# Exemplar Longest Common Subsequence

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Abstract. In the paper we investigate the computational and approximation complexity of the Exemplar Longest Common Subsequence of a set of sequences (ELCS problem), a generalization of the Longest Common Subsequence problem, where the input sequences are over the union of two disjoint sets of symbols, a set of mandatory symbols and a set of optional symbols. We show that different versions of the problem are APX-hard even for instances with two sequences. Moreover, we show that the related problem of determining the existence of a feasible solution of the Exemplar Longest Common Subsequence of two sequences is NP-hard. On the positive side, efficient algorithms for the ELCS problem over instances of two sequences where each mandatory symbols can appear totally at most three times or the number of mandatory symbols is bounded by a constant are given.

#### 1 Introduction

Algorithmic studies in comparative genomics have produced powerful tools for the analysis of genomic data which has been successfully applied in several contexts, from gene functional annotation to phylogenomics and whole genome comparison. A main goal in this research field is to explain differences in gene order in two (or more) genomes in terms of a limited number of rearrangement operations.

When there are no duplicates in the considered genomes, the computation of the similarity measure is usually polynomial-time solvable, e.g., number of breakpoints, reversal distance for signed genomes, number of conserved intervals, number of common intervals, maximum adjacency disruption, summed adjacency disruption. However, aside a few exceptions, several copies of the same gene or several highly homologous genes are usually scattered across the genome, and hence it is major problem to handle those duplicates when computing the similarity between two genomes. One approach to overcoming this difficulty is based on the concept of exemplar: for each genome, an exemplar sequence is constructed by deleting all but one occurrence of each gene family. Another approach is based on matching: in this two-step procedure, the two genomes are

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first made balanced (the number of occurrences of each gene from the same family must be the same in both genomes) by removing a minimum number of genes and next a one-to-one correspondence (among genes of each family) between genes of the genomes is computed.

Unfortunately, in the presence of duplicates, most similarity measures turn out to be **NP**-hard to compute for both the exemplar and the matching models, so that we generally have to rely on approximation algorithms or heuristic approaches. We discuss here one such general purpose heuristic approach (the EXEMPLAR LCS problem) which is basically a constrained string alignment problem. The basic idea of the general framework we propose here is based on the observation that, for most similarity measures and for both the exemplar and the matching models, specific common subsequences may correspond to highly conserved sets of genes. This suggests the following greedy heuristic algorithm: find a common subsequence of significant length – but compact enough – between the two genomes, replace in the two genomes the substring that contains the common subsequence (the substring that starts at the first character of the common subsequence and ends at the last character of the common subsequence) by a new letter and continue in a similar way.

At each iteration of this simple heuristic algorithm, one however has to be cautious in how to choose the common subsequence, as bad choices may have a disastrous impact for the rest of the algorithm. Let us take the exemplar model as a very simple explanatory example, and suppose that we are searching for a common subsequence between two precise substrings of the two genomes. For one, if one gene family has occurrences elsewhere in the two genomes, then taking or not one occurrence of this particular gene family in the common subsequence is thus not based on necessity but on the length of the obtained solution. For another, if there do not exist any other occurrences of one gene family except one in the two considered substrings, definitively one has to take this occurrence in the common subsequence (observe that in this case the obtained common subsequence may not be the longest one). This simple example suggests to consider a LCS-like problem that deals with two types of letters (mandatory and optional symbols) to allow greater flexibility in the searching process.

In this paper we will formally define such framework with a simple combinatorial problem that generalizes the well-known LCS problem and we will study its computational and approximation complexity. We show that different versions of the problem are **APX**-hard even for instances with two sequences and that even determining if a feasible solution exists or not is **NP**-hard. On a positive side the hardness of the problem can be limited in some cases, in fact we show that it is possible to determine efficiently a feasible solution, provided that each symbol appears at most three times totally in the input sequence. Finally we give a polynomial-time algorithm in case the number of mandatory symbols is a constant.

### 2 The Problems

The LONGEST COMMON SUBSEQUENCE problem (shortly LCS) is a well-known problem in Computational Biology. Let  $s = s[1], s[2], \ldots, s[m]$  and  $t = t[1], t[2], \ldots, t[l]$  be two sequences, s is a subsequence of t if for some  $j_1 < j_2 < \ldots < j_m$   $s[h] = t[j_h]$ . Let  $s_1, s_2$  be two sequences, a longest common subsequence of  $s_1$  and  $s_2$  is a sequence s of maximum length, such that s is a subsequence of both  $s_1$  and  $s_2$ . Let s be a set of sequences, then a longest common subsequence of s is a longest possible sequence s that is a subsequence of each sequence in s.

Table 1. Versions of EXEMPLAR LCS

Problem name	Occurrences	Occurrences
	mandatory	optional
	symbols	symbols
$ELCS(1, \leq 1)$	exactly 1	at most 1
ELCS(1)	exactly 1	unrestricted
$ELCS(\geq 1, \leq 1)$	at least 1	at most 1
$ELCS(\geq 1)$	at least 1	unrestricted

Given a set of sequences S, the LCS problem asks for a longest common subsequences of S. The complexity of LCS problem has been deeply studied in the past. In [7] it is shown that the problem is **NP**-hard even for sequences over an alphabet of size 2. However, when the instance of the prob-

lem consists of a fixed number of sequences, the LCS can be solved in polynomial time via dynamic programming algorithms [5, 4]. The input of the EXEMPLAR LCS problem (ELCS) consists of a set S of sequences over alphabet  $A_o \cup A_m$ ,  $A_o \cap A_m = \emptyset$ , where  $A_o$  is the set of optional symbols and  $A_m$  is the set of mandatory symbols. The output of the problem is a longest common subsequence of all sequences in S and containing all mandatory symbols.

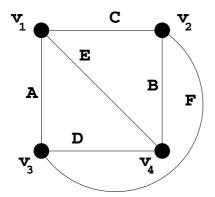
Given an instance S of ELCS, by exemplar common subsequence we mean a feasible solution of ELCS over S. It is possible to define different versions of the problem, according to the number of occurrences of each symbol in the solution, as represented in Table 1. In this paper we will deal with such different versions of ELCS. First notice that ELCS(1) and ELCS( $\geq 1$ ) are generalizations of the LCS problem, where no mandatory symbols are present. Therefore all the hardness results for LCS apply to ELCS(1) and ELCS( $\geq 1$ ). Moreover, we will show that the above problems are hard also on instances of only two sequences (while the LCS problem can be solved in polynomial time for any fixed number of sequences). When dealing with the restriction of ELCS containing only a fixed number of sequences, we will denote such restriction prefixing the problem name with the number of sequences, e.g. 2-ELCS(1,  $\leq 1$ ) is the restriction of ELCS(1,  $\leq 1$ ) to instances of two sequences.

### 3 The Results

**Theorem 1.** The 2-ELCS $(1, \leq 1)$  problem is **APX**-hard even when each symbol appears at most twice in each input sequence.

*Proof.* We prove the theorem describing an L-reduction from MAX INDEPENDENT SET on Cubic Graph to 2-ELCS $(1, \leq 1)$ , since the latter problem is

known to be **APX**-hard[1]. Let G = (V, E) be a cubic graph. Then for each vertex  $v_i$  there are three edges  $e_1(v_i)$ ,  $e_2(v_i)$ ,  $e_3(v_i)$  incident on it. In the reduction each vertex  $v_i$  is associated with a symbol  $v_i$  of  $A_o$  and a symbol  $x_i$ in  $A_m$ . Each edge is associated with a distinct symbol of  $A_m$ . Define a block associated with a vertex  $v_i$ , as a string consisting of a vertex symbol  $v_i$ , the symbols associated with edges incident to  $v_i$  in G and the symbols  $x_i$ . There are two possible blocks associated with  $v_i$ , one contained in  $s_1$  and defined as  $b_1(v_i) = v_i e_1(v_i) e_2(v_i) e_3(v_i) x_i$ , the second contained in  $s_2$  and defined as  $b_2(v_i) = e_1(v_i)e_2(v_i)e_3(v_i)v_ix_i$ . The instance of 2-ELCS $(1, \leq 1)$  consists of the following two sequences:  $s_1 = b_1(v_1)b_1(v_2)\cdots b_1(v_n), s_2 = b_2(v_1)b_2(v_2)\cdots b_2(v_n).$ Observe that since each symbol  $x_i$  is mandatory and it occurs only in blocks  $b_1(v_i), b_2(v_i)$  of  $s_1, s_2$  respectively, any symbol  $x_i$  in a feasible solution of 2-ELCS $(1, \leq 1)$  over  $s_1$  and  $s_2$  must be taken from  $b_1(v_i)$  and  $b_2(v_i)$ . It follows that if  $v_i$  is in an exemplar common subsequence, then the exemplar common subsequence does not contain any symbol of  $e_1(v_i)e_2(v_i)e_3(v_i)$  of  $b_1(v_i)$ and  $b_2(v_i)$ . Let s be a feasible solution of 2-ELCS $(1, \leq 1)$  over  $s_1, s_2$ , then s consists of  $f_1x_1 \dots f_ix_i \dots f_nx_n$ , where each  $f_i$  is either  $v_i$  or a subsequence of  $e_1(v_i)e_2(v_i)e_3(v_i)$ . Observe that each edge symbol is mandatory, which means that it must appear exactly once in a common subsequence. Moreover, an edge symbol encoding edge  $(v_i, v_j)$  appears in blocks  $b_1(v_i)$  and  $b_1(v_j)$  of  $s_1$  and in blocks  $b_2(v_i)$  and  $b_2(v_j)$  of  $s_2$ . Thus a common subsequence takes such edge symbol either from  $b_1(v_i)$  and  $b_2(v_i)$  or from  $b_1(v_i)$  and  $b_2(v_i)$ .



 $s_1 = v_1 CAEx_1 v_2 CFBx 2v_3 AFDx_3 v_4 EBDx_4$  $s_2 = CAEv_1 x_1 CFBv_2 x_2 AFDv_3 x_3 EBDv_4 x_4$ 

**Fig. 1.** Reducing the graph  $K_4$ 

Let I be the set of vertices appearing in s, we will show that I is an independent set of G. Assume that symbols  $v_i, v_j \in I$ . Then  $(v_i, v_j)$  is not an edge of G, otherwise s in  $f_i$  and  $f_i$  contains symbols  $v_i$  and  $v_i$  respectively. It follows that the edge symbol associated with  $(v_i, v_j)$ , that can appear only in  $f_i$  and  $f_i$ , is not contained in s. Since each edge symbol is mandatory, it must appear in any feasible solution of 2-ELCS $(1, \leq 1)$ , which is a

contradiction. Observe that the length of a feasible solution of 2-ELCS $(1, \leq 1)$  over  $s_1$ ,  $s_2$  is |V| + |E| + |I|, where I is an independent set of G. On the other side, let I be an independent set of G, it is easy to compute a feasible solution of 2-ELCS $(1, \leq 1)$  over  $s_1$ ,  $s_2$  of size |V| + |E| + |I|, retaining in the exemplar common subsequence only the symbols associated with vertices in I.

A similar proof can be given also for 2-ELCS( $\geq 1, \leq 1$ ).

**Theorem 2.** The 2-ELCS( $\geq 1, \leq 1$ ) problem is **APX**-hard even when each symbol appears at most twice in each input sequence.

*Proof.* The reduction is similar to the previous one, but for each vertex  $v_i$  of the graph, we have four symbols  $v_i^a v_i^b v_i^c v_i^d$  and the blocks  $b_1(v_i)$  and  $b_2(v_i)$  associated with  $v_i$  in sequences  $s_1$  and  $s_2$  respectively are defined as follows:  $b_1(v_i) = v_i^a v_i^b v_i^c v_i^d e_1(v_i) e_2(v_i) e_3(v_i) x_i$ ;  $b_2(v_i) = e_1(v_i) e_2(v_i) e_3(v_i) v_i^a v_i^b v_i^c v_i^d x_i$ .

Again the symbols  $x_i$  are mandatory. Since each  $x_i$  appears in blocks  $b_1(v_i)$  and  $b_2(v_i)$  of  $s_1$  and  $s_2$  respectively, it follows that any symbol  $x_i$  in an exemplar common subsequence must be taken from the blocks of  $s_1$ ,  $s_2$  associated with  $v_i$ , that is  $b_1(v_i)$  and  $b_2(v_i)$ . Since each mandatory edge symbols appears twice in each input sequence, it must appear once or twice in a common subsequence.

Clearly if sequence  $v_i^a v_i^b v_i^c v_i^d$  is in a feasible solution of 2-ELCS( $\geq 1, \leq 1$ ) over  $s_1, s_2$ , then this solution does not contain occurrence of symbols of sequence  $e_1(v_1)e_2(v_1)e_3(v_1)$  in  $b_1(v_i)$  and  $b_2(v_i)$ . This means that a feasible solution s of 2-ELCS( $\geq 1, \leq 1$ ) over  $s_1, s_2$  consists of  $g_1x_1 \dots g_ix_i \dots g_nx_n$ , where each  $g_i$  is either a subsequence of  $v_i^a v_i^b v_i^c v_i^d$  or a subsequence of  $e_1(v_i)e_2(v_i)e_3(v_i)$ . Observe that each edge symbol is mandatory, which means that it must appear exactly once in an exemplar common subsequence. Thus an exemplar common subsequence takes each edge symbol from one of the two blocks where it appears.

Let I be an independent set of G, then  $s = g_1x_1 \dots g_ix_i \dots g_nx_n$ , where each  $g_i = v_i^a v_i^b v_i^c v_i^d$  if  $v_i \in I$  and  $g_i = e_1(v_i)e_2(v_i)e_3(v_i)$  otherwise. It is immediate to note that s is a common subsequence of  $s_1$  and  $s_2$  of length |V| + 3|V| + |I| and that all mandatory symbols encoding an edge are included in s.

Assume now that there exists a feasible solution s of 2-ELCS( $\geq 1, \leq 1$ ) over  $s_1, s_2$  with length |V|+3|V|+|I|. We can assume that, for each block in  $s_1, s_2$ , either  $v_i^a v_i^b v_i^c v_i^d$  or  $e_1(v_i)e_2(v_i)e_3(v_i)$  appears as a substring of s. Let Y be the set of blocks for which  $v_i^a v_i^b v_i^c v_i^d$  is part of s. Hence the vertices corresponding to Y are an independent set of s. By a trivial counting argument, it is easy to show that for |I| blocks s includes  $v_i^a v_i^b v_i^c v_i^d$ . We claim that such blocks encode an independent set. W.l.o.g. assume that  $v_i^a v_i^b v_i^c v_i^d$  and  $v_i^a v_i^b v_i^c v_i^d$  are included in s, then there is no edge  $(v_1, v_2)$  in s, otherwise the mandatory symbol encoding such edge would not be in s.

A related problem is that, given an instance of 2-ELCS, of determining if a feasible solution exists. In what follows we will consider a general version of the 2-ELCS problem. Notice that both reductions described above hold for instances that are known to admit a feasible solution, therefore they are not sufficient for dealing with the problem. Observe that we can assume that both input sequences consist only of mandatory symbols, since only mandatory symbols are relevant for the existence of a solution.

**Theorem 3.** The problem of determining if a feasible solution exists for an instance of 2-ELCS where each mandatory symbol appears totally at most three times in the input sequences, can be solved in polynomial time.

*Proof.* We prove the theorem reducing an instance of 2-ELCS where each mandatory symbol appears totally at most three times in the input sequences to an instance of 2SAT. Notice that 2SAT can be solved in polynomial time [2].

For each symbol s, let  $occ_1(s)$  (respectively  $occ_2(s)$ ) be the set of positions of the input sequence  $s_1$  (resp.  $s_2$ ) where the s appears. Clearly both  $occ_1(s)$  and  $occ_2(s)$  are not empty and  $|occ_1(s)| + |occ_2(s)| \le 3$ . For each symbol s there are at most two pairs in  $occ_1(s) \times occ_2(s)$ , for otherwise  $|occ_1(s)| + |occ_2(s)| > 3$ , let us associate with each of such pairs a variable  $x_{s,i}$ , where  $i \in \{1,2\}$  if there are two pairs in  $occ_1(s) \times occ_2(s)$  and i = 1 if there is only one pair in  $occ_1(s) \times occ_2(s)$ .

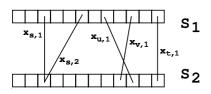


Fig. 2. Reducing 2-ELCS to 2SAT

Graphically the possible variables are represented in Fig. 2 with a line connecting two identical symbols belonging to different sequences. The case  $|occ_1(s)| + |occ_2(s)| = 3$  is represented by the two leftmost lines and the variables  $x_{s,1}, x_{s,2}$ , while the case  $|occ_1(s)| + |occ_2(s)| = 2$  is represented by the rightmost line and the variable  $x_{t,1}$ . Each truth assignment to

the variables can be viewed as picking the lines corresponding to true variables. Let C be the set of clauses of the instance of 2SAT that we are constructing. For each pair  $x_{s,1}$ ,  $x_{s,2}$  of variables, the clauses  $\neg x_{s,1} \lor \neg x_{s,2}$  and  $x_{s,1} \lor x_{s,2}$ are added to C. Moreover, for each symbol s such that there is only one pair in  $occ_1(s) \times occ_2(s)$ , add the clause  $x_{s,1}$  to C (this corresponds to forcing the variable  $x_{s,1}$  to be true). The fact that all these clauses are satisfied in any feasible solution of 2SAT, corresponds to pick exactly one of the lines associated with each symbol. Two lines (or two variables) are called *crossing* if they cross in the drawing built as in Fig. 2. More formally, notice that each variable  $x_{s,i}$  is associated with an occurrence of s in  $s_1$  (denoted as  $s_1(s,i)$ ) and one occurrence of s in  $s_2$  (denoted as  $s_2(s,i)$ ). A pair  $x_{s,i}, x_{t,j}$  of variables is crossing if in  $s_1$  the symbol  $s_1(s,i)$  precedes  $s_1(t,j)$  and in  $s_2$  the symbol  $s_2(s,i)$  does not precede  $s_2(t,j)$  or, symmetrically, if in  $s_1$  the symbol  $s_1(s,i)$  does not precede  $s_1(t,j)$ and in  $s_2$  the symbol  $s_2(s,i)$  precedes  $s_2(t,j)$ . For each pair  $x_{s,i}, x_{t,j}$  of crossing variables, the clause  $\neg x_{s,i} \vee \neg x_{t,j}$  is added to C. We can prove that the original instance of 2-ELCS has a feasible solution if and only if the instance of 2SAT is satisfiable, that is there is a truth assignment for all variables such that all clauses in C are evaluated true. Assume that there is a feasible solution z of the instance of 2-ELCS then, for each symbol s, we pick the lines connecting the symbols retained in z. By definition of common subsequence there cannot be two crossing lines, and exactly one of the lines associated with each symbol must be picked as  $|occ_1(s)| + |occ_2(s)| \leq 3$ , therefore we have constructed a feasible solution of 2SAT. Conversely given a truth assignment for all variables that satisfies all clauses in C, it is immediate to note that there are not two crossing lines, and that there is exactly one line for each symbol, therefore it is immediate to construct a feasible solution of 2-ELCS that contains all symbols.

Notice that the above result holds for all the restrictions of 2-ELCS considered here, as no symbol appears twice in both input sequences, therefore it can appear at most once in any solution. We will show in the following theorem that slightly relaxing this constraint makes the problem **NP**-hard.

**Theorem 4.** The problem of determining if a feasible solution exists for an instance of 2-ELCS where each mandatory symbol appears at most three times in each input sequence, is **NP**-hard.

Proof. We will prove the theorem reducing 3SAT to 2-ELCS, with a reduction very similar to the one shown before. Let  $C = \{C_1, \ldots, C_k\}$  be a set of clauses, each one consisting of at most three (possibly negated) literals. We construct an instance of 2-ELCS associating a block with each variable. The block of  $s_1$  associated with variable  $x_i$  is defined as the symbol  $x_i$ , followed by the sequence of clauses containing  $\neg x_i$ , where in each sequence the clauses are ordered according to the index in  $\{C_1, \ldots, C_k\}$ . In  $s_2$  the block associated with variable  $x_i$  is defined as the symbol  $x_i$ , followed by the sequence of clauses containing  $\neg x_i$ , followed by the sequence of clauses containing  $x_i$  (again the clauses are ordered according to the index in  $\{C_1, \ldots, C_k\}$ ). Both sequences  $s_1$  and  $s_2$  consist of the sequence of all blocks associated with the variables of the original instance of 3SAT. All symbols are mandatory, also notice that each symbol appear at most three times in each sequence as each clause contains at most three literals.

Each symbol  $x_i$  appears exactly once in each sequence, hence there is no ambiguity on which occurrence is retained in any exemplar common subsequence. Consequently each symbol retained must correspond to occurrences taken from the same block. Inside the block associated with  $x_i$ , retaining the clauses where  $x_i$  appears as a positive literal is mutually exclusive with retaining the clauses where  $x_i$  appears as a negative literal, by definition of exemplar common subsequence. The first case corresponds to setting  $x_i$  to true, while the second case corresponds to setting  $x_i$  to false. In both case the clauses retained are satisfied by the assignment of variables  $x_i$ . It is immediate to note that any feasible solution must contain all clauses, therefore we have computed a truth assignment of the variables that satisfies all clauses in C, completing the proof.

The above results have a definitive consequence on the approximability of the 2-ELCS problem where each mandatory symbol appears at most three times in both input sequences, as they rule out any possible polynomial-time approximation algorithm. Since the problem can be extended to instances consisting of a set of sequences, it is interesting to know if the above results can be made stronger. In fact, the well-known inapproximability results in [6] for the LCS problem, immediately apply also to the ELCS( $\geq 1$ ) problem, since ELCS( $\geq 1$ ) is more general than LCS. A closer inspection of their proofs shows that their results also apply to all versions of ELCS, as the optimal solutions in their reductions contain at most one occurrence of each symbol, excluding any  $O(n^{1-\epsilon})$  ratio polynomial-time approximation algorithm unless  $\mathbf{ZPP}{=}\mathbf{NP}$ , even if no mandatory symbol is allowed and all symbols appear at most twice in each sequence.

## 4 Restricting the Problem

In this section we consider the restriction of 2-ELCS(1) where the number of mandatory symbols is at most a constant. We describe a polynomial time algorithm for this restriction based on two phases: the first step consists of guessing the exact ordering of all mandatory symbols in the optimal solution, the second step basically fills in the gaps between each pair of mandatory symbol. Since each mandatory symbol appears exactly once in a feasible solution, the correct ordering of the mandatory symbol is a permutation of  $A_m$ , which can be computed in constant time, since  $|A_m|$  is a constant.

Let s be a permutation of mandatory symbol, the second phase consists of computing a longest common subsequence  $s^*$  of  $\{s_1, s_2\}$  such that s is a subsequence of  $s^*$ . Let us denote by s[i] the i-th character of the sequence s and by  $s[i \dots j]$  the substring of s starting with s[i] and ending with s[j]. The recurrence equation for  $\mathrm{EL}[i,j,k]$ , that is the length of an optimal solution over  $s_1[1 \dots i]$ ,  $s_2[1 \dots j]$  that is a supersequence of the sequence  $s[1] \dots s[k]$  is:

$$\mathrm{EL}[i,j,k] = \max \begin{cases} \mathrm{EL}[i-1,j-1,k] + 1 \text{ if } s_1[i] = s_2[j], \ s_1[i] \in A_o \\ \mathrm{EL}[i-1,j-1,k-1] + 1 \text{ if } s_1[i] = s_2[j] = s[k] \\ \mathrm{EL}[i-1,j,k], \mathrm{EL}[i,j-1,k] \text{ if } s_1[i] = s_2[j] \neq s[k], \ s_1[i] \in A_m \\ \mathrm{EL}[i-1,j,k], \mathrm{EL}[i,j-1,k] \text{ if } s_1[i] \neq s_2[j] \end{cases}$$

The boundary conditions are  $\mathrm{EL}[0,j,0]=0$  and  $\mathrm{EL}[i,0,0]=0$  for  $0\leq i\leq |s_1|$  and  $0\leq j\leq |s_2|$ . The value of the optimal solution can be read in  $\mathrm{EL}[|s_1|,|s_2|,|s|]$ . Once the matrix EL has been completely filled in the actual optimal subsequence can be constructed with standard backtracking techniques [3]. The recurrence equation described above can be easily modified for the 2-ELCS( $\geq 1$ ), by removing the requirement  $s_1[i]\in A_o$  in the first condition of the equation.

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