Sequence analysis

Genome analysis with inter-nucleotide distances

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Received on June 9, 2009; revised on August 19, 2009; accepted on August 21, 2009
Advance Access publication September 16, 2009
Associate Editor: John Quackenbush

ABSTRACT

Motivation: DNA sequences can be represented by sequences of
four symbols, but it is often useful to convert the symbols into
real or complex numbers for further analysis. Several mapping
schemes have been used in the past, but they seem unrelated to
any intrinsic characteristic of DNA. The objective of this work was
to find a mapping scheme directly related to DNA characteristics
and that would be useful in discriminating between different species.
Mathematical models to explore DNA correlation structures may
contribute to a better knowledge of the DNA and to find a concise
DNA description.

Results: We developed a methodology to process DNA sequences
based on inter-nucleotide distances. Our main contribution is a
method to obtain genomic signatures for complete genomes, based
on the inter-nucleotide distances, that are able to discriminate
between different species. Using these signatures and hierarchical
clustering, it is possible to build phylogenetic trees. Phylogenetic
trees lead to genome differentiation and allow the inference of
phylogenetic relations. The phylogenetic trees generated in this work
display related species close to each other, suggesting that the
inter-nucleotide distances are able to capture essential information
about the genomes. To create the genomic signature, we construct
a vector which describes the inter-nucleotide distance distribution
of a complete genome and compare it with the reference distance
distribution, which is the distribution of a sequence where the
nucleotides are placed randomly and independently. It is the residual
or relative error between the data and the reference distribution that
is used to compare the DNA sequences of different organisms.

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1 INTRODUCTION

DNA sequences have been converted to numerical signals using
different mappings. A commonly used mapping is to consider binary
dependencies that describe the position of each symbol (Voss, 1992).
The binary representation is certainly one of the earliest and one of
most popular mappings of DNA. However, several other different
mappings have been proposed (Akhatar et al., 2007; Anastassiou,
2003; Brodzik and Peters, 2005; Budnyrev et al., 1995; Cristea, 2003;
Jeffrey, 1990; Liao et al., 2005; Nair and Mahalakshmi, 2005; Ning
et al., 2003; Randic, 2008; Silverman and Linsker, 1986; Zhang and
Zhang, 1994).

Some of the mappings used in DNA processing do not have a
simple numerical interpretation and others do not have biological
motivation. Also, some of the representations are not reversible and
do not take into account the sequence structure. Currently, there
is no ideal mapping to analyze every type of correlation in DNA
sequences.

The inter-nucleotide distances introduced by Nair and Mahalakshmi (2005)
provide a new DNA numerical methodology profile and a new mapping to explore the distance structure of
DNA. This representation converts any DNA sequence into a unique
numerical sequence with the same length, where each number represents
the distance of a symbol to the next occurrence of the
same symbol. The global inter-nucleotide distance representation
is reversible, but does not explore the individual behavior of each
nucleotide.

We explore the inter-nucleotide representation introduced by Nair
and Mahalakshmi (2005) and develop new methodologies to analyze
this representation and extract some interesting features of the DNA
correlation structure. Nair and Mahalakshmi (2005) applied Fourier
analysis to the distance sequence and showed that this mapping has
a discriminatory capability for highlighting the promoter region of
gene sequences. However, Akhtar and Epps (2008) found that it has
poor exon prediction accuracy.

In our approach, we introduced four sequences, one for
each nucleotide, to represent the inter-nucleotide distances. This
methodology allows to perform comparative analysis between
the behavior of the four nucleotides and of the global sequence.
We studied the five inter-nucleotide distance distributions and we
present one residual analysis to characterize organisms and to do
multiple organism comparisons.

Phylogenetic trees reproduce the evolutionary tree that represents
the historical relationships between the species. Recent phylogenetic
tree algorithms use nucleotide sequences. Typically, these trees are
constructed with multiple sequence alignment (Hodge and Cope,
2000), which is a computationally demanding task. We propose an
algorithm based on the inter-nucleotide distance behavior that is
able to efficiently building phylogenetic trees.

2 METHODS

Consider the alphabet \( \mathcal{A} = \{A, C, G, T\} \) and let \( \omega = (\omega_1, \omega_2, \ldots, \omega_N) \) be a symbolic sequence defined in \( \mathcal{A} \). Consider a numerical sequence, \( d^\omega \), that represents...
the inter-nucleotide distances to the symbol \( x \in \{ A, C, G, T \} \). We show below, as an example, the four inter-nucleotide distance sequences for a short DNA fragment AAACCCGTGTCAGTT:

\[
d^0 = (1, 1, 9, 4), d^1 = (1, 1, 5, 8), d^2 = (2, 4, 9), d^3 = (2, 4, 1, 8),
\]

considering that the symbolic sequence is cyclic.

It is possible, for small sequences, to visualize the four inter-nucleotide distance sequences, as exemplified in Figure 1 for gene \( g(NM_{032427.1}) \) from \( H. sapiens \).

Another distance sequence, originally introduced by Nair and Mahalakshmi (2005), is the global inter-nucleotide distance sequence, \( \delta \). This global distance sequence is exemplified below for the same short DNA segment used previously,

\[
d = (1, 1, 9, 1, 5, 2, 4, 4, 8, 4, 9, 1, 8),
\]

which is slightly different from the non-cyclic approach used by Nair and Mahalakshmi (2005).

The length \( \delta \) of the global distance sequence, \( \delta \), is equal to the sum of the lengths of the four inter-nucleotide distance sequences \( N^0, N^1, N^2, N^3 \). Thus,

\[
\sum_{x \in A} N^\delta = N.
\]

If the positions of the first occurrence of each nucleotide are known, \( k_0^x \), \( k_1^x \), \( k_2^x \) and \( k_3^x \) (\( x = s \) and \( x = t \) for \( 0 < c < k \)), then the positions of all the nucleotides in the complete sequence may be determined from the inter-nucleotide distance sequences,

\[
k_i^x = \sum_{s \in A} d^i + k_s^x.
\]

Naturally, we have: \( k_i^t - k_{i-1}^t = d_i \) and \( N = \sum_{x \in A} d_i, x \in A \).

In order to illustrate the reversibility of the mapping, we show how to reconstruct the DNA sequence used in the example above from the initial positions of the symbols and the global distance sequence. We start by assigning the first symbols to their positions in the sequence,

\[
\begin{align*}
[1 & 4 7 8] \quad A \cdot C \cdot GT---
\end{align*}
\]

Then considering each distance in the sequence we reconstruct iteratively the symbol sequence

\[
\begin{align*}
d_1 &= 1 \quad A \cdot C \cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_2 &= 1 \quad A \cdot AC\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_3 &= 9 \quad A \cdot ACC\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_4 &= 1 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_5 &= 5 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_6 &= 1 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_7 &= 2 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_8 &= 2 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_9 &= 4 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_{10} &= 4 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_{11} &= 4 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_{12} &= 4 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_{13} &= 9 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_{14} &= 1 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_{15} &= 1 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_{16} &= 8 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

\[
\begin{align*}
d_{17} &= 8 \quad A \cdot ACC\cdot C\cdot GT---
\end{align*}
\]

There is some redundancy in the four inter-nucleotide distance sequences and three of them would be sufficient to determine the complete nucleotide sequence.

### 2.1 Distribution of the distance sequences

In order to calculate some statistical properties of various genomes, we will study the characteristics of the inter-nucleotide distance distribution. Consider \( p^0, p^1, p^2 \) and \( p^3 \) as the occurrence probabilities of nucleotides \( A, C, G \) and \( T \), respectively. If the nucleotide sequences were generated by an independent and identically distributed (i.i.d.) random process, then each of the inter-nucleotide distance sequences, \( d^i \), would follow a geometric distribution. In fact, the probability distribution of the inter-nucleotide distances of the symbol \( x \) is

\[
f^i(x) = P(d^i = k) = P(d = k|x) = p^i(1-p^i)^{k-1}, \quad k = 1, 2, \ldots,
\]

its distribution function is

\[
F^i(x) = P(d^i \leq k) = 1 - (1-p^i)^k,
\]

the expected value is \( 1/p^i \) and the variance is \((1-p^i)/(p^i)^2\). To estimate the nucleotide occurrence probability, \( p^i \), we use relative frequencies, \( N^\delta \), computed from the original nucleotide sequence. The term reference distribution, applied to a DNA sequence, describes the distribution that the inter-nucleotide distances for that sequence would follow, if its nucleotides were randomly determined, with probabilities equal to the relative frequencies, independently of each other.

Figure 2 shows the measured and the reference distributions of the inter-nucleotide distance sequences for gene \( g(NM_{032427.1}) \) from \( H. sapiens \). Although the nucleotide distance distribution from DNA shows a power law behavior, it differs from the reference distribution. This power law behavior is expected, since the reference distribution was established under the assumption of a i.i.d. random process with constant nucleotide relative frequencies estimated from the DNA sequence.

To compare the distribution of the inter-nucleotide distance sequences with the reference distribution several measures may be used. Some examples are the Kolmogorov–Smirnov distance, Kolbék-Leibler distance and the correlation coefficient. In this work, we use the Kolmogorov–Smirnov distance to assess how significantly different the distribution of the measured distance sequence and the reference distribution are. The comparison between the distribution obtained from the data and the reference distribution may be carried out for the nucleotide distance sequences and also for the global distance sequence.

As mentioned above, the reference distribution function for each nucleotide is geometric, assuming that the DNA sequence was generated

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**Fig. 1.** Inter-nucleotide distances for the \( g(NM_{032427.1}) \) gene of \( H. sapiens \).
The histograms of the distance sequences were computed for each nucleotide coding region. The global distance sequence distribution is given by an independent random process with constant parameters, and the observed distances and the solid line shows the reference distribution with parameters estimated from the data.

We setup to investigate how similar (or different) are the distance distributions and the reference distributions of various species. The species used in this work are listed in Table 1.

<table>
<thead>
<tr>
<th>Species Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. sapiens</em> (human) Build 36.3</td>
</tr>
<tr>
<td><em>Pan troglodytes</em> (chimpanzee) Build 2.1</td>
</tr>
<tr>
<td><em>Macaca mulatta</em> (Rhesus macaque) Build 1.1</td>
</tr>
<tr>
<td><em>Mus musculus</em> (mouse) Build 37.1</td>
</tr>
<tr>
<td><em>Rattus norvegicus</em> (brown rat) Build 4.1</td>
</tr>
<tr>
<td><em>Equus caballus</em> (horse) Build 2.1</td>
</tr>
<tr>
<td><em>Canis familiaris</em> (dog) Build 2.1</td>
</tr>
<tr>
<td><em>Bos taurus</em> (cow) Build 4.1</td>
</tr>
<tr>
<td><em>Ornithorhynchus anatinus</em> (platypus) Build 1.1</td>
</tr>
<tr>
<td><em>Gallus gallus</em> (chicken) Build 2.1</td>
</tr>
<tr>
<td><em>Xenopus tropicalis</em> (Western clawed frog) Build 4.1</td>
</tr>
<tr>
<td><em>Danio rerio</em> (zebrafish) Build 3.1</td>
</tr>
<tr>
<td><em>Apis mellifera</em> (honey bee) Build 4.1</td>
</tr>
<tr>
<td><em>Caenorhabditis elegans</em> (nematode) NC003279</td>
</tr>
<tr>
<td><em>Vitis vinifera</em> (grape vine) Build 1.1</td>
</tr>
<tr>
<td><em>Populus trichocarpa</em> (California poplar) Build 1.0</td>
</tr>
<tr>
<td><em>Arabidopsis thaliana</em> (thale cress) AGI 7.2</td>
</tr>
<tr>
<td><em>Saccharomyces cerevisiae</em> str.S228C (budding yeast) SGD 1</td>
</tr>
<tr>
<td><em>Schizosaccharomyces pombe</em> (fission yeast) Build 1.1</td>
</tr>
<tr>
<td><em>Dictyostelium discoideum</em> str.AX4 (amoeba) Build 2.1</td>
</tr>
<tr>
<td><em>Plasmodium falciparum</em> 3D7 (protozoan) Build 2.1</td>
</tr>
<tr>
<td><em>Escherichia coli</em> str.K12 subsp.MG1655 (bacterium) NC000913</td>
</tr>
<tr>
<td><em>Bacillus subtilis</em> str.168 (bacterium) NC000964</td>
</tr>
<tr>
<td><em>Chlamydia trachomatis</em> str.D/UW-3JCX (bacterium) NC000117</td>
</tr>
<tr>
<td><em>Mycoplasma genitalium</em> str.G37 (bacterium) NC000908</td>
</tr>
<tr>
<td><em>Streptococcus mutans</em> str.UA159 (bacterium) NC004350</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em> str.ATCC 700669 (bacterium) NC011900</td>
</tr>
<tr>
<td><em>Aeropyrum pernix</em> str.K1 (archaeota) NC000854</td>
</tr>
</tbody>
</table>

where \( f(k) \) is the observed relative frequency of the distance \( k \), and \( f(k) \) is the relative frequency of the reference distribution.

It is known that coding regions usually have different characteristics when compared with the complete genome. To explore these differences, we carried out an experiment to compare the behaviour of the global distance distributions of the complete genome and coding regions of *H. sapiens*. The distances between nucleotides within each gene were considered as separate sequences and the distance distribution was computed from all the genes. The data for the human coding regions was obtained from the RNA file at the NCBI ftp site.

### 3 RESULTS

#### 3.1 Inter-nucleotide distances analysis

Table 2 shows the results of the Kolmogorov–Smirnov test between the distance relative frequencies distributions of all the human chromosome pairs. Only the first 100 distances were used. The results of the test show that for a significance level of 5% it is not possible to say that the distributions of the distances for the various chromosomes are different. The need for limiting the distances to the first 100 represents a compromise between two extremes. On one hand, if all or a very large number of distances are used, the distributions will be very sparse and difficult to interpret. On the other hand, if the number is too small, the vector of distances may not contain enough information about the inter-nucleotide distributions. We have found that the limitation to the first 100 distances, which was carried out...
Table 2. P-values from Kolmogorov–Smirnov test to compare inter-nucleotide distance relative frequencies distributions between the chromosomes of H. sapiens

|   | C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8 | C9 | C10 | C11 | C12 | C13 | C14 | C15 | C16 | C17 | C18 | C19 | C20 | C21 | C22 | CX | CY |
|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| C1| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 0.4| 1.0| 0.9| 1.0| 0.3|
| C2| – 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 0.9| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 0.7| 1.0| 1.0| 0.3| 0.9| 0.8| 0.9| 1.0| 0.2|
| C3| – – 1.0| 1.0| 1.0| 1.0| 0.9| 1.0| 0.8| 1.0| 1.0| 1.0| 0.6| 1.0| 1.0| 0.3| 0.8| 0.7| 0.8| 1.0| 0.1|
| C4| – – – 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 0.7| 1.0| 1.0| 0.3| 1.0| 0.9| 1.0| 1.0| 0.2|
| C5| – – – – 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 0.6| 1.0| 1.0| 0.3| 1.0| 0.8| 1.0| 1.0| 0.1|
| C6| – – – – – 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 0.6| 1.0| 1.0| 0.3| 1.0| 0.8| 1.0| 1.0| 0.2|
| C7| – – – – – – 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 0.9| 1.0| 1.0| 0.7| 1.0| 1.0| 1.0| 1.0| 1.0| 0.2|
| C8| – – – – – – – – 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 0.7| 1.0| 1.0| 0.3| 1.0| 1.0| 1.0| 1.0| 0.2|
| C9| – – – – – – – – – 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 1.0| 0.7| 1.0| 1.0| 0.6| 1.0| 0.9| 1.0| 0.1|
| C10| – – – – – – – – – – 1.0| 1.0| 1.0| 1.0| 1.0| 0.8| 1.0| 1.0| 0.4| 1.0| 1.0| 1.0| 0.2|
| C11| – – – – – – – – – – – 1.0| 1.0| 1.0| 1.0| 1.0| 0.8| 1.0| 1.0| 0.4| 1.0| 0.9| 1.0| 0.2|
| C12| – – – – – – – – – – – – 1.0| 1.0| 1.0| 1.0| 1.0| 0.6| 1.0| 1.0| 0.4| 1.0| 0.9| 1.0| 0.2|
| C13| – – – – – – – – – – – – – 1.0| 1.0| 1.0| 0.6| 1.0| 1.0| 0.3| 1.0| 0.9| 1.0| 0.2|
| C14| – – – – – – – – – – – – – – 1.0| 0.6| 1.0| 0.3| 1.0| 0.8| 1.0| 1.0| 0.2|
| C15| – – – – – – – – – – – – – – – 1.0| 0.8| 1.0| 0.2| 1.0| 0.9| 1.0| 0.1|
| C16| – – – – – – – – – – – – – – – – 1.0| 0.8| 0.8| 1.0| 0.8| 1.0| 1.0| 0.6|
| C17| – – – – – – – – – – – – – – – – – 1.0| 1.0| 0.6| 1.0| 1.0| 1.0| 1.0| 0.2|
| C18| – – – – – – – – – – – – – – – – – – 1.0| 0.3| 1.0| 1.0| 1.0| 1.0| 0.1|
| C19| – – – – – – – – – – – – – – – – – – – 1.0| 0.6| 0.8| 0.8| 0.7| 0.9|
| C20| – – – – – – – – – – – – – – – – – – – – 1.0| 1.0| 1.0| 1.0| 0.2|
| C21| – – – – – – – – – – – – – – – – – – – – – 1.0| 1.0| 1.0| 0.6|
| C22| – – – – – – – – – – – – – – – – – – – – – – 1.0| 1.0| 1.0| 1.0|
| CX| – – – – – – – – – – – – – – – – – – – – – – – 1.0| 1.0| 0.3|
| CY| – – – – – – – – – – – – – – – – – – – – – – – – 1.0|

Only the first 100 distances were used.

Table 3. P-values from the Kolmogorov–Smirnov test to compare inter-nucleotide distance relative frequencies distributions between nucleotides in H. sapiens

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>C</th>
<th>G</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>0.00032</td>
<td>0.00032</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>–</td>
<td>1</td>
<td>1</td>
<td>0.00058</td>
</tr>
<tr>
<td>G</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>0.00058</td>
</tr>
<tr>
<td>T</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1</td>
</tr>
</tbody>
</table>

Only the first 100 distances were used.

in all experiments described in this article, provides an adequate compromise.

Our results confirm that the distribution of the first distances contains information about the genome of each species, and that it may be interpreted as a genetic signature. The approach is justified by the similarity between the distance relative frequencies distributions of all the chromosomes (high P-values). The same similarity was also found on the DNA of the other organisms used in this study, with some exceptions for the Gallus gallus.

We have also compared the inter-nucleotide distance relative frequencies distribution of the four nucleotides, by applying the Kolmogorov–Smirnov test to the distance relative frequencies distribution for the complete genome. The results of the comparative tests are shown in Table 3.

The results in Table 3 show that the distance relative frequencies distribution of the nucleotide T, and the distance relative frequencies distribution of C is identical to that of G, but the distributions for A (or T) and C (or G) are significantly different. Notice that the DNA complementary signature was not used in the computation of the inter-nucleotide distance relative error for the inter-nucleotide distance distribution relative error. These identical distance distributions for the nucleotides A/T and C/G are present in all the human chromosomes and also on the genome of all the other species used in this work.

We may use the relative error, as defined in (1), to compare the distance distributions, both for inter-nucleotide and global sequences, with the reference distributions. Figure 3 shows the relative error for the inter-nucleotide distance in H. sapiens and Figure 4 shows the relative error for the global distance.

For the human genome, the first two distances have a higher frequency than the corresponding random sequences, and the following 10 distances have lower frequencies. For distances higher than 12 the relative error is always positive (this behavior is similar in all chromosomes). The higher frequencies of the first two distances of the human genome highlight constitutive repeat elements [see Doggett (2001) for an overview of repeating structures in the human genome] and a tendency in this species to have repeated nucleotides separated by a different nucleotide.

The behavior of the relative error in the coding regions of the human DNA is different from the behavior in the complete DNA (compare Figs. 5 and 6 with Figs. 3 and 4). In the coding regions, the first distance continues to have a higher relative frequency than in the corresponding random sequences, but the relative error shows a kind of oscillating behavior for the first distances that may indicate some form of underlying periodicity.
From the values shown in Table 4, we observe that the \( P \)-values between distance relative frequencies distributions of the nucleotides do not have the same similarity relations that were found for the complete genome. In the coding regions, the similarity is only significant for the nucleotides \( A/C \) and \( A/T \).

We have used the Discrete Fourier Transform (DFT) to characterize the periodicity observed in the plots of the relative error for the coding regions (Figs. 5 and 6). Figure 7 shows the spectrum of the relative error for the coding regions of the human genome and Figure 8 shows the spectrum of the complete human genome. Figure 7 reveals a local peak at \( k = N/3 \), which corresponds to a period of three samples. It is known that the symbolic autocorrelation spectrum of protein coding DNA regions typically has a peak at \( k = N/3 \).
Genome analysis with inter-nucleotide distances

3.2 Analysis of multiple organisms

The relative error vectors of each complete genome may be used as a genomic signature that identifies each species, thus allowing the comparison of species. These vectors were used to build dendrograms that show hierarchical clusters which could be interpreted as phylogenetic trees. The dendrograms were built using complete linkage clustering and the similarity matrix was computed using the Euclidean distance.

4 CONCLUSION

The inter-nucleotide distance mapping characterizes completely a DNA sequence, in the sense of providing an invertible mapping: the original sequence can be reconstructed from the inter-nucleotide distances. The results obtained in this work suggest that for the addressed species there is a genetic signature, a pattern, that is a distinguishing characteristic of that species. The pattern, which is obtained from the distribution of the inter-nucleotide distances, is contained in any of the chromosomes of all species used in this work.
Another interesting feature of the inter-nucleotide approach is the significant similarity found for the A/T and C/G nucleotides. This similarity may be explained by the existence of inverted repeats. We used the inter-nucleotide distance to build dendrograms that may have a biological interpretation and may be considered as a kind of phylogenetic tree. The dendrograms for the species used in this work are in accordance with the expected similarities between species.

We expect that the inter-nucleotide distance mapping may stimulate further investigations and improve our knowledge about the correlation structure of DNA.

Funding: Fundação para a Ciência e a Tecnologia (FCT); European Social Fund (to S.P.G.); Ministério da Ciência, Tecnologia e Ensino Superior (MCTES, to S.P.G.).

Conflict of Interest: none declared.

REFERENCES