Algorithms in Bioinformatics: A Practical Introduction

Genome Alignment

Complete genomes

- About 1000 bacterial genomes plus a few dozen higher organisms are sequenced

- It is expected many genomes will be available in the future.

- How can we study the similarities and differences of two or more related genomes?

Can we compare two genomes using Smith-Waterman (SW) algorithm?

- SW algorithm is designed for comparing two genes or two proteins.
- SW algorithm is too slow for comparing genomes
- Also, SW algorithm just reports locally similar regions (conserved regions) between two genomes. It cannot report the overall similarity.
- We need better solutions for comparing genomes.

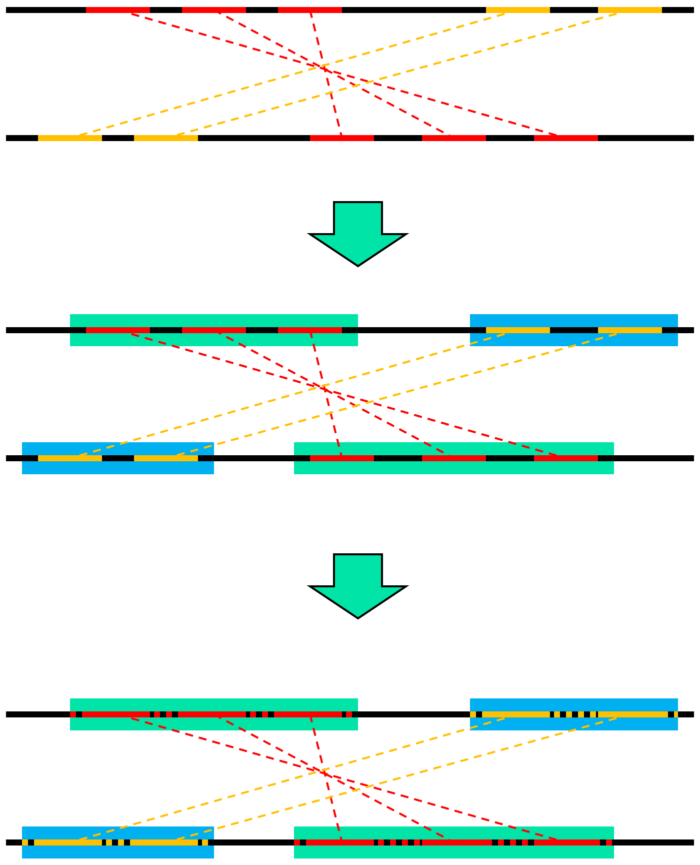
Existing tools for comparing genomes

- MUMmer, Mutation Sensitive Alignment, SSAHA, AVID, MGA, BLASTZ, and LAGAN

- All existing genome alignment methods assume the two genomes should share some conserved regions.
- They align the conserved regions first; then, they extend the alignment to cover the non-conserved regions.

General Framework

- Phase 1: Identifies potential anchors (highly similar regions).
- Phase 2: Identify a set of co-linear anchors, which forms the basis of the alignment (conserved regions).
- Phase 3: Close the gaps between the anchors to obtain the final alignment.



Agenda

- MUMmer (Versions 1 to 3)
- Mutation Sensitive Alignment

MUMmer 1

- Phase 1: Identifying anchors based on Maximal Unique Match (MUM).
- Phase 2: Identify a set of co-linear MUMs based on longest common subsequence.
- Phase 3: Fill-in the gaps

PHASE 1:
IDENTIFYING ANCHORS (MUM)

What is an anchor?

- Although conserved regions rarely contain the same entire sequence, they usually share some short common substrings which are unique in the two genomes.

- For example, consider below two regions.
  - GCTA is a common substring that is unique.
  - GCTAC is a maximal common substring that is unique
  - TAC is a common substring that is not unique.
  - GCTACT is not a common substring.

Genome1: ACGACTCAGCTACTGGTCAGCTATTACTTACCGC

Genome2: ACTTCTCTGCTACGGTCAGCTATTCACTTACCGC

Maximal Unique Match (MUM)

- In this lecture, we discuss MUM, a type of anchor.
- MUM is a common substring of two genomes of length at least some threshold d such that
  - The common substring is maximal, that is, the substring cannot be extended on either end without incurring a mismatch
  - The common substring is unique in both sequences
- For instance, almost all conserved genes share some short common substrings which are unique since they need to preserve functionality.

In our experiment, we set d=20.

Examples of finding MUMs

- S=acgactcagctactggtcagctattacttaccgc#
- T=acttctctgctacggtcagctattcacttaccgc$
- There are four MUMs: ctc, gctac, ggtcagctatt, acttaccgc.

- Consider S=acgat#, T=cgta$
- There are two MUMs: cg and t

How to find MUMs?

- Brute-force approach:

  Input: Two genome sequences $S[1..m_1]$ and $T[1..m_2]$

  - For every position i in S
    - For every position j in T
      - Find the longest common prefix P of $S[i..m_1]$ and $T[j..m_2]$
      - Check whether $|P| \geq d$ and whether P is unique in both genomes. If yes, report it as a MUM.

- This solution requires at least $O(m_1 m_2)$ time. Too slow!

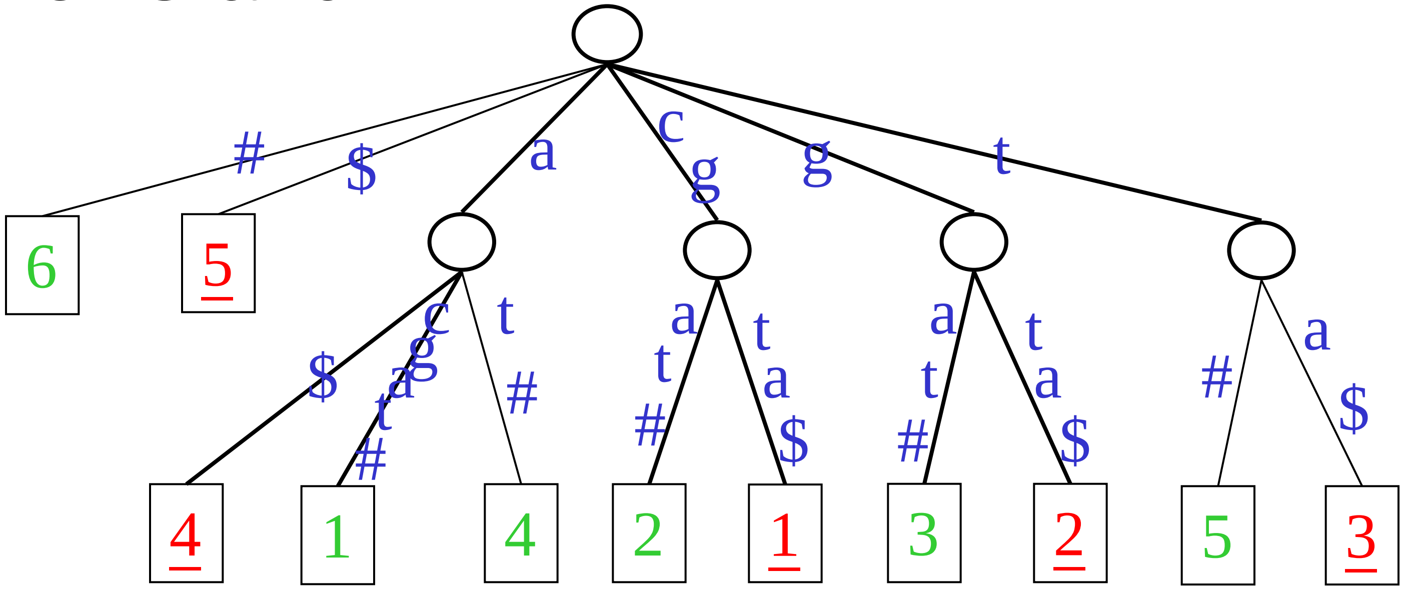
Finding MUMs by suffix tree!

- MUMs can be found in $O(m_1+m_2)$ time by suffix tree!

1. Build a generalized suffix tree for S and T
2. Mark all the internal nodes that have exactly two leaf children, which represent both suffixes of S and T.
3. For each marked node, WLOG, suppose it represents the i-th suffix S_i of S and the j-th suffix T_j of T. We check whether $S[i-1]=T[j-1]$. If not, the path label of this marked node is an MUM.

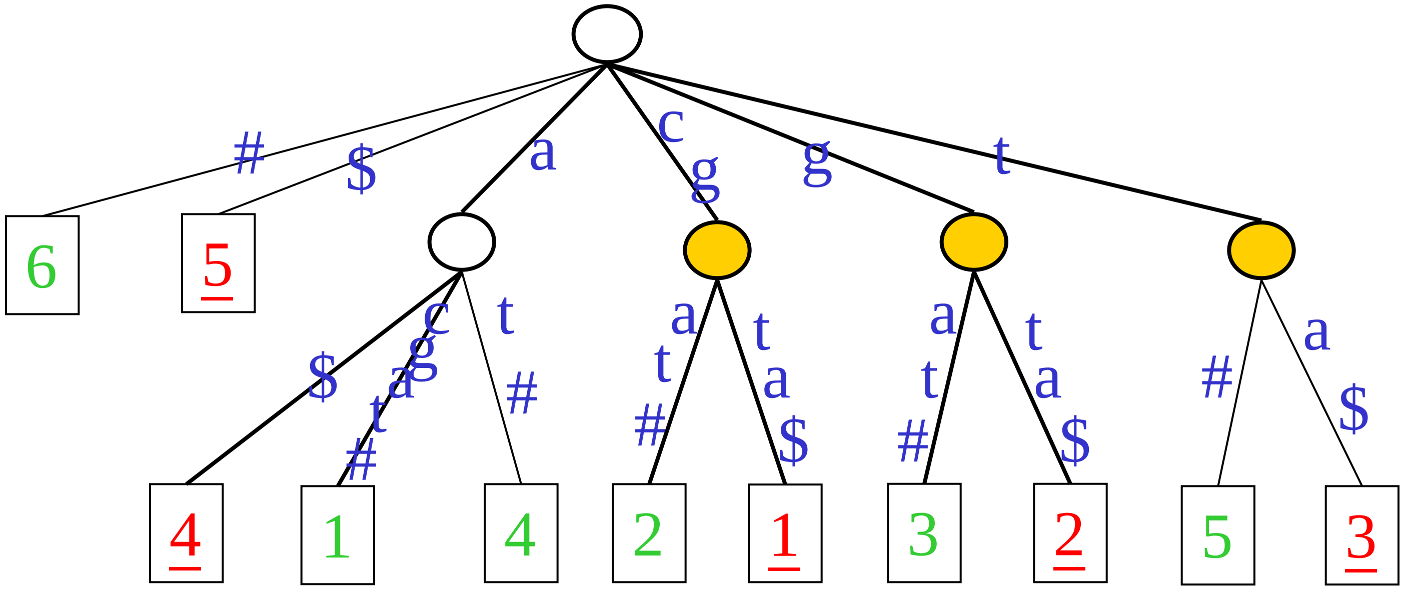
Example of finding MUMs (I)

- Consider S=acgat#, T=cgta$
- Step 1: Build the generalized suffix tree for S and T.



Example of finding MUMs (II)

- Step 2: Mark all the internal nodes that have exactly two leaf children, which represent both suffixes of S and T.



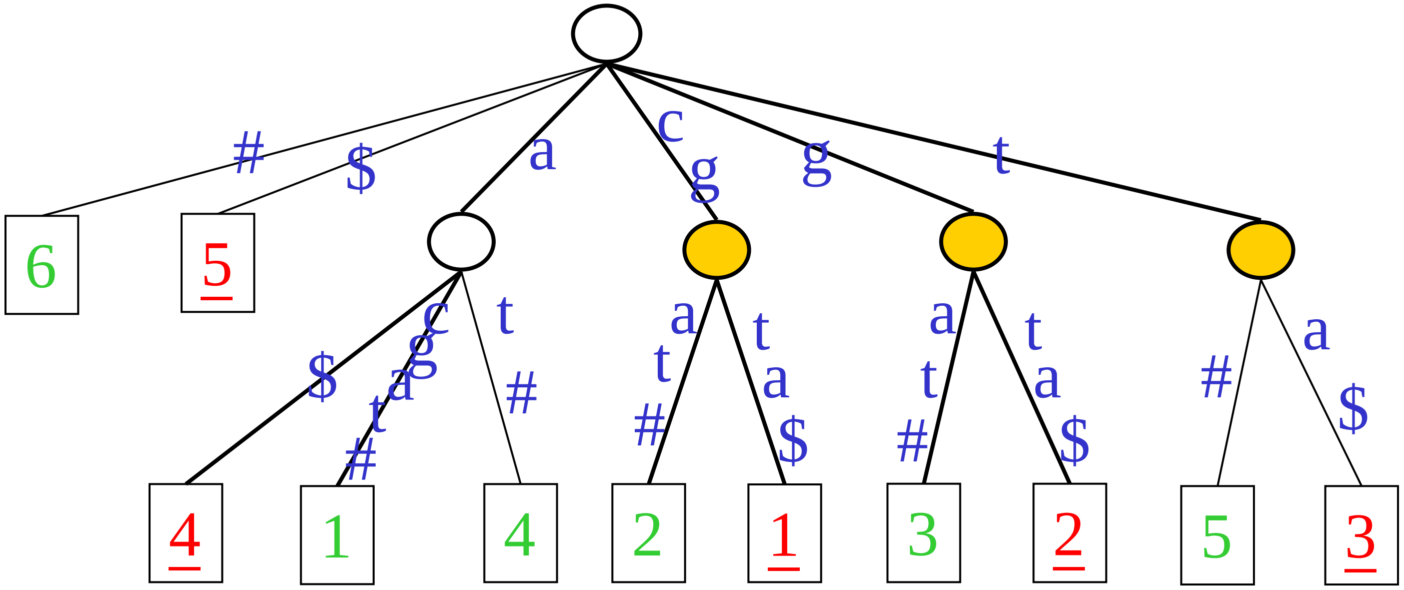
Example of finding MUMs (III)

- Step 3: For each marked node, WLOG, suppose it represents the i-th suffix S_i of S and the j-th suffix T_j of T. We check whether S[i-1]=T[j-1]. If not, the path label of this marked node is an MUM.

Output:

cg, t

S=acgat#,
T=cgta$



Phase 1: Time analysis

- Step 1: Building suffix tree takes $O(m_1+m_2)$ time.
- Step 2: Mark internal nodes takes $O(m_1+m_2)$ time.
- Step 3: Extracting MUM also takes $O(m_1+m_2)$ time.

- In total, $O(m_1+m_2)$ time.

Validating MUMs

- Mouse and human are closely related species. They share a lot of gene pairs.
- Do those gene pairs share MUMs?
- Good news!
  - MUMs appear in nearly 100% of the known conserved gene pairs.

Mouse Chr No.	Human Chr No.	# of Published Gene Pairs
2	15	51
7	19	192
14	3	23
14	8	38
15	12	80
15	22	72
16	16	31
16	21	64
16	22	30
17	6	150
17	16	46
17	19	30
18	5	64
19	9	22
19	11	93

Data is extracted from http://www.ncbi.nlm.nih.gov/Homology

Are all MUMs correspond to conserved regions?

- It seems that the answer is No!

Mouse Chr No.	Human Chr No.	# of Published Gene Pairs	# of MUMs
2	15	51	96,473
7	19	192	52,394
14	3	23	58,708
14	8	38	38,818
15	12	80	88,305
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
19	9	22	62,296
19	11	93	29,814

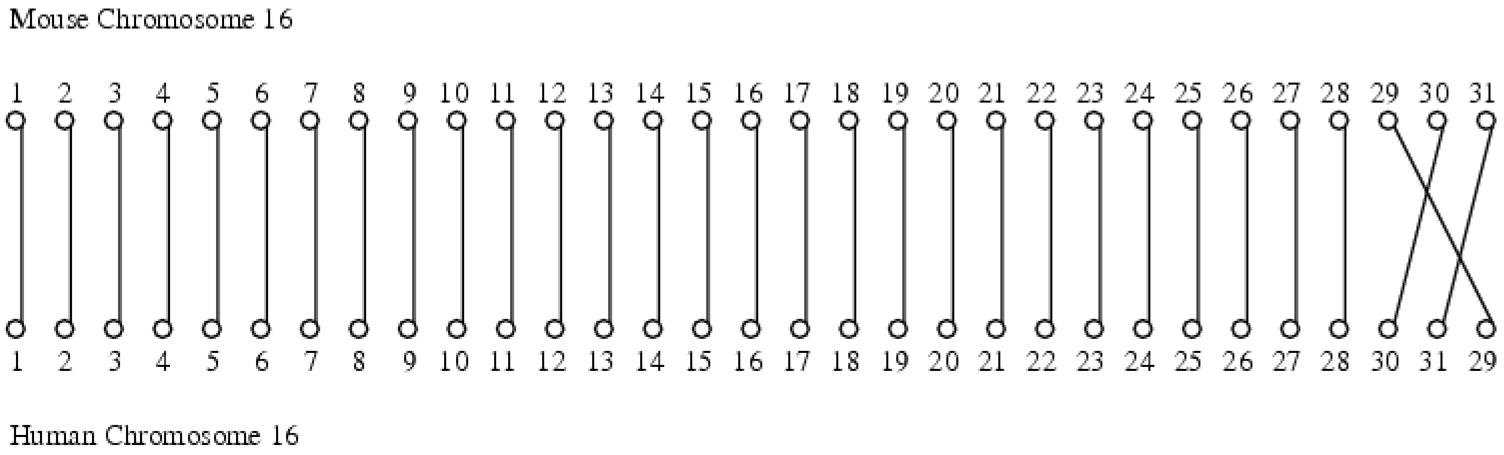
No. of MUMs >> no. of gene pairs!
There are many noise!

How can we extract the right MUMs?

PHASE 2:
IDENTIFYING CO-LINEAR MUMS

Why identify co-linear MUMs ?

- Two related species should preserve the ordering of most conserved genes!
- Example:
  - Conserved genes in Mouse Chromosome 16 and Human Chromosome 16

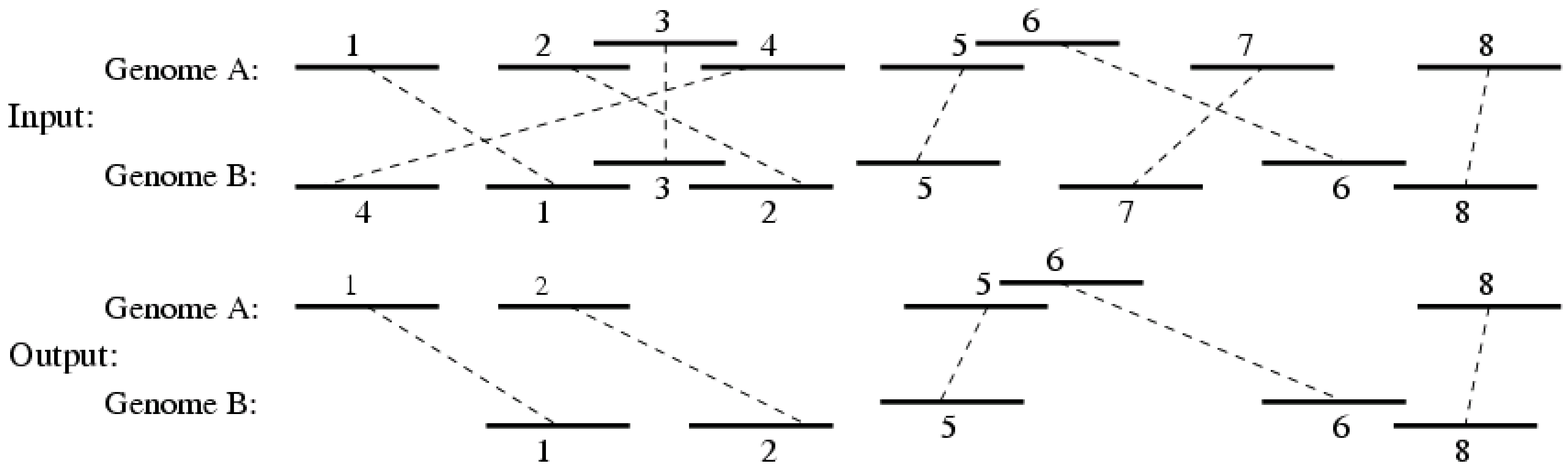


(a) There are 31 conserved gene pairs found in Mouse chromosome 16 and Human chromosome 16. The genes are labeled according to the positions of the genes in the mouse chromosome from the 5' end. The corresponding genes in human are drawn according to their relative positions from the 5' end of human chromosome.

How to identify co-linear MUMs?

- Instead of reporting all MUMs,
  - we compute the longest common subsequence (LCS) of all MUMs.
- We report only the MUMs on the LCS.
- Hopefully, this approach will not report a lot of noise.

Example of LCS



12345678

41325768

$\longrightarrow$

12345678

41325768

The longest common subsequence (LCS) problem

- Suppose there are n MUMs.
- Input: two sequences $A[1..n]=a_1a_2\ldots a_n$ and $B[1..n]=b_1b_2\ldots b_n$ of n distinct characters.
- Output: the longest common subsequence.

How to find LCS in $O(n^2)$ time?

- Let $C_i[j]$ be the length of the longest common subsequence of A[1..i] and B[1..j].
- Let $\delta(i)$ be the index of the character in B such that $a_i = b_{\delta(i)}$
- Note that $C_i[0]=C_0[j]=0$ for all $0 \le j \le n$; and

$$C_i[j] = \max \begin{cases} C_{i-1}[j] \\ 1 + C_{i-1}[\delta(i)-1] \quad \text{if } j \ge \delta(i) \end{cases}$$

- Note that the length of the LCS(A,B) = $C_n[n]$.
- By dynamic programming, the problem is solved in $O(n^2)$ time.

Example (I)

- A[1..8]=12345678
- B[1..8]=41325768

C	0	1	2	3	4	5	6	7	8
0									
1									
2									
3									
4									
5									
6									
7									
8									

Example (II)

- A[1..8]=12345678
- B[1..8]=41325768

- Base cases:
  - $C_i[0]=0$ and $C_0[j]=0$

C	0	1	2	3	4	5	6	7	8
0	0	0	0	0	0	0	0	0	0
1	0								
2	0								
3	0								
4	0								
5	0								
6	0								
7	0								
8	0								

Example (III)

- A[1..8]=12345678
- B[1..8]=41325768

- Fill the table row by row with the recursive formula:

$$C_i[j] = \max\begin{cases} C_{i-1}[j] \\ 1 + C_{i-1}[\delta(i)-1] & if\ j \geq \delta(i) \end{cases}$$

$C_2[4]$=LCS(A[1..2],B[1..4]).

By the recursive formula, $C_2[4]=\max\{C_1[4], 1+C_1[3]\}=2$
(Note: $\delta(2)=4$.)

C	0	1	2	3	4	5	6	7	8
0	0	0	0	0	0	0	0	0	0
1	0	0	1	1	1	1	1	1	1
2	0	0	1	1					
3	0								
4	0								
5	0								
6	0								
7	0								
8	0								

Example (IV)

- A[1..8]=12345678
- B[1..8]=41325768

- Fill the table row by row with the recursive formula:

$$C_i[j] = \max\begin{cases} C_{i-1}[j] \\ 1 + C_{i-1}[\delta(i)-1] & if\ j \geq \delta(i) \end{cases}$$

C	0	1	2	3	4	5	6	7	8
0	0	0	0	0	0	0	0	0	0
1	0	0	1	1	1	1	1	1	1
2	0	0	1	1	2	2	2	2	2
3	0	0	1	2	2	2	2	2	2
4	0	1	1	2	2	2	2	2	2
5	0	1	1	2	2	3	3	3	3
6	0	1	1	2	2	3	3	4	4
7	0	1	1	2	2	3	4	4	4
8	0	1	1	2	2	3	4	4	5

LCS(A,B)=C_8[8]=5.

We can extract more information

- As a side-product, we can retrieve LCS(A[1..i], B[1..j]), where $1 \le i,j \le n$, in O(1) time.

Sparsification

- Observation:
  - $C_i[1] \leq C_i[2] \leq \ldots \leq C_i[n]$
- Instead of storing $C_i[0..n]$ explicitly, we can store only the boundaries at which the values change.
- Precisely, we store $(j, C_i[j])$ for all j such that $C_i[j] > C_i[j-1]$.
- Example: suppose $C_i[0..9]$=0001122233.
  - We store (3,1), (5,2), (8,3).

- We can store all the tuples $(j, C_i[j])$ in a binary search tree T_i. Then, every search, insert, delete operation takes O(log n) time.

- Given T_{i-1}, we can compute C_i [j] in O(log n) time as follows.

$$C_i[j] = \max\begin{cases} C_{i-1}[j] \\ 1 + C_{i-1}[\delta(i) - 1] \quad \textit{if } j \geq \delta(i) \end{cases}$$

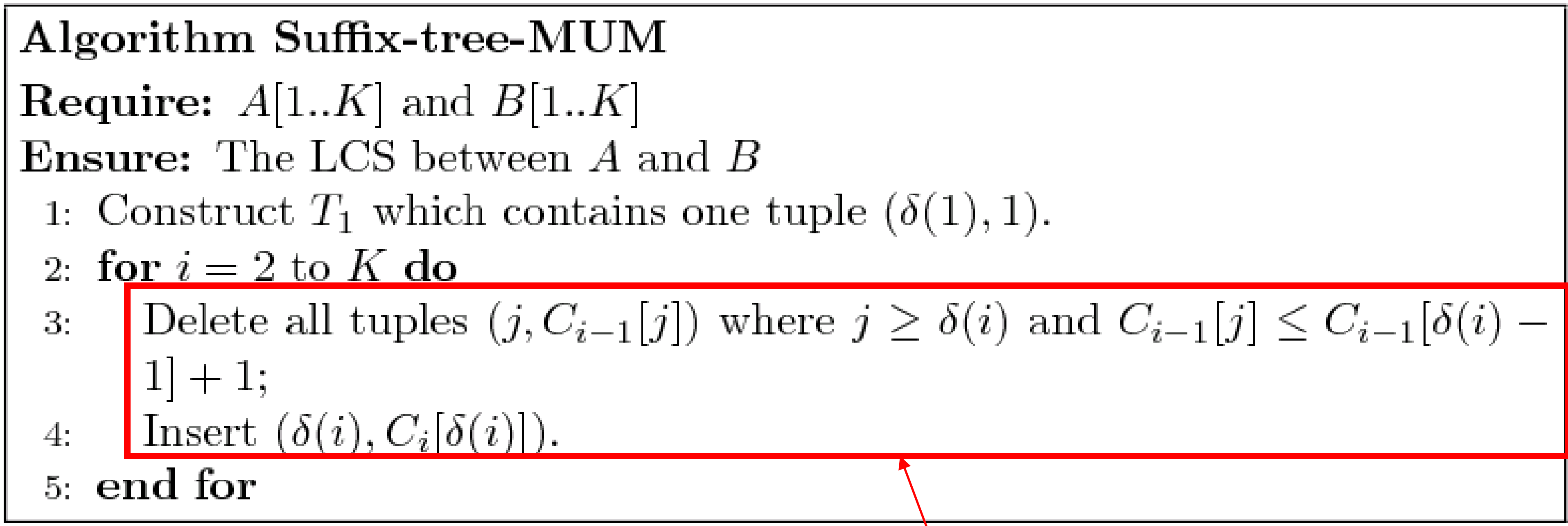
Lemma

- Let j' be the smallest integer greater than $\delta(i)$ such that $C_{i-1}[\delta(i)-1]+1 < C_{i-1}[j']$. We have

$$C_i[j] = \begin{cases} C_{i-1}[\delta(i)-1]+1 & \text{if } \delta(i) \le j \le j'-1 \\ C_{i-1}[j] & \text{otherwise} \end{cases}$$

- Proof:
  - When $j<\delta(i)$, by definition, $C_i[j]=C_{i-1}[j]$.
  - When $\delta(i)\le j<j'$, by definition, $C_{i-1}[\delta(i)-1]+1 \ge C_{i-1}[j'] \ge C_{i-1}[j]$, hence,
    - $C_i[j]=\max\{C_{i-1}[j], C_{i-1}[\delta(i)-1]+1\}= C_{i-1} [\delta(i)-1]+1$.
  - When $j> j'$, by definition, $C_{i-1}[\delta(i)-1]+1 < C_{i-1}[j'] \le C_{i-1}[j]$, hence,
    - $C_i[j]=\max\{C_{i-1}[j], C_i[\delta(i)-1]+1\}=C_{i-1}[j]$.

Algorithm



Algorithm Suffix-tree-MUM

```
Require: $A[1..K]$ and $B[1..K]$
Ensure: The LCS between $A$ and $B$
1: Construct $T_1$ which contains one tuple $(\delta(1), 1)$.
2: for $i = 2$ to $K$ do
3:     Delete all tuples $(j, C_{i-1}[j])$ where $j \geq \delta(i)$ and $C_{i-1}[j] \leq C_{i-1}[\delta(i) - 1] + 1$;
4:     Insert $(\delta(i), C_i[\delta(i)])$.
5: end for
```

Construct T_i from T_{i-1}

Example: Transform T_7 to T_8

```
  123456789
A=123456789
B=245831697
```

- $\delta(1)=6$, $\delta(2)=1$, $\delta(3)=5$, $\delta(4)=2$, $\delta(5)=3$, $\delta(6)=7$, $\delta(7)=9$, $\delta(8)=4$, $\delta(9)=8$.

- $C_7[0..9]=0123333445$ $T_7=(1,1),(2,2),(3,3),(7,4),(9,5)$

- Note that $C_7[\delta(8)-1]+1=4$
- $T_7 \rightarrow$ remove (7,4), insert (4,4) $\rightarrow T_8$

- $C_8[0..9]=0123444445$ $T_8=(1,1),(2,2),(3,3),(4,4),(9,5)$

Time analysis

- To build T_i from T_{i-1}, suppose we need to delete α_i tuples.
- Then, T_i can be constructed in $O((\alpha_i+1)\log n)$ time.
- In total, T_n can be constructed in $O((n+\alpha_1+\alpha_2+\ldots+\alpha_n) \log n)$ time.
- Since we can delete at most n tuples, T_n can be constructed in $O(n \log n)$ time.

We can extract more information

- As a side-product, we can retrieve LCS(A[1..i], B[1..j]), where $1 \le i,j \le n$, in O(log n) time.
  - Idea: By searching the tuple (j', C_i [j']) in T_i such that j' is just smaller than j.
  - Then, we report C_i[j'].
  - Searching in T_i takes O(log n) time.

Analysis

- In conclusion, LCS can be computed in O(n log n) time.

PHASE 3:
FILLING THE GAPS

Phase 3: Filling the gaps

- Using Smith-Waterman alignment, gaps are filled to identify
  - Large inserts,
  - Repeats,
  - Small mutated regions,
  - Tandem repeats, and
  - SNPs.

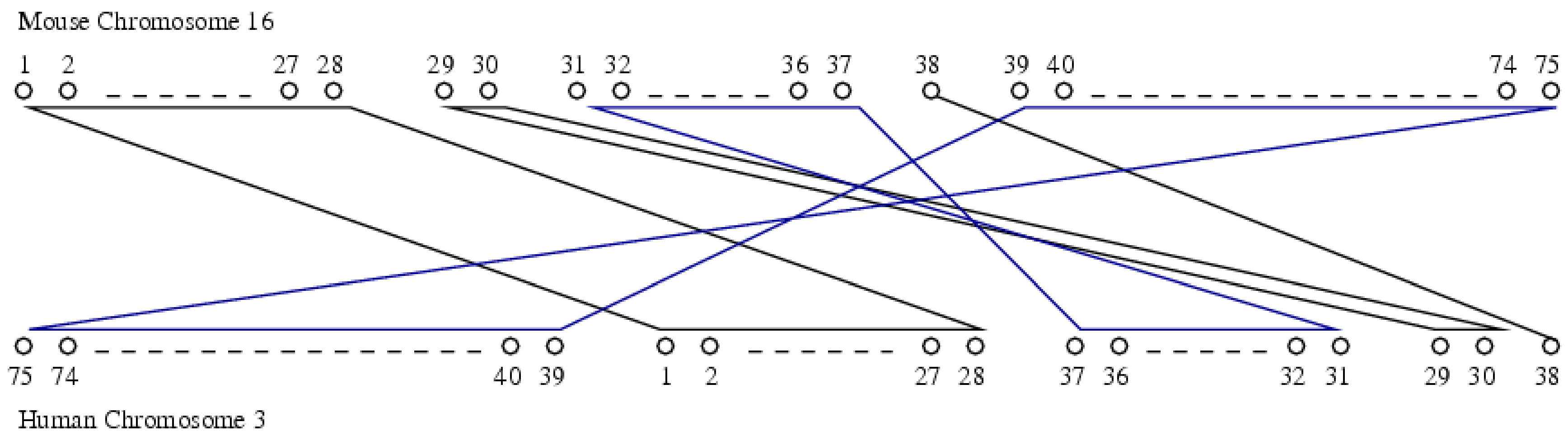
- Combing the three phases, we have MUMmer1.

Problem of this approach

- This approach assumes there exist a single long alignment. Moreover, such assumption may not be always true.

- Therefore, for many cases, LCS can only discover few genes.

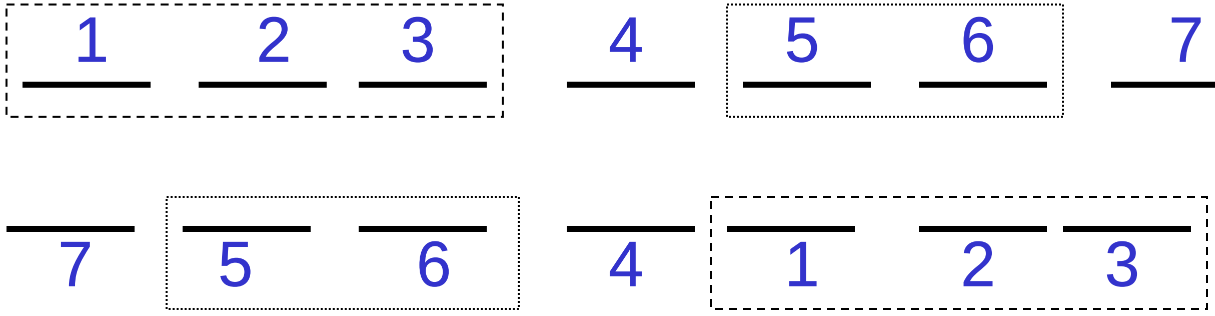
Common genes in Mouse Chromosome 16 and Human Chromosome 3



(b) There are 31 conserved gene pairs found in Mouse chromosome 16 and Human chromosome 3. The genes are labeled as in (a). Note that the relative ordering of Genes 31 to 37 in human chromosome is exactly the reverse of that in the mouse chromosome. The same situation occurs in Genes 39 to 75.

Observation 3

- A pair of conserved genes are likely corresponding to a sequence of MUMs that are consecutive and close in both genomes and have sufficient length.



- The set of such substrings is called a cluster.

Solution 3

- Based on Observation 3, MUMmer2 and MUMmer3 try to identify maximal clusters in the genomes.
- This approach is quite good. In our experiment, MUMmer3 can identify ~76.6% of the published gene pairs.

Can we further improve?

- Yes. We propose the Similar Subsequence Problem.
- In our experiment, we can identify ~91.3% of the published gene pairs.

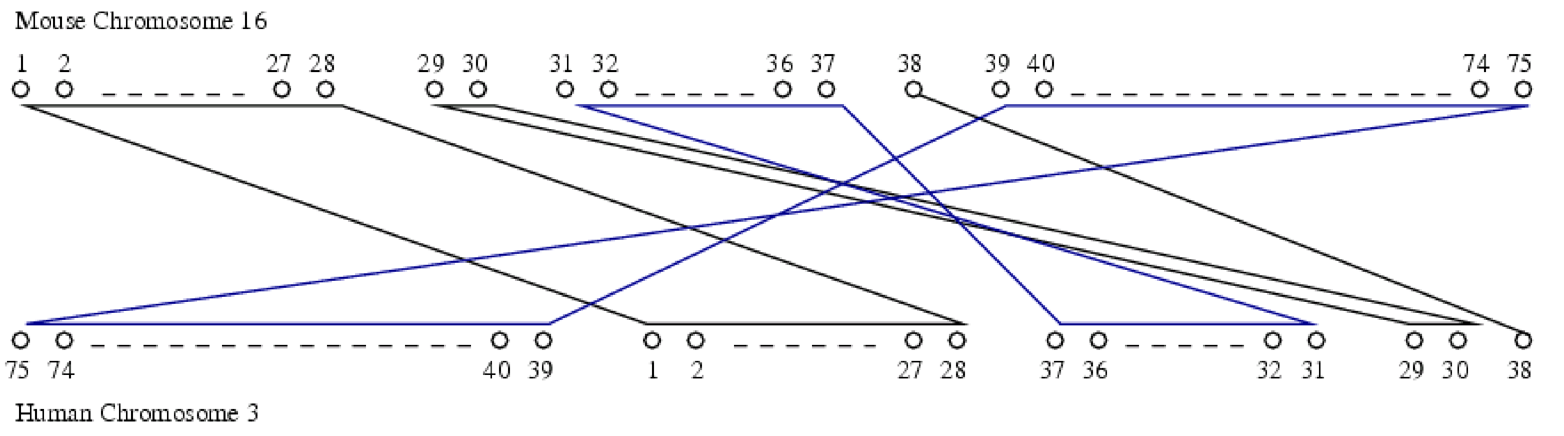
Mutation Sensitive Alignment (MSA) Algorithm

Observation 4

- If two genomes are closely related, they can be transformed from each other using a few transpositions/reversals.

Example

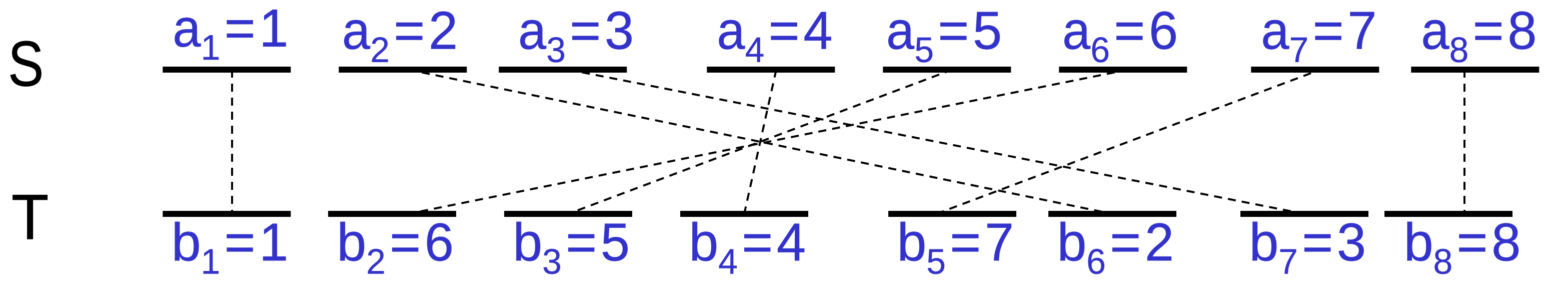
- By two transposition/reversal operations, we can transform Mouse Chr 16 to Human Chr 16.



(b) There are 31 conserved gene pairs found in Mouse chromosome 16 and Human chromosome 3. The genes are labeled as in (a). Note that the relative ordering of Genes 31 to 37 in human chromosome is exactly the reverse of that in the mouse chromosome. The same situation occurs in Genes 39 to 75.

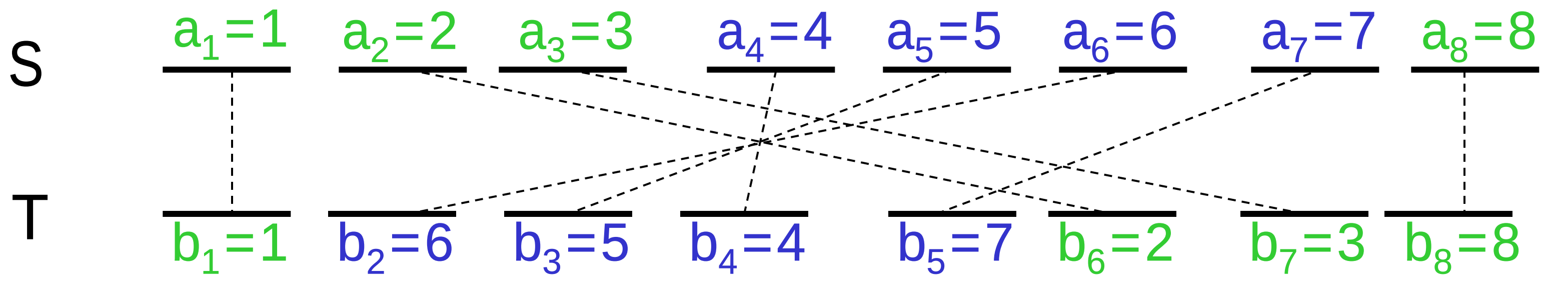
Input

- Given two genomes S and T. Assume we already know the n MUMs.
- Let $A=(a_1,a_2,\ldots,a_n)$ and $B=(b_1,b_2,\ldots,b_n)$, respectively, be the order of the n MUMs in S and T.



Common subsequence

- A sequence $C=(c_1,c_2,\dots,c_m)$ is a common subsequence of A and B if C is a subsequence of both A and B
- For example, C=(1,2,3,8) is a common subsequence of A and B.
- The weight of a common subsequence is the total weight of the MUMs
- A maximum weight common subsequence (MWCS) of A and B is a subsequence with the heaviest weight.



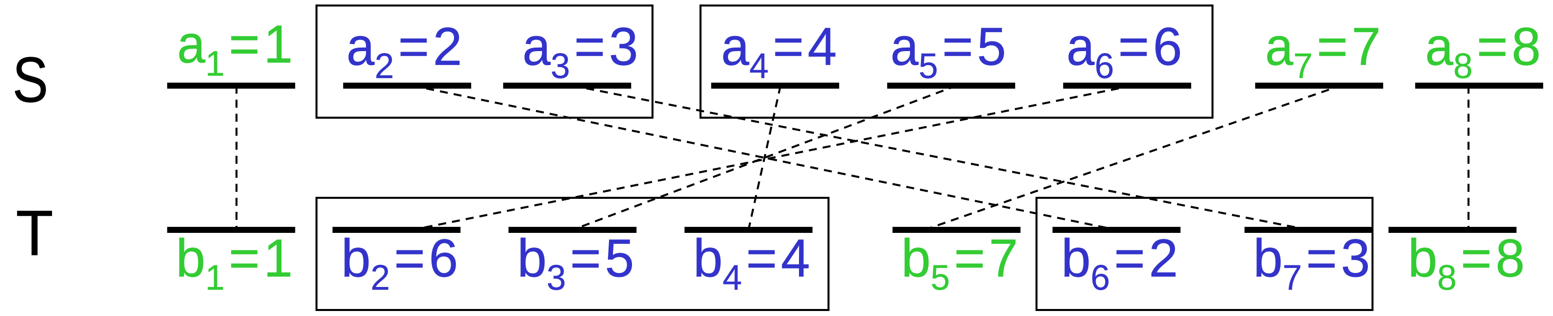
Maximum weight common subsequence (MWCS) problem

- Given A[1..n] and B[1..n],
  - we can compute an MWCS of A and B in O(n log n) time.
- Idea: similar to the computation of LCS.

- Remark: as a side-product, we can retrieve MWCS of A[1..i] and B[1..j], where $1 \leq i,j \leq n$, in O(log n) time.

Similar Subsequence

- A k-similar subsequence consists of k blocks and a backbone.
  - The backbone is a common subsequence with k blocks inserted into it.
  - Each block is a common subsequence or reversed common subsequence while all of them are disjoint.
- Below is an example of 2-similar subsequence.
- In some sense, k-similar subsequence models k transpositions/reversals.



Similar Subsequence Problem

- Given two sequences A and B and a parameter k,
- the Similar Subsequence Problem finds a k-similar subsequence with the heaviest weight.

- This problem is NP-complete in general.
- For a constant k, we can solve the problem in $O(n^{2k+1} \log n)$ time.
- We devise a heuristic algorithm to solve it in $O(n^2(\log n + k))$ time.

Heuristic algorithm: idea

1. Find the backbone first.
2. For every interval i..j, compute the score of inserting such subsequence into the backbone.
3. Find k non-overlapping intervals which maximizes the total score.

Heuristic algorithm: Step 1

- Find the MWCS of A and B. Treat this as the backbone.
  - O(n log n) time

Heuristic algorithm: Step 2

- This step compute the score for inserting one block A[i..j] to B[δ(i)..δ(j)]
- Example: Moving A[1..3] to B[8..5]
  - Note: This is a transposition and reversal
  - A = $\underline{123}456789$
  - B = $4769\underline{3251}8$

- This step consists of two substeps.

Heuristic algorithm: Step 2.1

- Compute MWCS(A[i..j], B[δ(i)..δ(j)]) for all $1 \le i,j \le n$.
  - Brute force: $O(n^3 \log n)$ time
  - Better algorithm: $O(n^2 \log n)$ time
    - For each i,
      - Find the MWCS for A[i..n] and B[δ(i)..n] in O(n log n) time
      - Find the MWCS for A[i..n] and reverse of B[1..δ(i)] in O(n log n) time
      - Retrieve MWCS(A[i..j], B[δ(i)..δ(j)]) in O(log n) time for every $j \ge i$

Heuristic algorithm: Step 2.2

- For every interval i..j,
  - Define Score(i..j) to be
    - MWCS(A[i..j], B[δ(i)..δ(j)]) –
    - the total weight of chracters in the backbone that fall into A[i..j] or B[δ(i)..δ(j)]

Example

- A[1..8]=12345678
- B[1..8]=41325768

- Backbone is 12568
  - A[1..8]=12345678
  - B[1..8]=41325768
- Consider mutating A[3..4] to B[δ(3)..δ(4)])=B[3..1].
  - A[1..8]=12345678
  - B[1..8]=41325768
- After mutation, we have
  - A[1..8]=12345678
  - B[1..8]=41325768

Note:
MWCS(A[3..4],B[δ(3)..δ(4)])=2
‘1’ falls in B[1..3].
So, Score(3..4)=2-1=1

Heuristic algorithm: Step 3

- Among all intervals,
  - Find k intervals $i_1..j_1$, $i_2..j_2$, …, $i_k..j_k$ such that they are mutually disjoint and maximize the sum of their scores, that is, $\Sigma_{p=1,2,\ldots,k}\mathrm{Score}(i_p..j_p)$.

- This step can be done in $O(k\ n^2)$ time by dynamic programming. [Exercise]

Heuristic algorithm: Step 4

- Refine the k intervals i..j so that B[δ(i)..δ(j)] are disjoint.
- While there exists δ(i)..δ(j) and δ(i')..δ(j') that are overlapping,
  - We examine all possible ways to shrink the intervals i..j and i'..j' so that the score is maximize and δ(i)..δ(j) and δ(i')..δ(j') are not overlap.
- O(k^2) time

Heuristic algorithm: summery

- The total time is $O(n^2(\log n + k))$.

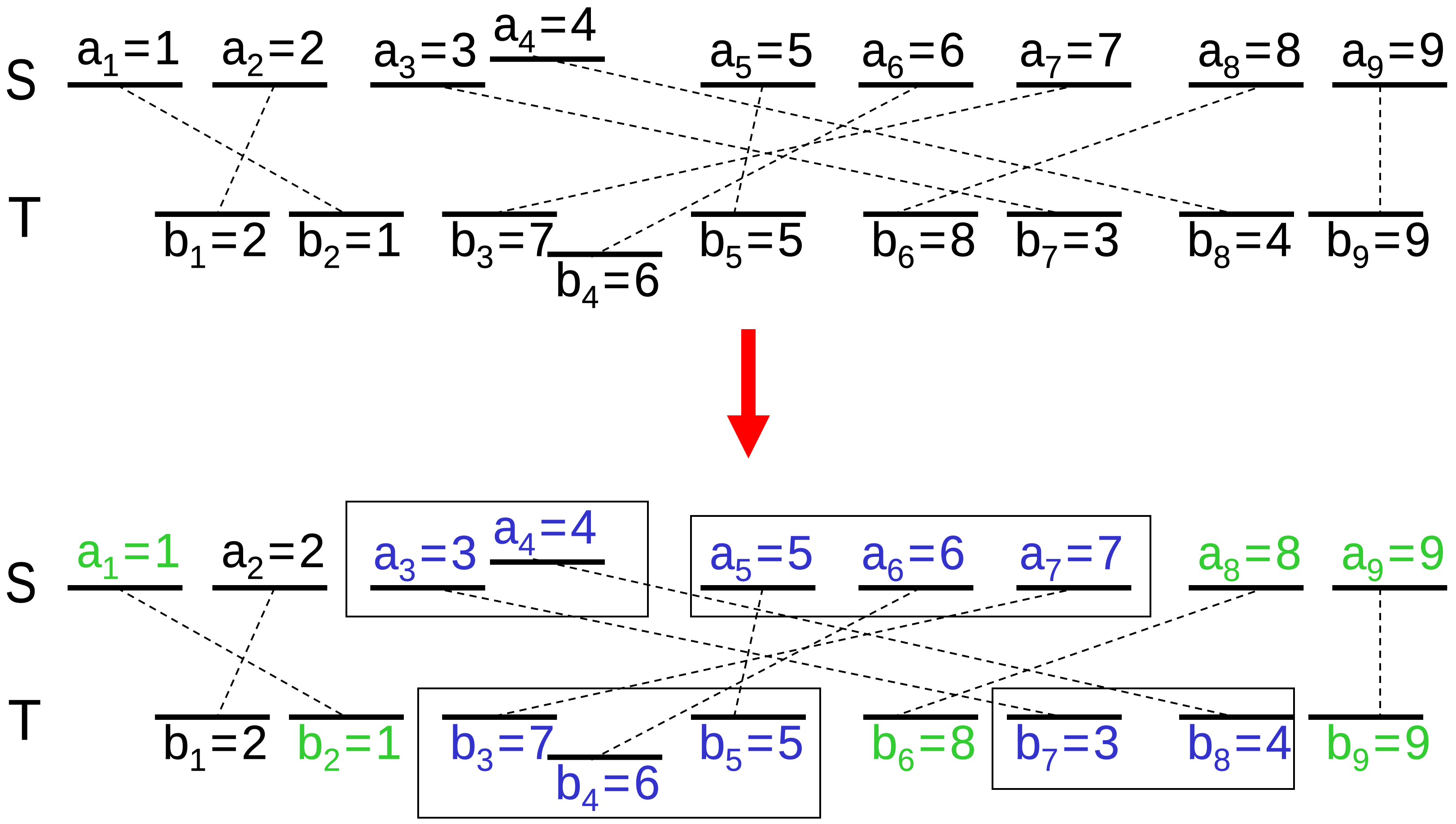
Solution 4

- Given two genomes S and T,

Mutation Sensitive Alignment (MSA) Algorithm

1. Find all the MUMs
2. Solve the similar subsequence problem
3. Report all the MUMs on the k-similar subsequence.

Example


S
$a_1=1$
$a_2=2$
$a_3=3$
$a_4=4$
$a_5=5$
$a_6=6$
$a_7=7$
$a_8=8$
$a_9=9$
T
$b_1=2$
$b_2=1$
$b_3=7$
$b_4=6$
$b_5=5$
$b_6=8$
$b_7=3$
$b_8=4$
$b_9=9$

Experiment on human and mouse

- We apply MUMmer3 and MSA to the following 15 pairs of chromosomes.

For MSA, we set k=4!

Mouse Chr No.	Human Chr No.	# of Published Gene Pairs	# of MUMs
2	15	51	96,473
7	19	192	52,394
14	3	23	58,708
14	8	38	38,818
15	12	80	88,305
15	22	72	71,613
16	16	31	66,536
16	21	64	51,009
16	22	30	61,200
17	6	150	94,095
17	16	46	29,001
17	19	30	56,536
18	5	64	131,850
19	9	22	62,296
19	11	93	29,814

Experiment on human and mouse

	Coverage		Preciseness	
Exp. No.	MUMmer	MSA	MUMmer	MSA
1	76.50%	92.20%	21.70%	22.70%
2	71.40%	91.70%	21.30%	25.10%
3	87.00%	100.00%	24.80%	25.50%
4	76.30%	94.70%	27.40%	26.70%
5	92.50%	96.30%	32.50%	32.00%
6	72.20%	95.80%	31.20%	32.90%
7	67.70%	87.10%	13.50%	17.80%
8	78.10%	90.60%	37.20%	36.70%
9	80.00%	86.70%	40.70%	49.70%
10	82.00%	92.00%	30.90%	32.10%
11	65.20%	89.10%	30.50%	36.00%
12	60.00%	80.00%	27.50%	41.90%
13	89.10%	95.30%	18.20%	18.40%
14	72.70%	86.40%	10.40%	12.60%
15	78.50%	91.40%	30.00%	29.70%
average	76.60%	91.30%	26.50%	29.30%

- Coverage: % of published genes covered
- Preciseness: % of MUMs reside in some published gene pairs.

Experiment result on Baculoviridae genomes that are in the same genus

Experiment	Virus	Virus	Length	# of MUMs	# of Conserved Genes
1	AcMNPV	BmNPV	133K*128K	35,166	134
2	AcMNPV	HaSNPV	133K*131K	64,291	98
3	AcMNPV	LdMNPV	133K*161K	65,227	95
4	AcMNPV	OpMNPV	133K*131K	59,949	126
5	AcMNPV	SeMNPV	133K*135K	66,898	100
6	BmNPV	HaSNPV	128K*131K	63,939	98
7	BmNPV	LdMNPV	128K*161K	63,086	93
8	BmNPV	OpMNPV	128K*131K	58,657	122
9	BmNPV	SeMNPV	128K*135K	66,448	99
10	HaSNPV	LdMNPV	131K*161K	57,618	92
11	HaSNPV	OpMNPV	131K*131K	59,125	95
12	HaSNPV	SeMNPV	131K*135K	64,980	101
13	LdMNPV	OpMNPV	161K*131K	75,906	98
14	LdMNPV	SeMNPV	161K*135K	62,545	102
15	OpMNPV	SeMNPV	131K*135K	63,261	101
16	CpGV	PxGV	123K*100K	59,733	97
17	CpGV	XcGV	123K*178K	63,258	107
18	PxGV	XcGV	100K*178K	81,020	99

- We apply MUMmer3 and MSA to the following 15 pairs of viruses.
- MUM pairs of length at least three amino acids
- For MSS, k=20

Experiment result on Baculoviridae genomes that are in the same genus

Experiment	Coverage		Preciseness	
	MUMmer	MSS	MUMmer	MSS
1	100% (134)	100% (134)	44%	91%
2	58% (57)	80% (78)	80%	85%
3	58% (55)	69% (66)	64%	80%
4	83% (105)	95% (120)	91%	94%
5	61% (61)	68% (68)	70%	85%
6	59% (58)	73% (72)	78%	87%
7	58% (54)	69% (64)	47%	79%
8	83% (101)	94% (115)	86%	94%
9	63% (62)	69% (68)	65%	86%
10	75% (69)	85% (78)	75%	85%
11	53% (50)	68% (65)	77%	83%
12	75% (76)	87% (88)	71%	93%
13	60% (59)	67% (66)	52%	89%
14	74% (75)	75% (77)	65%	90%
15	52% (53)	63% (64)	66%	82%
16	61% (59)	85% (82)	83%	89%
17	58% (62)	74% (79)	83%	84%
18	61% (60)	76% (75)	76%	86%
average	66%	78%	71%	87%

- Coverage: % of published genes covered
- Preciseness: % of MUMs reside in some published gene pairs.

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