Speeding Hirschberg Algorithm for Sequence Alignment

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**Abstract.** The use of Hirschberg algorithm reduces the spatial cost of recovering the Longest Common Subsequence to linear space. The same technique can be applied to similar problems like Sequence Alignment. However, the price to pay is a duplication of temporal cost. We present here a technique to reduce this time overhead to a negligible amount.

**Keywords:** Dynamic Programming, Hirschberg’s Algorithm, Sequence Alignment

1. Introduction

The answer to many Dynamic Programming problems includes not only the score of the optimal solution but also the sequence of decisions that led to it. For example, given two sequences, it is usually more interesting to find the best alignment between them than the score of that alignment. This poses a problem since the memory costs associated to the recovery of the alignment using a direct Dynamic Programming approach are much higher than the costs of finding the score of that alignment. Concretely, when aligning two sequences of length \( m \) and \( n \), the score of the alignment

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can be obtained in $O(mn)$ steps. Storing the trellis (or at least backpointers) for recovering the actual alignment implies using $O(mn)$ memory space.

To remedy this, it is possible to use a technique due to Hirschberg [Hir75] and popularized for biological alignments by Myers and Miller [MM88] that only requires $O(n + m)$ memory at the cost of duplicating the execution time. This technique was developed for solving the Longest Common Subsequence problem and for that particular problem it can be accelerated using bit vector algorithms since the difference in the contents of neighbor cells in the trellis is 0 or 1 [CIP03]. This is however not applicable to other problems like Sequence Alignment.

Here we present a novel approach that reduces the time overhead to a small fraction of the original with a memory cost that is still $O(n + m)$. Hirschberg’s method combines a forward pass of the first half of the trellis with a backward pass of the second to find one intermediate point and recurses to find the optimal path. This reduces memory cost with a time overhead factor of 2. Our proposal is to use $k$ intermediate points and find them in a forward pass. This leads to a time overhead factor of $\frac{k}{k-1}$.

2. Sequence Alignment

The problem we will tackle is Sequence alignment. Let there be given two sequences $a = a_1 \ldots a_m$ and $b = b_1 \ldots b_n$. Assume all symbols of those sequences belong to an alphabet $\mathcal{A}$. Let $\bot$ be a new symbol not belonging to $\mathcal{A}$ that represents a gap. An alignment of $a$ and $b$ is a pair of sequences $(a', b')$ such that both $a'$ and $b'$ have symbols from $\mathcal{A} \cup \{\bot\}$, both have the same length, and such that the sequences obtained by taking out the gaps from $a'$ and $b'$ are $a$ and $b$, respectively. For instance, given the sequences of DNA bases, $a = ACCACTA$ and $b = ACGATC$, the pair $(ACCACTA, ACGA\bot TC)$ is an alignment. It is possible to score an alignment by defining a similarity measure between symbols and then adding the similarities of the corresponding symbols in the two sequences of the alignment. For instance, let us assign a score of $+2$ to a pair of equal symbols and $-1$ to a pair of different symbols. The previous alignment has then a score of 5 as seen below:

\[
\begin{array}{cccccc}
A & C & C & A & C & T & A \\
A & C & G & A & \bot & T & C \\
+2 & +2 & -1 & +2 & -1 & +2 & -1 \\
\end{array}
\]

Obviously, there are many other possible alignments, for example:

\[
\begin{array}{cccccc}
A & C & C & A & C & T & A \\
A & C & G & A & T & \bot & C \\
+2 & +2 & -1 & +2 & -1 & -1 & -1 \\
\end{array}
\]

which has a score of 2. We are interested in finding one alignment with the maximum score (in general, there could be more than one, in that case, any will do). In our example, the first alignment presented happens to be optimal.

The usual approach to finding the best alignment is to use Dynamic Programming, this technique can be found in any book on algorithms like [CLRS09]. In our case, define $A(i, j)$ to be the score of
the best alignment between the prefixes \( a_1 \ldots a_i \) and \( b_1 \ldots b_j \) (when \( i \) or \( j \) is zero, we assume that the corresponding prefixes are empty). It is easy to see that:

\[
A(i, j) = \begin{cases} 
0, & \text{if } i = 0 \text{ and } j = 0, \\
A(i-1, 0) + s(a_i, \perp), & \text{if } i \neq 0 \text{ and } j = 0, \\
A(0, j-1) + s(\perp, b_j), & \text{if } i = 0 \text{ and } j \neq 0, \\
\max\{A(i-1, j) + s(a_i, \perp), A(i, j-1) + s(\perp, b_j), A(i-1, j-1) + s(a_i, b_j)\}, & \text{otherwise.}
\end{cases}
\] (1)

Where \( s \) is the similarity between two symbols\(^1\). Then, the score of the best alignment is just \( A(m, n) \). A direct recursive implementation of \( A \) will be prohibitively costly, but using memoization it can be computed in \( O(mn) \) time. Just consider \( A \) as a matrix (usually called trellis) and fill it in. Also, create a matrix \( BP \) of back pointers that stores for each pair \((i, j)\) the argument that achieved the maximum in Equation (1).

A simple iterative approach suffices:

\begin{algorithm}
\caption{Iterative version of the alignment algorithm}
\begin{algorithmic}
\State \textbf{Input:} Two strings: \( a \) and \( b \) of length \( m \) and \( n \)
\State \textbf{Output:} The optimal alignment of \( a \) and \( b \)
\State \( A \leftarrow \text{matrix}(m, n) \);
\State \( BP \leftarrow \text{matrix}(m, n) \);
\State \( A[0, 0] \leftarrow 0 \);
\State \( BP[0, 0] \leftarrow (-1, -1) \);
\For {\( i \leftarrow 1 \) to \( m \)}
\State \( A[i, 0] \leftarrow A[i-1, 0] + s(a_i, \perp) \);
\State \( BP[i, 0] \leftarrow (i-1, 0) \);
\EndFor
\For {\( j \leftarrow 1 \) to \( n \)}
\State \( A[0, j] \leftarrow A[0, j-1] + s(\perp, b_j) \);
\For {\( i \leftarrow 1 \) to \( m \)}
\State \( A[i, j] \leftarrow \text{maximize}\{(i-1, j), (i, j-1), (i-1, j-1)\} \);
\State \( BP[i, j] \leftarrow \text{choose}\{(i-1, j), (i, j-1), (i-1, j-1)\} \);
\EndFor
\EndFor
\State \textbf{return} \( \text{recoverAlignment}(a, b, BP) \);
\end{algorithmic}
\end{algorithm}

Here, we use \texttt{maximize} and \texttt{choose} to represent the maximization process and the election of the

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\(^1\)This equation does not allow the alignment of two gaps, which makes little sense in this context. Through the rest of the paper, we will assume that \( s(\perp, \perp) = -\infty \).
predecessor. In this case, maximize is

\[
\text{maximize}\{(i - 1, j), (i, j - 1), (i - 1, j - 1)\} = \max\{A[i - 1, j] + s(a_i, \bot), \\
A[i, j - 1] + s(\bot, b_j), \\
A[i - 1, j - 1] + s(a_i, b_j)\}
\]

and choose returns the pair corresponding to the maximum. Obviously, they are not implemented as separate functions and the corresponding values are computed simultaneously in actual code.

The function recoverAlignment recovers the alignment from the back pointers by simply following them until it finds \((-1, -1)\).

The execution of that algorithm in our example stores the following scores in \(A\):

|     | A | C | C | A | G | A | T | C |
|-----|---|---|---|---|---|---|---|---|
| -7  | -4| -1| -1| 2 | 5 | 5 |
| -6  | -3| 0 | 0 | 3 | 6 | 5 |
| -5  | -2| 1 | 1 | 4 | 4 | 6 |
| -4  | -1| 2 | 2 | 5 | 4 | 3 |
| -3  | 0 | 3 | 3 | 2 | 1 | 3 |
| -2  | 1 | 4 | 3 | 2 | 1 | 0 |
| -1  | 2 | 1 | 0 | -1 | -2 | -3 |
| 0   | -1| -2| -3| -4 | -5 | -6 |

The lines between the scores of the cells represent the back pointers. The darker path is the optimum and corresponds to the first alignment of the example.

All in all, the total spatial cost is \(O(mn)\), which for sequences of more than a few thousand elements is too high. A first step to reduce the cost is the observation that the internal loop (that of \(i\)) only uses scores from the previous column, so a simple trick suffices to eliminate the need to keep \(A\) \([CLRS09]\). Only two columns are kept (\(c\), which is the current column, and \(p\), the previous) and swapped as needed. Algorithm 2 returns the alignment score using only \(O(m)\) space.

Now maximize is slightly changed. Taking into account that \(j - 1\) corresponds to \(p\) and \(j\) to \(c\), we obtain:

\[
\text{maximize}\{(i - 1, j), (i, j - 1), (i - 1, j - 1)\} = \max\{c[i - 1] + s(a_i, \bot), \\
\quad \quad \quad p[i] + s(\bot, b_j), \\
\quad \quad \quad p[i - 1] + s(a_i, b_j)\}
\]

Unfortunately, it is not possible to do the same with the backpointers. The whole \(BP\) matrix is needed to recover the alignment. In the following section we will see how to use the proposal of Hirschberg to recover the alignment using linear memory at the cost of duplicating the time.
Algorithm 2: Reduced space version of the alignment algorithm

Input: Two strings: $a$ and $b$ of length $m$ and $n$
Output: The optimal alignment of $a$ and $b$

$c \leftarrow \text{vector}(m)$;
$p \leftarrow \text{vector}(m)$;
$c[0] \leftarrow 0$;
for $i \leftarrow 1$ to $m$ do
    $c[i] \leftarrow c[i-1] + s(a_i, \perp)$;
end
for $j \leftarrow 1$ to $n$ do
    $p, c \leftarrow c, p$;
    $c[0] \leftarrow p[0] + s(\perp, b_j)$;
    for $i \leftarrow 1$ to $m$ do
        $c[i] \leftarrow \text{maximize}\{(i-1,j),(i,j-1),(i-1,j-1)\}$;
    end
end
return $c[n]$;

3. Hirschberg’s method

Although Hirschberg presented his idea for the problem of finding a maximal common subsequence of two sequences \[Hir75\], it can be adapted for the case of the alignment.

The idea of the method is to find the point of the alignment path that passes through the middle column of the trellis. Let $\pi = \pi_1 \ldots \pi_l \ldots \pi_{|\pi|}$ be an optimal path in the trellis for the alignment of $a$ and $b$. Each $\pi_i$ is a pair $(i, j)$ that marks the alignment of the corresponding prefixes of both sequences. Now consider the prefix $\pi_1 \ldots \pi_l$. It is an optimal path for the prefixes $a_1 \ldots a_i$ and $b_1 \ldots b_j$ since otherwise there would be a path $\rho$ for those prefixes with better score and then the path $\rho \pi_{l+1} \ldots \pi_{|\pi|}$ would be better than $\pi$. A similar reasoning leads to the observation that $\pi_{l+1} \ldots \pi_{|\pi|}$ is an optimal path for $a_{i+1} \ldots a_n$ and $b_{j+1} \ldots b_m$. Now, let $\pi_c = (n/2, i)$ be a point of $\pi$ in column $n/2$ like in Figure 1 left.

The key observation is that the total score of the alignment can be computed in two steps:

- First, compute the $c$ column for the alignment of $a$ with the first half of $b$, i.e. $b_1 \ldots b_{n/2}$.

- Second, do the same for $a$ reversed ($a^R = a_m a_{m-1} \ldots a_1$) and the reversed second half of $b' = b_n b_{n-1} \ldots b_{n/2+1}$. This gives a second column, $c'$.

- Combine $c$ and $c'$ by adding the value of $c[i]$ to $c'[m-i+1]$. The maximum of those values is the score of the alignment.

In our example, the two alignments are:
Therefore, $c$, $c'$ and their combination are:

|     | -7 | -4 | -1 | -1 |
|-----|----|----|----|----|
| $-c$ | -6 | -3 | 0  | 0  |
| $-c'$| -5 | -2 | 1  | 1  |
| $-c$ | -4 | -1 | 2  | 2  |
| $-c'$| -3 | 0  | 3  | 3  |
| $-c$ | -2 | 1  | 4  | 3  |
| $-c'$| -1 | 2  | 1  | 0  |
| $-c$ | 0  | -1 | -2 | -3 |

With this, we have found two facts: that the best alignment has a score of 5 and, more importantly, that it aligns ACC with ACG and ACTA with ATC. So, to recover the rest of the alignment, it suffices to recursively apply the same procedure to the pairs (ACC, ACG) and (ACTA, ATC). Note that the spatial cost has been reduced to $O(m + n)$.

We can recover the alignment as shown in Algorithm 3.

Here, lastColumn simply computes the alignment score like in Algorithm 2 and returns the last column instead of only the value in its end. It is interesting to note that Hirschberg’s method disposes of the backpointers completely.

The other function, trivialAlignment deals with two simple cases: when $b$ is the empty string or has only one symbol. The alignment corresponding to the first is simply the string $a$ with $n$ gaps
Algorithm 3: Version of Hirschberg’s algorithm for sequence alignment

**Input:** Two strings: \( a \) and \( b \) of length \( m \) and \( n \)

**Output:** The optimal alignment of \( a \) and \( b \)

if \( n \leq 1 \) then
  return trivialAlignment\((a, b)\);
else
  \( c \leftarrow \text{lastColumn}(a, b_{1} \ldots b_{n/2}) \);
  \( c' \leftarrow \text{lastColumn}(a^{R}, b_{n} b_{n-1} \ldots b_{n/2+1}) \);
  \( i \leftarrow \text{argmax}_{i} \text{combine}(c, c')[i] ; \)
  // Recurse on the two halves
  \( (a_{l1}, b_{l1}) \leftarrow \text{Alignment}(a_{1} \ldots a_{i}, b_{1} \ldots b_{n/2}) \);
  \( (a_{l2}, b_{l2}) \leftarrow \text{Alignment}(a_{i+1} \ldots a_{n}, b_{n/2+1} \ldots b_{n}) \);
  return \((a_{l1} a_{l2}, b_{l1} b_{l2})\);
end

and for the second case there are two possibilities: either \( b_{1} \) is aligned to a gap or to one of the symbols of \( a \). This is reflected in Algorithm 4.

Algorithm 4: Algorithm TrivialAlignment

**Input:** Two strings: \( a \) and \( b \) of length \( m \) and \( n \) with \( n \leq 1 \)

**Output:** The optimal alignment of \( a \) and \( b \)

if \( n = 0 \) then
  return \((a, \bot^{m})\);
else // \( n = 1 \)
  if \( \text{max}_{i} (s(a_{i}, b_{1}) - s(a_{i}, \bot)) < s(\bot, b_{1}) \) then
    return \((\bot a, b \bot^{m})\);
  else
    \( i \leftarrow \text{argmax}_{i} (s(a_{i}, b_{1}) - s(a_{i}, \bot)) \);
    return \((a, \bot^{i-1} b \bot^{n-i})\);
end

To find the temporal cost, first note that it is dominated by the cost of the calls to \text{lastColumn} which is linear in \( mn \), so it can be approximated as \( lmn \). Similarly, the call to \text{trivialAlignment} has a cost linear in \( m \), and we approximate it as \( l'm \). Note also that the recursive calls only touch the shadowed regions of Figure 1 and that the total area of these regions is \( \frac{mn}{2} \), no matter the value of \( i \).
Therefore, we arrive to the following recurrence:

\[
C(n, m) = \begin{cases} 
  l'm, & \text{if } n = 1, \\
  lmn + C(n/2, m), & \text{if } n > 1.
\end{cases}
\]  

(2)

This can be easily solved assuming \(n\) to be a power of two:

\[
C(n, m) = lmn + C(n/2, m) = lmn + \frac{lnm}{2} + C(n/2^2, m) \\
= \cdots = l'm + \sum_{i=0}^{\log_2 n} \frac{lnm}{2^i} \approx 2lnm.
\]

Therefore, the cost of having linear space is the duplication of the execution time.

4. The k-col method

Now, we will show how we can reduce the overhead of path recovery so that the total time will be similar to that of using the full trellis of backpointers but without the memory overhead. Let’s return to Figure 1. Remember that the key issue is to find the position of \(\pi_c\). We want to do that in a forward pass of the algorithm. We need a backpointer from the top right position of the trellis indicating the row of \(\pi_c\), since we already know the column \((n/2)\). With this backpointer it will be possible to perform the recursive call. We will also keep a backpointer from \(\pi_c\) to the corner for its recursive call. Although this backpointer will always be 0, we keep it to ease the formulation of the full algorithm. The diagram in the left of Figure 1 represents those pointers.

Let us consider how can we find \(\pi_c\). First, note that this is the point in which the best path from \((m, n)\) to \((0, 0)\) cuts the column at \(\frac{n}{2}\). Define \(bp_j(i)\) as the row in which the best path from \((i, j)\) to \((0, 0)\) cuts column \(\frac{n}{2}\). Clearly, the value of \(bp_{\frac{n}{2}}(i) = i\). And for a \(j\) greater than \(\frac{n}{2}\) the value of \(bp_{j+1}(i)\) is equal to the value of \(bp_j(i)\) where \((i', j')\) is the predecessor of \((i, j)\). Therefore a forward version of Hirschberg’s algorithm can be implemented by initializing a column vector in column \(\frac{n}{2}\) and updating it. As mentioned above, to keep the algorithm uniform, a column will be also initialized to zeros in the first position.

With this, we arrive to Algorithm 5. In it, the variable \(bpc\) keeps the backpointers of the current column and \(bpp\) those of the previous column. The function \texttt{maximize} has the same form as in Algorithm 2. And assuming \((i', j')\) is the predecessor of \((i, j)\) in the optimal path, the value of \texttt{choose} is:

\[
\texttt{choose}\{(i-1,j), (i,j-1), (i-1,j-1)\} = \begin{cases} 
  bpc[i-1], & \text{if } (i-1,j) = (i', j'), \\
  bpp[i], & \text{if } (i, j-1) = (i', j'), \\
  bpp[i-1], & \text{if } (i-1, j-1) = (i', j').
\end{cases}
\]

Algorithm 5 does not give any reduction of costs over Hirschberg’s method but it opens the possibility of storing more intermediate columns, like in Figure 2.
Algorithm 5: Forward version of Hirschberg algorithm

**Input:** Two strings: \(a\) and \(b\) of length \(m\) and \(n\)

**Output:** The optimal alignment of \(a\) and \(b\)

if \(n \leq 1\) then
  return trivialAlignment\((a, b)\);
end

\(p \leftarrow \text{vector}(m); \ bpp \leftarrow \text{vector}(m);\)
\(c \leftarrow \text{vector}(m); \ bpc \leftarrow \text{vector}(m);\)
\(cols \leftarrow \emptyset;\)
\(c[0] \leftarrow 0;\)

for \(i \leftarrow 1\) to \(m\) do
  \(c[i] \leftarrow c[i - 1] + s(s_i, \bot);\)
  \(bpc[i] \leftarrow 0;\)
end

for \(j \leftarrow 1\) to \(n\) do
  \(c[0] \leftarrow p[0] + s(\bot, b_j);\)
  for \(i \leftarrow 1\) to \(m\) do
    \(c[i] \leftarrow \text{maximize}\{(i - 1, j), (i, j - 1), (i - 1, j - 1)\};\)
    \(bpc[i] \leftarrow \text{choose}\{(i - 1, j), (i, j - 1), (i - 1, j - 1)\};\)
  end
  \(p \leftarrow c;\)
  if \(j = n/2\) or \(j = n\) then
    push\((cols, bpc)\);
    for \(i \leftarrow 1\) to \(m\) do
      \(bpp[i] \leftarrow i;\)
    end
  else
    \(bpp, bpc \leftarrow bpc, bpp;\)
  end
end
\(c \leftarrow \text{pop}(cols);\)
\(i \leftarrow c[n];\)
// Recurse on the two halves
\((al_2, bl_2) \leftarrow \text{Alignment}(a_{i+1}...a_n, b_{n/2+1}...b_n);\)
\((al_1, bl_1) \leftarrow \text{Alignment}(a_1...a_i, b_1...b_{n/2});\)
return \((al_1, al_2, bl_1, bl_2);\)
Algorithm 6: The algorithm k-col

**Input:** Two strings: $a$ and $b$ of length $m$ and $n$

**Output:** The optimal alignment of $a$ and $b$

1. If $n \leq 1$
   - Return `trivialAlignment(a, b)`
2. Let $p \leftarrow \text{vector}(m)$; $bpp \leftarrow \text{vector}(m)$;
   \hspace{1em} $c \leftarrow \text{vector}(m)$; $bpc \leftarrow \text{vector}(m)$;
   \hspace{1em} $cols \leftarrow \emptyset$;
   \hspace{1em} $c[0] \leftarrow 0$;
3. For $i \leftarrow 1$ to $m$
   - $c[i] \leftarrow c[i - 1] + s(s_i, \perp)$;
   \hspace{1em} $bpc[i] \leftarrow 0$;
4. End for
5. For $j \leftarrow 1$ to $n$
   - $c[0] \leftarrow p[0] + s(\perp, b_j)$;
   \hspace{1em} For $i \leftarrow 1$ to $m$
     - $c[i] \leftarrow \text{maximize}\{(i - 1, j), (i, j - 1), (i - 1, j - 1)\}$
     \hspace{1em} $bpc[i] \leftarrow \text{choose}\{(i - 1, j), (i, j - 1), (i - 1, j - 1)\}$
   \hspace{1em} End for
6. $p \leftarrow c$;
7. If `isSpecial(j)` then
   - Push $(cols, bpc)$
   \hspace{1em} For $i \leftarrow 1$ to $m$
     - $bpp[i] \leftarrow i$
   \hspace{1em} End for
8. Else
   - $bpp, bpc \leftarrow bpc, bpp$;
9. End if
10. $i \leftarrow n$;
11. For $j \leftarrow k$ down to $1$
   - $c \leftarrow \text{pop}(cols)$;
   \hspace{1em} $i' \leftarrow c[i]$;
   \hspace{1em} $(al_j, bl_j) \leftarrow \text{Alignment}(a_{i'+1} \ldots a_i, b_{(j-1)\cdot n/k+1} \ldots b_{j\cdot n/k})$;
   \hspace{1em} $i \leftarrow i'$;
12. End for
13. Return $(al_1 \ldots al_k, bl_1 \ldots bl_k)$;
This gives rise to Algorithm 6.

The function `isSpecial` returns true when the column is a special one, i.e. is of the form \( \frac{ln}{k} \) adequately rounded. When that is the case, the current backpointer column is pushed in `cols`.

To understand the reduction on the cost, note that the total area of the shadowed regions in Figure 2, left, is \( nm\frac{k}{k} \), which can be substantially lower than Hirschberg’s \( nm\frac{n}{2} \) for small values of \( k \). To compute the cost of Algorithm 6, we can use the following recursion:

\[
C(n,m) = \begin{cases} 
  t'm, & \text{if } n = 1, \\
  tnm + C(n/k, m), & \text{if } n > 1.
\end{cases}
\]

If we expand the recursion we arrive to:

\[
C(n,m) = tnm + C(n/k, m) = tnm + \frac{tnm}{k} + C(n/k^2, m) = \cdots = t'm \sum_{i=0}^{\log_k n} \frac{nm}{k^i} \approx \frac{k}{k-1} tnm.
\]

So the total cost depends on a constant \( t \) that will be slightly higher than the \( l \) of Hirschberg for the need of managing the backpointers and the fraction \( \frac{k}{k-1} \) that rapidly approaches 1. So as long as the ratio of \( t \) to \( l \) is kept lower than two, the overhead will be very low with a memory cost of a modest \( O(km) \).

5. Experiments

To test k-col, we aligned two sequences corresponding to the human and mouse versions of the Titin protein. Each sequence has approximately 35 thousand aminoacids. The matrix used to evaluate the distance between the aminoacids was blosum 62.
Implementation Considerations  The different algorithms were coded in *rust* and their implementation is freely available in github ([https://github.com/DavidLlorens/SequenceAlignment](https://github.com/DavidLlorens/SequenceAlignment)). The election of the programming language was motivated by efficiency considerations and to avoid the influence of garbage collectors.

All the executions were done in a Linux workstation equipped with an Intel Core i7-7700 CPU and 32Gb of RAM. The times were measured by the program using the `Instant` structure of rust library `std::time`. Memory occupation was measured as the maximum resident size reported by the `time` utility of GNU. All the results presented are the averages of ten executions of the program.

Some improvements were done over the naive implementation of the algorithms as presented.

The recursive algorithms used the basic quadratic memory implementation when the number of cells in the trellis was small enough. Different number of nodes were considered as recursion base size and their impact on the running time and memory usage was analyzed.

Another optimization was the use of a single column of the trellis together with a few auxiliary variables. Since only two cells from the previous column are needed to compute the value of a cell in the current column, a bit of “juggling” with the variables allows the saving of the memory associated to a column.

A final optimization was also used in k-col to reduce cache misses. The vector corresponding to the column of the trellis and the vector with the backpointers where joined in a single vector of pairs.

Baseline Results  Two baseline measures were considered. First, the cost of finding only the score without the alignment. Second, the use of the quadratic space algorithm (i.e. storing the whole trellis) to recover the alignment.

The results can be seen in this table:

| Algorithm      | time (s) | size (KB) |
|----------------|----------|-----------|
| Only score     | 1.55     | 2,736     |
| Quadratic space| 2.66     | 1,185,988 |

It is clear that recovering the alignment has a cost in time and memory.

Effect of the Recursion Base Size  Analyzing Figure 3 it is clear that using the quadratic space algorithm when the number of nodes is small enough saves space and has a negligible effect on time in the case of Hirschberg’s algorithm. Also, it is interesting to see that the overhead of recovering the alignment is almost the same as the overhead of the quadratic space algorithm. This can be attributed to the large number of cache misses incurred in by the quadratic algorithm while filling the trellis.

The effect of the recursion base size is similar in the case of k-col. For example, it can be seen in Figure 4 that for the case \( k = 32 \), once the recursion base size is big enough there is a reduction in memory used while the effect on the time is negligible.

Effect of the value of \( k \)  You can see in Figure 5 the results for a recursion base size of 30,000 nodes. It is clear from that figure that using a value of \( k \) equal to 16, the increment of time needed to recover
Figure 3. Resource usage of the implementation of Hirschberg’s algorithm as function of the recursion base size.

| R. base | Time | Memory |
|---------|------|--------|
| 0       | 2.71 | 13,696 |
| 100     | 2.68 | 8,330  |
| 300     | 2.69 | 7,781  |
| 1,000   | 2.68 | 7,308  |
| 3,000   | 2.66 | 7,051  |
| 10,000  | 2.67 | 6,623  |
| 30,000  | 2.67 | 6,442  |
| 100,000 | 2.66 | 6,633  |
| 300,000 | 2.66 | 6,592  |
| 1,000,000 | 2.66 | 6,618 |

Figure 4. Resource usage of the implementation of k-col with $k = 32$ as function of the recursion base size.

| R. base | Time | Memory |
|---------|------|--------|
| 0       | 2.12 | 16,477 |
| 100     | 2.12 | 16,478 |
| 300     | 2.12 | 16,446 |
| 1,000   | 2.13 | 16,462 |
| 3,000   | 2.09 | 14,020 |
| 10,000  | 2.10 | 13,790 |
| 30,000  | 2.10 | 13,762 |
| 100,000 | 2.10 | 13,768 |
| 300,000 | 2.09 | 13,780 |
| 1,000,000 | 2.09 | 13,751 |
the alignment is reduced from the 1.12s of Hirschberg to 0.61s with a small increase of memory. Using a value of $k$ equal to 32, the increase of memory is still acceptable and the time overhead of recovering the alignment is reduced to 0.55s.

6. Conclusions

Recovering the alignment or in general the optimal solution to a Dynamic Programming problem can involve large spatial costs if a backpointer structure needs to be kept in memory. Hirschberg’s approach reduces this cost to a linear factor of the input size. This is achieved by considering where the optimal solution crosses the central column of the trellis. We have shown how to further reduce the cost using k-col, an approach that keeps the intersections of the optimal solution with $k$ columns of the trellis. And these intersections are computed during a forward traversal, instead of the combination of forward and backward traversals performed by Hirschberg’s algorithm.

The experiments presented show that for the problem of protein alignment the overhead incurred for recovering the optimal solution is reduced to nearly a half.

References

[CIP03] Maxime Crochemore, Costas S. Iliopoulos, and Yoan J. Pinzon. Speeding-up Hirschberg and Hunt-Szymanski LCS algorithms. Fundamenta Informaticae, 56(1-2):89–103, 2003.

[CLRS09] Thomas H. Cormen, Charles E. Leiserson, Ronald L. Rivest, and Clifford Stein. Introduction to Algorithms. MIT Press, third edition, 2009.
D.S. Hirschberg. A linear space algorithm for computing maximal common subsequences. *Communications of the ACM*, 18(6):341–343, June 1975.

Eugene W Myers and Webb Miller. Optimal alignments in linear space. *Computer applications in the biosciences : CABIOS*, 4(1):11–7, March 1988.