance as measurement of sequence similarities, the smaller the Euclidean distance is, the more similar the DNA sequences are. That is to say, the distances between evolutionary closely related species are smaller, while those between evolutionary disparate species are larger.
Method. The compositions of trinucleotides among DNA sequences of various species are universally different, which can be seen from Fig. 3. In order to find some of the invariants sensitive to the form of the TN curve, we use a vector relating to trinucleotides usages composed of 64 components as descriptors to represent DNA sequence. Here, we employ a symmetric matrix.
whose \((i, j)\) is defined as the Euclidean distance between sequence \(i\) and \(j\) to describe the mutual distance of two sequences. Based on this vector, the Euclidean distance between two sequences can be defined as follows:

\[
D(S_i, S_j) = \sqrt{\sum_{m=1}^{64} (P_{m}^{i} - P_{m}^{j})^2},
\]

where \(P_{m}^{i}\) and \(P_{m}^{j}\) are the usage probability of \(m\)th trinucleotide among the 64 kinds of trinucleotides in sequences \(S_i\) and \(S_j\), respectively. With the help of TN curve, one can get each kind of trinucleotide's usage probability in a given DNA sequence without complicated computation. In the sample of Table 2, it is easy to count the number of each trinucleotide easily. For example, we want to obtain the usage probability of trinucleotide GGT in a DNA sequence, which can be accomplished with the following formula:

\[
P_{GGT} = \frac{N_{GGT}}{N_{tot}},
\]

where \(N_{tot}\) is the total number of all trinucleotides in given DNA sequence, \(N_{GGT}\) denotes the number of GGT, which can be got by counting out these dots with \(x = -2\) and \(y = 4\) from map \(\phi\). In the sample of Table 2, the numbers of GGT is 1, the total number of all trinucleotides is 8, then the usage probability of trinucleotide GGT is 12.5%. Similarly, we can also compute the probabilities of other trinucleotides.

Method 2. In Discussions 1 and 2, we elaborate the significations of the six parameters \(x, y, z, x', y', z'\). Here, we use a vector composed of six components as numerically descriptors for a given sequence. Having a vector representation of a DNA sequence, we can compare similarities of different sequences by using the Euclidean distance between two vectors representing them. The Euclidean distance based on the 6-components vector between sequences \(S_i\) and \(S_j\) is defined as follows:

\[
D(S_i, S_j) = \sqrt{\sum_{n=1}^{6} (V_{n}^{i} - V_{n}^{j})^2},
\]

where, \(V = \{x, y, z, x', y', z'\}\) is the descriptors vector, \(V_{n}^{i}\) and \(V_{n}^{j}\) are the \(n\)th component of the 6D vector of sequences \(S_i\) and \(S_j\), respectively.

Although methods 1 and 2 are based on two vectors composed of different descriptors of DNA sequences, their hypostasis is identity, for both methods can represent the trinucleotides' compositions. Tables 6 and 7 are the similarities matrices of the coding sequences of the fist exon and complete coding sequences among the 11 species based on 64-components vector, respectively. Tables 8 and 9 are the corresponding similarities matrices based on 6-components vector, respectively. Observing Table 6, we find gallus (the only non-mammal among them) and Opossum (the most remote species from the remaining mammals) are most dissimilar to others among the 11 species. On the other hand, human–gorilla has the smallest distance, so they are the most similar species pairs. Human–chimpanzee, goat–bovine, mouse–gorilla, mouse–chimpanzee, rabbit–chimpanzee, and gorilla–chimpanzee have smaller distance, so they are more similar species pairs. Similar results are also obtained from Tables 6 to 8, which are coincided with the results in recent

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**Table 6**

| Species | Human | Goat | Opossum | Gallus | Lemur | Mouse | Rabbit | Rat | Gorilla | Bovine | Chimpanzee |
|---------|-------|------|---------|--------|-------|-------|--------|-----|---------|--------|------------|
| Human   | 0     | 47.435 | 72.592 | 224.64 | 40.987 | 108.88 | 38.569 | 93.976 | 34.964 | 76.534 | 27.528     |
| Goat    | 0     | 60.001 | 57.513 | 267.78 | 15.861 | 146.12 | 32.153 | 120.12 | 69.595 | 31.427 | 55.033     |
| Opossum | 0     | 81.315 | 68.348 | 247.28 | 57.513 | 121.96 | 81.315 | 88.352 | 68.348 | 78.567 | 62.949     |
| Gallus  | 0     | 122.19 | 104.22 | 0      | 140.32 | 117.1  | 117.1  | 117.1  | 117.1  | 117.1  | 117.1      |
| Lemur   | 0     | 138.82 | 42.835 | 138.82 | 0      | 39.483 | 138.82 | 42.835 | 138.82 | 42.835 | 138.82     |
| Mouse   | 0     | 78.094 | 117.09 | 117.09 | 117.09 | 0      | 117.09 | 117.09 | 117.09 | 117.09 | 117.09     |
| Rabbit  | 0     | 138.82 | 42.835 | 138.82 | 138.82 | 138.82 | 0      | 117.09 | 117.09 | 117.09 | 117.09     |
| Rat     | 0     | 138.82 | 42.835 | 138.82 | 138.82 | 138.82 | 138.82 | 0      | 117.09 | 117.09 | 117.09     |
| Gorilla | 0     | 138.82 | 42.835 | 138.82 | 138.82 | 138.82 | 138.82 | 138.82 | 0      | 117.09 | 117.09     |
| Bovine  | 0     | 138.82 | 42.835 | 138.82 | 138.82 | 138.82 | 138.82 | 138.82 | 138.82 | 0      | 117.09     |
| Chimpanzee | 0 | 138.82 | 42.835 | 138.82 | 138.82 | 138.82 | 138.82 | 138.82 | 138.82 | 138.82 | 0          |

**Table 9**

Similarity matrix of the complete coding sequences of 11 species based on six-components vector.

| Species | Human | Goat | Opossum | Gallus | Lemur | Mouse | Rabbit | Rat | Gorilla | Bovine | Chimpanzee |
|---------|-------|------|---------|--------|-------|-------|--------|-----|---------|--------|------------|
| Human   | 0     | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |
| Goat    | 0     | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |
| Opossum | 0     | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |
| Gallus  | 0     | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |
| Lemur   | 0     | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |
| Mouse   | 0     | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |
| Rabbit  | 0     | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |
| Rat     | 0     | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |
| Gorilla | 0     | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |
| Bovine  | 0     | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |
| Chimpanzee | 0 | 0    | 0       | 0      | 0     | 0     | 0      | 0   | 0       | 0      | 0          |

**Fig. 7.** PCA is performed on the 6D vector. (A) Is the results of projection of 11 6-component vectors on the first two principal components, here: 1—human, 2—goat, 3—opossum, 4—gallus, 5—lemur, 6—mouse, 7—rabbit, 8—rat, 9—gorilla, 10—bovine, and 11—chimpanzee and (B) shows the contributions of each principal component.
papers (Cao et al., 2008; He and Wang, 2002; Liao and Ding, 2006; Qi and Fan, 2007; Wang and Zhang, 2006; Zhang and Chen, 2006).

In method 2, we construct a six-components vector as descriptor of DNA sequence. To validate the efficiencies of this 6D vector, we perform principal component analysis (PCA) on the six parameters. Fig. 7A shows the projection the 6D vectors of the complete coding sequences of 11 species on a 2D property space composed of PC 1 and PC 2, where PC 1 and PC 2 are the first two principal components. From Fig. 7A, we can find that opossum and gallus are most dissimilar with other species, while human–gorilla has the smallest distance. Besides, human–chimpanzee, gorilla–chimpanzee, goat–bovine are the more similar species. These results are overall in agreement with the results above. We calculate the contribution proportion of the six components, as shown in Fig. 7B, from which we find that the cumulative contribution proportion of the first two principal components is 92% of the total inertia of the six-dimension space vector. These results denote the six-components vector do well in numerically representing DNA sequences.

4. Conclusion

Visual inspection and numerical description of DNA sequences are major functions of graphical representations. By classifying the 64 kinds of trinucleotides into four categories, we construct a novel 3D graphical representation of DNA sequence. In this paper, the utilities of TN curve are illustrated by relevant applications, such as visual inspection and graphical analysis similarities of different DNA sequences, discriminating conserving sequences and similarities/dissimilarities of orthologous genes among different species. We also propose six descriptors which can be obtained without complex calculations for DNA sequences from this novel model, and the PCA validate their efficiencies. Meanwhile, two simple methods are outlined to analyze similarities/dissimilarities among DNA sequences, and these two approaches can be easier to perform with low cost of runtime.

Comparison with other geometrical models, TN curve has following advantages: (1) It is the first approach that allows us to display the trinucleotides information in a space within 3D space. (2) It contains more information, as introduced in Section 2, we can obtain information of not only trinucleotides but also dinucleotides. (3) It provides straightforwardly visual biological information of DNA sequence, such as compositions of trinucleotides and recognizing similarities among different sequences. (4) Based on trinucleotides, TN curve can provide efficient method in sequences especially coding sequences analysis. Therefore, TN curve can provide convenient tools for both computational scientists and molecular biologists in Bioinformatics researches.

Competing interests

The authors declare that they have no competing interests.

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