CS612 – Algorithms in Bioinformatics

Homework Assignment 1 – 02/16/2023

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Part 1 – Practice

1. Sequence alignment hands-on exercise. We have given the following protein sequence:

>protein
TCPFADPAALYSRQDTTSGQSPLAAYEVDDSTGYLTSDVGGPIQDQTSLKAGIRGPTLLEDFMFRQK
IQHFDHERVPERAV

The sequence is also available at the course webpage: http://www.cs.umb.edu/nurith/cs612/protein.fasta .

Solution:

(a) In this protein sequence we need to perform the protein Blast from http://blast.ncbi.nlm.nih.gov.

Select "Protein Blast" to get to the **BlastP** website. Paste the above sequence to the top window. Use the default parameters – **nr** database (nonredundant protein sequence database). We will be getting the following.

Y7S2DKNY016-Alignment.docx

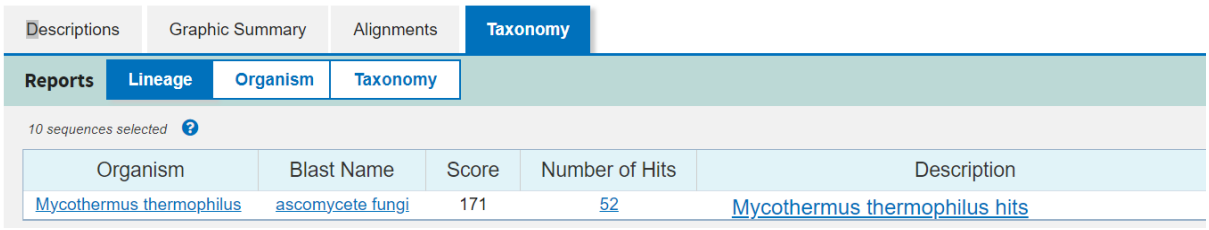
(b) In this we need to Repeat the search above with the **UniprotKB**/**SwissProt** database and attach it first 2 pages as part of your homework
We will be getting the following as the output.

Y7WWEBCM01R-Alignment.docx

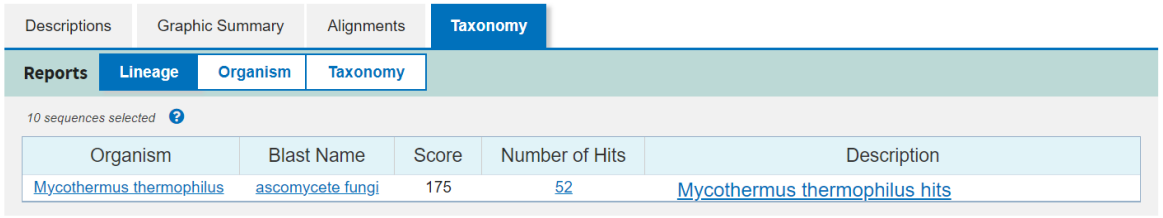
(c) Repeat search a. above with **PAM30** as a substitution matrix. This can be done in the **blastP** homepage by opening "algorithm parameters" at the bottom of the page.
We can have the following differences highlighted in the attachment.

We have below ranked for A and C and name of the protein sequences are as above.

Default matrix



Substitution matrix



2. DNA sequence alignment: The following sequence was constructed by NCBI scientist Mark Boguski for Michael Chrichton's "The Lost World" of the Jurassic Park series:

The sequence is available at the course webpage:

http://www.cs.umb.edu/ nurith/cs612/dino.fasta

(a) What are the two main species used to construct the dinosaur DNA sequence?

(I) Gallus gallus (chicken)

(ii) Xenopus laevis (African clawed frog)

(b) with Blastx

(i) Gallus gallus (chicken)

(ii) Cygnus olor (mute swan)

(iii) Parus major (Great Tit)

(iv) Catharus ustulatus (Swainson's thrush)

b. Now we need to Repeat the search with blastx (DNA vs. protein sequence) using the default non-redundant protein sequence database. Look at the top sequence alignment we get the below ones.

YXZYK0M3013-Alignment.txt

Part 2 – Theory

1. Lesk book question 5.3: The edit distance between the strings agtcc and cgctca is 3, consistent with the following alignment:

Solution: To convert the string "agtcc" to "cgctca" using a minimum of 3 edit operations, we can use the following sequence of operations:

Replace "a" with "c" at position 1: "cgtcc"

agtcc
|
cgtcc

Insert "g" at position 2: "cggtcc"

agtcc
/
cggtcc

Replace "c" with "a" at position 4: "cggtca"

agtcc
\
cggtca

This sequence of operations results in the desired string "cgctca" and requires a minimum of 3 edit operations: one replacement, one insertion, and one replacement.

2.1.jpg

2. Dynamic programming:

(a) Use the Needleman Wunsch global alignment Dynamic programming formula in slide set no. 2 to find the sequence alignment score of the two DNA sequences ATCGAACTGCC and TACGCACTCCA.

2 A.jpg

(b) Smith waterman local alignment

2 B.jpg

(c) Semi global alignment

2C.jpg

3.a) Given the Longest Common Subsequence (LCS) of two sequences X and Y, you can obtain the shortest common super sequence (SCS) of the two sequences by following these steps:

Initialize two pointers, one pointing to the start of the LCS and the other pointing to the start of the sequences X and Y, respectively.

Iterate through the LCS, and for each element in the LCS, do the following:

Append all the characters in X and Y that come before the current element of the LCS to the SCS.

Append the current element of the LCS to the SCS.

Move the X and Y pointers to the characters immediately following the current element in the LCS.

After iterating through the entire LCS, append all the remaining characters in X and Y to the SCS.

The resulting sequence is the shortest common super sequence of X and Y.

For example, suppose we have two sequences X = "ABCBDAB" and Y = "BDCABA", and their LCS is "BCBA". To obtain the SCS of X and Y, we can follow these steps:

Initialize two pointers, one pointing to the start of the LCS "BCBA" and the other pointing to the start of X ("A") and Y ("B"), respectively.

Iterate through the LCS "BCBA", and for each element in the LCS, do the following:

Append all the characters in X and Y that come before the current element of the LCS to the SCS. In this case, we append "A" to the SCS.

Append the current element of the LCS to the SCS. In this case, we append "B", "C", "B", and "A" to the SCS.

Move the X and Y pointers to the characters immediately following the current element in the LCS. In this case, we move the X and Y pointers to "D" and "D", respectively.

After iterating through the entire LCS, append all the remaining characters in X and Y to the SCS. In this case, we append "D", "A", and "B" to the SCS.

The resulting sequence is "ABCBADAB".

b. We are given two sequences that are TACGGGTAT and GGACGTACG.

To find the shortest common sequence of two strings, we can use a technique called the

"Longest common substring" algorithm, which finds the longest substring that is common to both strings. However, in this case, there is no common substring that is shared between the two sequences.

TACGGGTAT

GGACGTACG

3 b.jpg

Therefore, the shortest common sequence of "TACGGGTAT" and "GGACGTACG" is simply an empty sequence or string "".

4.Substuition Matrix:

We have given the two sequences.

THISSEQ

THATSEQ

From the given BLOSUM-62 matrix matrix, we can obtain these values and

(a)

4 a.jpg

(b) From the given PAM -250 matrix, we can obtain these values and


4 b.jpg

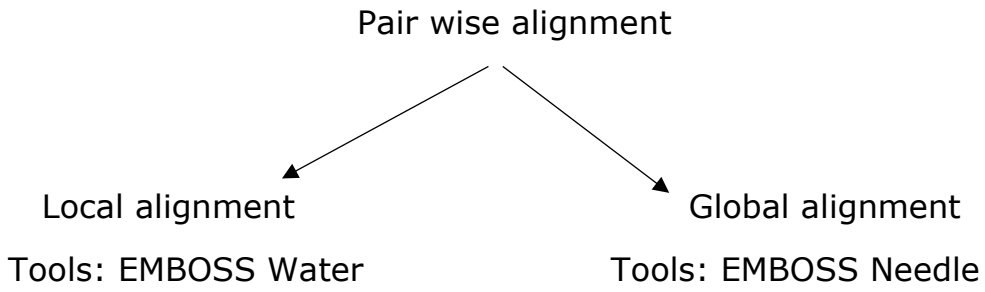
5. Multiple Sequence Alignment for extended dynamic programming.

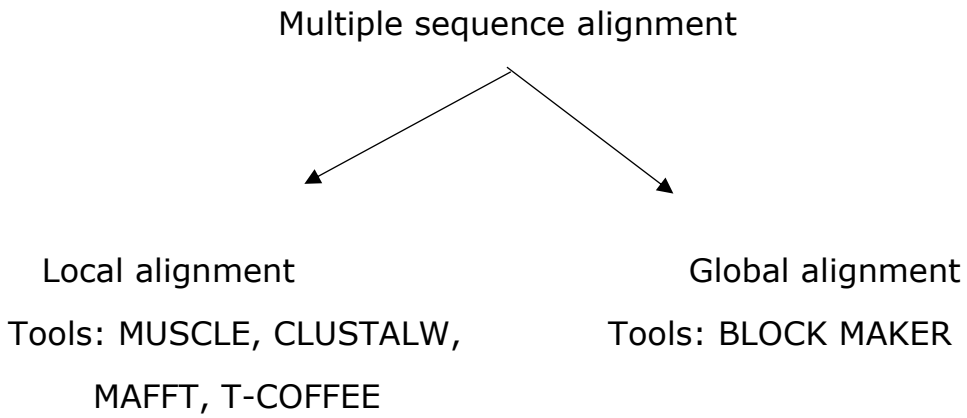
-> A multiple sequence alignment is basically an alignment of more than two sequences.

-> A pair wise alignment tells you about the similarities of two sequences but a multiple Sequence tells you about the similarity among the multiple sequences.

-> Local alignment is to identify small highly similar regions of two proteins or two genes With minimum gaps.

-> Global alignment aims end to end alignment of two sequences, reflecting overall Sequence variations. Below is the brief description of them.





-> To extend the dynamic programming formula for multiple sequence alignment to three dimensions, we will introduce a new variable and a new dimension to the dynamic programming matrix.

-> Suppose we have three sequences A, B, and C of lengths p, q, and r, respectively. We will define a 3D matrix S of size (p +1) x (q +1) x (r +1),

where S [i][j][k] represents the score of the optimal alignment of the i first characters of sequence A, the j first characters of sequence B, and the k first characters of sequence C.

The dynamic programming formula for three dimensions is as follows:

S[i][j][k] = max(S[i-1][j-1][k-1] + Z(A[i], B[j], C[k]), # match/mismatch

S[i-1][j][k] + Z(A[i], GAP, GAP), # gap in sequence B and C

S[i][j-1][k] + Z(GAP, B[j], GAP), # gap in sequence A and C

S[i][j][k-1] + Z(GAP, GAP, C[k])) # gap in sequence A and B

where Z(A[i], B[j], C[k]) is the score of aligning the characters A[i], B[j], and C[k].

If the characters are the same, we assign a positive score to the match.

If they are different, we assign a negative score to the mismatch.

We also assign a negative score to the gaps.

The runtime of the dynamic programming algorithm for three-dimensional multiple sequence alignment is O(pqr), which is cubic in the length of the sequences.

The number of cases we need to compare is the number of paths from the vertex (0,0,0) to the vertex (p,q,r) in a cubic grid of size (p+1) x (q+1) x (r+1).

Each path corresponds to a possible alignment of the three sequences, and there are (p+q+r) choose ' r ' paths.

This is because we need to choose r steps out of a total of (p+q+r) steps, and the order in which we choose them does not matter.

Therefore, the number of cases we need to compare is (p+q+r) choose r.

THANKING YOU

YOURS SINCERALY.