AltAVisT: Comparing alternative multiple sequence alignments

Burkhard Morgenstern1,∗, Sachin Goel1, Alexander Sczyrba2 and Andreas Dress3

1International Graduate School in Bioinformatics and Genome Research, 2Faculty of Technology, Research Group in Practical Computer Science and 3Department of Mathematics, University of Bielefeld, Postfach 10 01 31, 33501 Bielefeld, Germany

Received on July 18, 2002; revised on September 18, 2002; accepted on September 28, 2002

ABSTRACT
Summary: We introduce a WWW-based tool that is able to compare two alternative multiple alignments of a given sequence set. Regions where both alignments coincide are color-coded to visualize the local agreement between the two alignments and to identify those regions that can be considered to be reliably aligned.

Availability: http://bibiserv.techfak.uni-bielefeld.de/altavist/
Contact: burkhard@TechFak.Uni-Bielefeld.DE

Sequence alignment is the most fundamental tool for sequence data analysis in molecular biology. Practically all methods of computational sequence analysis rely in one way or the other on sequence comparison, so their results depend on the quality of the underlying alignments. Pairwise and multiple alignment therefore continue to be among the most active areas of bioinformatics research.

There are two major challenges in the context of sequence alignment: (a) it can be hard to distinguish weak local homologies from random similarities and (b) alignment programs can only detect those homologies that appear in the same relative order in the input sequences. The latter problem is inherent in sequence alignment and means that, for many data sets, correct alignment of one homologous region necessarily prevents other homologies from being properly aligned.

No single alignment procedure can be expected to construct biologically reasonable alignments in all possible situations. The reason for this is that every alignment program tries (explicitly or implicitly) to find optimal alignments according to some relatively simple mathematical scoring function. Yet it cannot be expected that any given scoring function will, under all conditions, be in accordance with biology giving the mathematically highest score to the biologically correct alignments. Consequently, human intervention is often necessary to check the results of automated alignment procedures and to obtain meaningful alignments.

A popular way of testing the (local) reliability of pairwise or multiple alignments is to construct alternative alignments of the same sequences using different alignment methods. Notredame et al. (2000) used this idea systematically and developed a software tool that integrates results from different multi-alignment methods into one single output alignment.

For multiple alignment, a variety of software programs are now available that rely on very different objective functions and optimization techniques. The results of these methods can therefore be quite diverse, see Notredame (2002) for an excellent review of the state-of-the-art multi-alignment algorithms and Thompson et al. (1999b) and Lassmann and Sonnhammer (2002) for systematic evaluation of the corresponding software tools.

If two alignments have been constructed by different methods, those regions where both alignments coincide are generally considered to be more reliable than regions where the two methods disagree. However, manually comparing different multiple alignments is a tedious task. Herein, we introduce AltAVisT (Alternative Alignment Visualization Tool), a WWW-based tool that compares two different multiple alignments of a given data set and highlights regions where both alignments coincide. Two input options are available:

(1) It is possible to enter a family of sequences. In this case, our program runs DIALIGN (Morgenstern, 1999) and CLUSTAL W (Thompson et al., 1994) on the input sequences and compares the resulting alignments to each other. These two methods are currently among the most popular multi-alignment tools. They rely on fundamentally different algorithmical approaches, so agreement between them should indicate (local) correctness of the alignments.

*To whom correspondence should be addressed.
The alignment of DIALIGN is:

```
GNEF--EFAYE---QTYMDYFPE---TFHSHFSEP---FD---FN
EAYF---QMEEFSYDPPE---TFHSHFSEP---FD---FN
EAYF---QTYMDYFPE---TFHSHFSEP---FD---FN
DPYF---QTYMDYFPE---TFHSHFSEP---FD---FN
DPYF---QTYMDYFPE---TFHSHFSEP---FD---FN
DPYF---QTYMDYFPE---TFHSHFSEP---FD---FN
DPYF---QTYMDYFPE---TFHSHFSEP---FD---FN
```

With lower case letters not considered to be aligned.
The alignment of CLUSTAL is:

```
PGEF---EFAYE---QTYMDYFPE---TFHSHFSEP---FD---FN
EAYF---QMEEFSYDPPE---TFHSHFSEP---FD---FN
EAYF---QTYMDYFPE---TFHSHFSEP---FD---FN
DPYF---QTYMDYFPE---TFHSHFSEP---FD---FN
DPYF---QTYMDYFPE---TFHSHFSEP---FD---FN
DPYF---QTYMDYFPE---TFHSHFSEP---FD---FN
DPYF---QTYMDYFPE---TFHSHFSEP---FD---FN
```

With different colors used to distinguish groups where the alignments coincide within groups but not between different groups.

Fig. 1. AltAVisT applied to a small test sequence set. The first alignment has been produced by DIALIGN, the second one by CLUSTAL. For each column in the first alignment, those residue pairs are colored that also appear in one common column in the second alignment. The same holds true for the two Cs in the same column of the DIALIGN alignment; they also appear in one column in the CLUSTAL alignment (column four). However, the Ms and Cs belong to different columns in the CLUSTAL alignment so different colors are used. All lower-case residues in the DIALIGN alignment are printed in black because they are not considered aligned by DIALIGN. In the second alignment, all residues have the same color as in the first alignment even though they are not aligned together in the first alignment, see for example column 21 in the second alignment.

(2) It is possible to enter two different pre-calculated alignments of a sequence family set that may have been produced by any method; this way the user can compare the output of arbitrary alignment methods.

With the second option, it is possible to distinguish between upper-case and lower-case letters in the input alignments and to consider only upper-case letters for the alignment comparison. This can be used in situations where only subareas of an alignment are of interest; it corresponds to the output of DIALIGN where lower-case letters are not considered to be aligned. With either option, those residue pairs that are aligned to each other in both alignments are colored. Different colors are used to distinguish groups of residues where the alignments coincide within groups but not between different groups; see Figure 1 for an example.

REFERENCES


