Smith & Waterman Algorithm for Pairwise Local Alignment

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Lecture Outline

1. Sequence Alignment
2. Sequence Edits
3. Score Matrix
4. Dynamic Programming
5. Local Sequence Alignment
6. Smith & Waterman Algorithm
7. Example

1 Sequence Alignment

2 Sequence Edits

3 Score Matrix

4 Dynamic Programming

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7 Example

Sequence Alignment

- Why do we need to align sequence?

Why do we need to align sequence?

- Comparing DNA/protein sequences for
  - Similarity
  - Homology
- Prediction of function
- Construction of phylogeny Shotgun assembly
  - End-space-free alignment / overlap alignment
- Finding motifs
- Understanding Evolutionary Relationships

Sequence Alignment

- Procedure of comparing to (Pairwise) or more (Multiple) sequences by searching for a series of individual characters that are in the same order in the sequence.

```
G  C  T  A  G  T  C  A  G  A  T  C  T  G  A  C  G  C  T  A
      |     |  |  |  |     |  |  |  |  |  |  |  |  |
      T  G  G  T  C  A  C  A  T  C  T  G  C  C  G  C
```

Sequence Alignment

- **Definition**

  Given two strings $x = x_1 x_2 ... x_m$ and $y = y_1 y_2 ... y_n$,
  an alignment is an assignment of gaps to positions 0 ... M in x and 0 ... N in y, so as to line up each letter in one sequence with either a letter or a gap in the other sequence.

A Simple Alignment

- Let us try to align two short nucleotide sequences:
  -AATCTATA and AAGATA

- Without considering any gaps (insertions/deletions) there are 3 possible ways to align these sequences

```
A A T C T A T A      A A T C T A T A      A A T C T A T A
A A G A T A            A A G A T A            A A G A T A
```

- Which one is better?

What is a Good Alignment

A G G C T A G T T , A G C G A A G T T

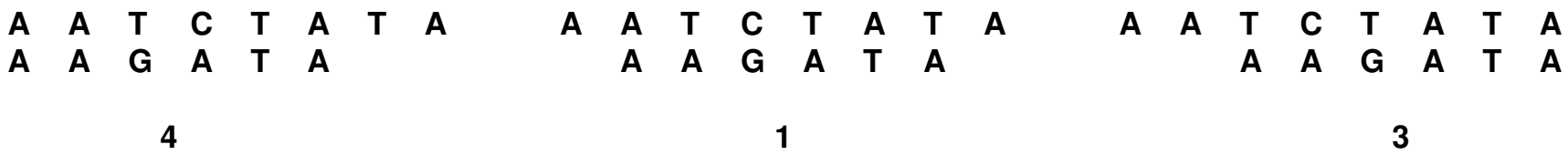
A G G C T A G T T - **A G C G A A G T T T**	**Matches = 6** **Mistatches = 3** **Gap = 1**
A G G C T A - G T T - **A G - C G A A G T T T**	**Matches = 7** **Mismatches = 1** **Gaps = 3**
A G G C - T - G T T - **A G - C G - A A G T T**	**Matches = 7** **Mismatches = 0** **Gaps = 5**

Scoring the Alignments

- We need to have a scoring mechanism to evaluate alignments
  - match score
  - mismatch score
- We can have the total score as:

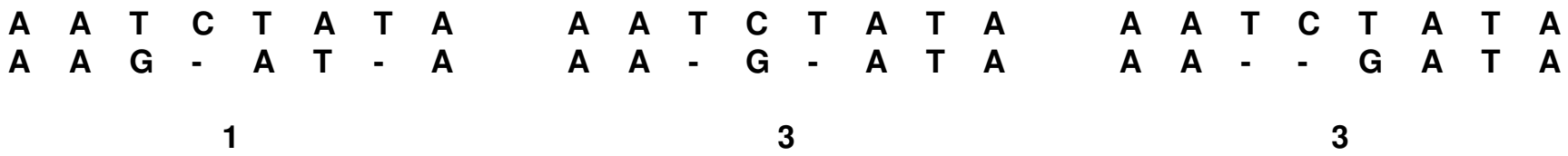
$$\sum_{i=1}^{n} \textit{match or mismatch score at position } i$$

- For the simple example, assume a match score of 1 and a mismatch score of 0:



Simple Alignment with Gaps

- Considering gapped alignments vastly increases the number of possible alignments:



- If gap penalty is -1, what will be the new scores?

1 Sequence Alignment

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Sequence Edits

Lets do some sequence edits and view scores

Sequence Edits

Three types of sequence edits

1. Mutations
2. Insertions
3. Deletions

Mutations

A G G C C T C
A G G A C T C

Insertions

A	G	G	C	C	T	C	
A	G	G	G	C	C	T	C

Deletions

A G G C C T C
A G G . C T C

Scoring Function

Match: +m

Mismatch: -s

Gap: -d

Score F = (# matches) x m - (# mismatches) x s - (# gaps) x d

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Score Matrix

- Assign scores to each pair of symbol
  - Higher score means more similarity.

Score Matrix

- DNA
  - Match = +1
  - Mismatch = -3
  - Gap penalty = -5
  - Gap extension penalty = -2
- Protein sequences
  - Blossum62 matrix
  - Gap open penalty = -11
  - Gap extension penalty = -1

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- How do we compute the best alignment?

Alignment is Additive

- Observation:
  The score of aligning $x_1 \ldots x_M$ and $y_1 \ldots y_N$ is additive

  Say that $x_1 \ldots x_i \quad x_{i+1} \ldots x_M$
  aligns to $y_1 \ldots x_j \quad x_{j+1} \ldots x_N$

  The two scores add up:

  F(x[1:M], y[1:N]) = F(x[1:i], y[1:j]) + F(x[i+1:M], y[j+1:N])

Types of Alignment

- Global
  - Strings of similar size
    - Genes with a similar structure
    - Larger regions with a preserved order (syntenic regions)
- Local
  - Finding similar regions among:
    - Dissimilar regions
    - Sequences of different lengths

Dynamic Programming

- Instead of evaluating every possible alignment, we can create a table of partial scores by breaking the alignment problem into subproblems.
- Consider two sequences CACGA and CGA
  - we have three possibilities for the first position of the alignment

First Position	Score	Remaining seqs
C C	+1	ACGA GA
– C	-1	CACGA GA
C –	-1	ACGA CGA

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Local Sequence Alignment

- Suppose we have a long DNA sequence (eg 4000 bp) and we want to compare it with the complete yeast genome (12.5Mbp)
- What if only a portion of our query, say 200 bp length, has strong similarity to a gene in yeast.

Local Sequence Alignment Problem

- Given two strings

$$x = x_1 \ldots\ldots x_M$$

$$y = y_1 \ldots\ldots x_N$$

Find substring y', x' whose similarity (optimal global alignment value) is maximum.

$$x = aaaacc\underline{cccggg}gtta$$

$$y = tt\underline{cccggg}aaccaacc$$

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Smith & Waterman Algorithm

- $F(i, j)$= optimal local similarity among suffixes $A(1 : i)$ and $B(1 : j)$
- Recurrence relation
  - $F(i, 0) = 0$
  - $F(0, j) = 0$
  - F(i,j) = max $\begin{cases} 0 \\ F(i, j-1) + s(-, B(j)) \\ F(i-1, j) + s(A(i), -) \\ F(i-1, j-1) + s(A(i), B(j)) \end{cases}$

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Example

Q = E Q L L K A L E F K L P = K V L E F G Y

Linear gap model

Gap= -1
Match= 4
Mismatch= -2

	–	E	Q	L	L	K	A	L	E	F	K	L
–												
K												
V												
L												
E												
F												
G												
Y												

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F(i,0) = 0
F(0,j) = 0

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–	0	0	0	0	0	0	0	0	0	0	0	0
K	0											
V	0											
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Algorithm

F(i, j) = max [0, F(i,j-1) + s(-,Q(j)),F(i-1,j) + s(P(i),-),F(i-1,j-1) + s(P(i),Q(j)]

	–	E	Q	L	L	K	A	L	E	F	K	L
–	0	0	0	0	0	0	0	0	0	0	0	0
K	0	0										
V	0											
L	0											
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–	0	0	0	0	0	0	0	0	0	0	0	0
K	0	0	0									
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K	0	0	0	0								
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	–	E	Q	L	L	K	A	L	E	F	K	L
–	0	0	0	0	0	0	0	0	0	0	0	0
K	0	0	0	0	0	4						
V	0											
L	0											
E	0											
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	–	E	Q	L	L	K	A	L	E	F	K	L
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K	0	0	0	0	0	4	3	2	1	0	4	3
V	0											
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K	0	0	0	0	0	4	3	2	1	0	4	3
V	0	0	0	0	0	3	2	1	0	0	3	2
L	0	0	0	4	4	3	2	6	5	4	3	7
E	0	4	3	3	3	2	1	5	10	9	8	7
F	0	3	2	2	2	1	0	4	9	14	13	12
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Alignment

Q: . . . . . F
P: . . . . . F

	–	E	Q	L	L	K	A	L	E	F	K	L
–	0	0	0	0	0	0	0	0	0	0	0	0
K	0	0	0	0	0	4	3	2	1	0	4	3
V	0	0	0	0	0	3	2	1	0	0	3	2
L	0	0	0	4	4	3	2	6	5	4	3	7
E	0	4	3	3	3	2	1	5	10	9	8	7
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K	0	0	0	0	0	4	3	2	1	0	4	3
V	0	0	0	0	0	3	2	1	0	0	3	2
L	0	0	0	4	4	3	2	6	5	4	3	7
E	0	4	3	3	3	2	1	5	10	9	8	7
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K	0	0	0	0	0	4	3	2	1	0	4	3
V	0	0	0	0	0	3	2	1	0	0	3	2
L	0	0	0	4	4	3	2	6	5	4	3	7
E	0	4	3	3	3	2	1	5	10	9	8	7
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	–	E	Q	L	L	K	A	L	E	F	K	L
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K	0	0	0	0	0	4	3	2	1	0	4	3
V	0	0	0	0	0	3	2	1	0	0	3	2
L	0	0	0	4	4	3	2	6	5	4	3	7
E	0	4	3	3	3	2	1	5	10	9	8	7
F	0	3	2	2	2	1	0	4	9	14	13	12
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K	0	0	0	0	0	4	3	2	1	0	4	3
V	0	0	0	0	0	3	2	1	0	0	3	2
L	0	0	0	4	4	3	2	6	5	4	3	7
E	0	4	3	3	3	2	1	5	10	9	8	7
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K	0	0	0	0	0	4	3	2	1	0	4	3
V	0	0	0	0	0	3	2	1	0	0	3	2
L	0	0	0	4	4	3	2	6	5	4	3	7
E	0	4	3	3	3	2	1	5	10	9	8	7
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V	0	0	0	0	0	3	2	1	0	0	3	2
L	0	0	0	4	4	3	2	6	5	4	3	7
E	0	4	3	3	3	2	1	5	10	9	8	7
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P: K V - L E F

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K	0	0	0	0	0	4	3	2	1	0	4	3
V	0	0	0	0	0	3	2	1	0	0	3	2
L	0	0	0	4	4	3	2	6	5	4	3	7
E	0	4	3	3	3	2	1	5	10	9	8	7
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K	0	0	0	0	0	4	3	2	1	0	4	3
V	0	0	0	0	0	3	2	1	0	0	3	2
L	0	0	0	4	4	3	2	6	5	4	3	7
E	0	4	3	3	3	2	1	5	10	9	8	7
F	0	3	2	2	2	1	0	4	9	14	13	12
G	0	2	1	1	1	0	0	3	8	13	12	11
Y	0	1	0	0	0	0	0	2	7	12	11	10

References

- https://ocw.metu.edu.tr/course/view.php?id=37
- https://www.cs.cmu.edu/ ckingsf/bioinfo-lectures/local.pdf

Thank you

Stay Home, Stay Safe