Mansoura University
Faculty of Computers and Information
Department of Computer Science
First Semester: 2020-2021

[MED121] Bioinformatics: Sequence Alignment Algorithms

Grade: Third Year (Medical Informatics Program)

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AGENDA

- Sequence Alignment
- Scoring Metrics
- Local Vs. Global Alignments
- Pairwise Vs. Multiple Alignments
- Needleman-Wunsch algorithm
- Smith-Waterman algorithm

SEQUENCING TECHNOLOGIES

ps://www.biocompare.com/23967-Ne

https://ngisweden.scilifelab.se/technologies/pacific-biosciences/pacbio-sequel/

https://www.technologyreview.com/2016/02/24/8993/with-patent-suit-illumina-looks-to-tame-emerging-british-rival-oxford-nanopore/

NOTES

Reads

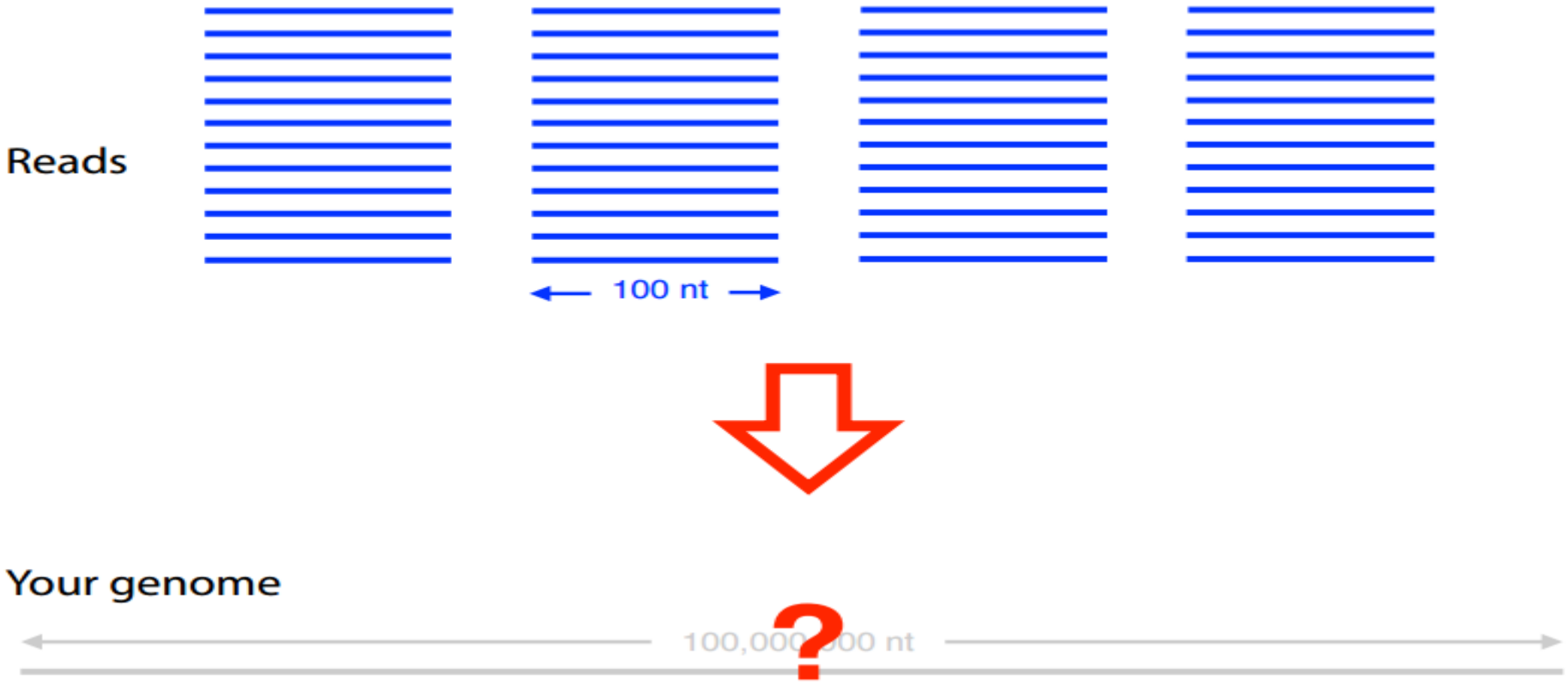
GTATGCACGCGATAG	TATGTCGCAGTATCT	CACCCTATGTCGCAG	GAGACGCTGGAGCCG
TAGCATTGCGAGACG	GGTATGCACGCGATA	TGGAGCCGGAGCACC	CGCTGGAGCCGGAGC
TGTCTTTGATTCCTG	CGCGATAGCATTGCG	GCATTGCGAGACGCT	CCTATGTCGCAGTAT
GACGCTGGAGCCGGA	GCACCCTATGTCGCA	GTATCTGTCTTTGAT	CCTCATCCTATTATT
TATCGCACCTACGTT	CAATATTCGATCATG	GATCACAGGTCTATC	ACCCTATTAACCACT
CACGGGAGCTCTCCA	TGCATTTGGTATTTT	CGTCTGGGGGGTATG	CACGCGATAGCATTG
GTATGCACGCGATAG	ACCTACGTTCAATAT	TATTTATCGCACCTA	CCACTCACGGGAGCT
GCGAGACGCTGGAGC	CTATCACCCTATTAA	CTGTCTTTGATTCCT	ACTCACGGGAGCTCT
CCTACGTTCAATATT	GCACCTACGTTCAAT	GTCTGGGGGGTATGC	AGCCGGAGCACCCTA
GACGCTGGAGCCGGA	GCACCCTATGTCGCA	GTATCTGTCTTTGAT	CCTCATCCTATTATT
TATCGCACCTACGTT	CAATATTCGATCATG	GATCACAGGTCTATC	ACCCTATTAACCACT
CACGGGAGCTCTCCA	TGCATTTGGTATTTT	CGTCTGGGGGGTATG	CACGCGATAGCATTG

Your genome

CGTCTGGGGGGTATGCACGCGATAGCATTGCGAGACGCTGGAGCCGGAGCACCCTATGTCGCAGTATCTGTCTTTGATTCCTG

Slide Credit: Ben Langmead course of Algorithms for DNA Sequencing

NOTES

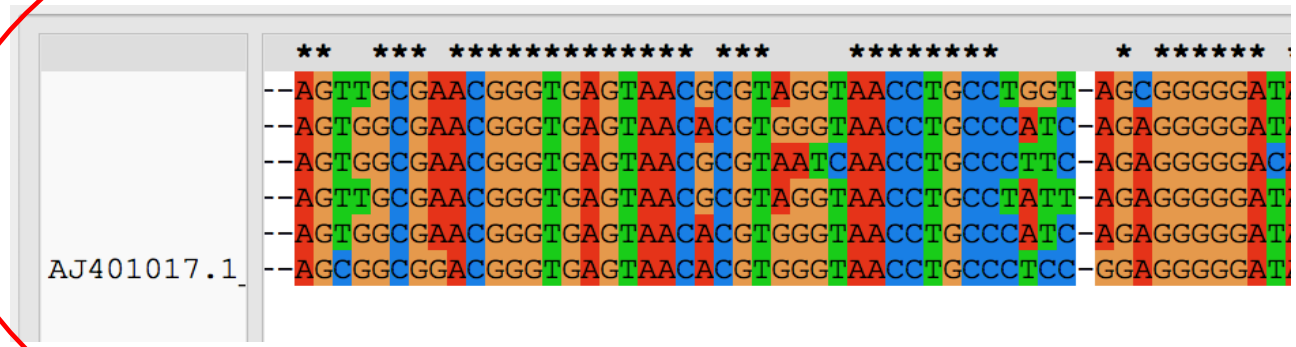


Slide Credit: Ben Langmead course of Algorithms for DNA Sequencing

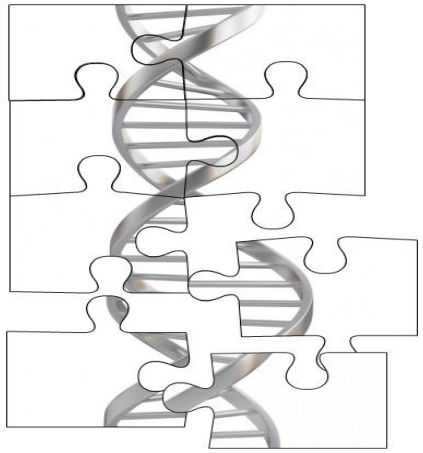
What is Next?

Sequence Analysis

Alignment



Assembly



Sequence alignment

Sequencing Reads

Reference Genome

Slide Credit: Ben Langmead course of Algorithms for DNA Sequencing

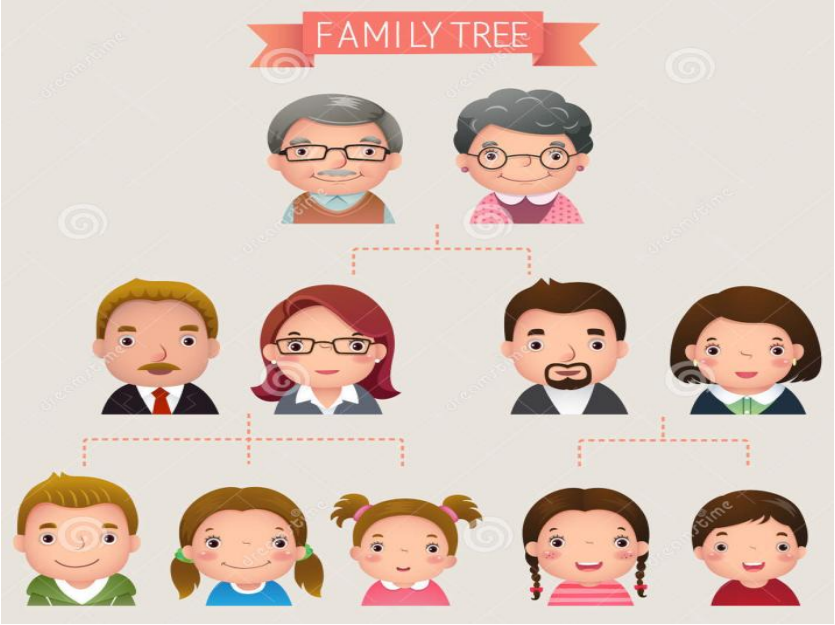
Sequence alignment

- **Sequence alignment** or sequence comparison lies at heart of the bioinformatics, which describes the way of arrangement of DNA/RNA or protein sequences, in order to identify the regions of similarity among them.

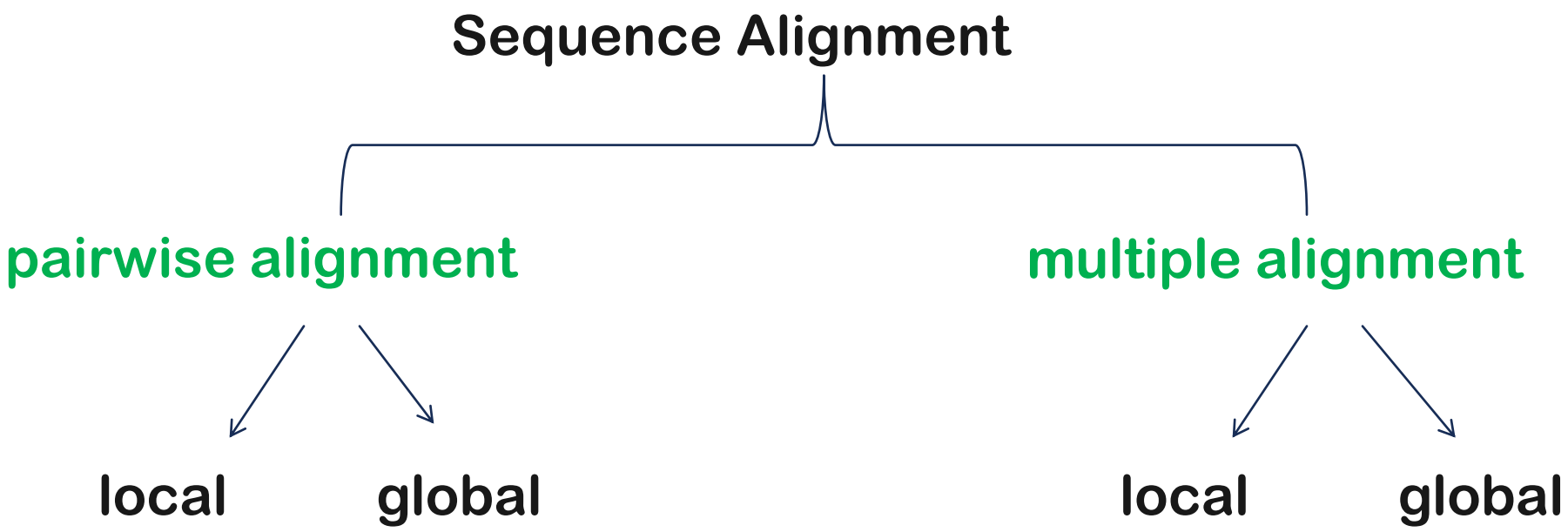
- **Causes for sequence (dis) similarity**:
  - Mutation or substitution (i.e. ACT → AGT)
  - Insertion (i.e. ACT → ACGT)
  - Deletion (i.e. ACT → AT)
  - Indels (Insertion/Deletion)

Sequence alignment (Why)

- Predicting functions.
- Database searching.
- Gene finding.
- Sequence evolutionary.



Sequence alignment



Sequence alignment

- Try to align these two sequences: AGTCTT, ATCT?

```
AGTCTT
A-TCT-
```

  - Is there a better alignment? How can we compare the “goodness” of two alignments?

scoring an alignment

- Simple scoring scheme is **Identity score** which is defined by the following equation:

$$id(x, y) = \begin{cases} 1 & \text{if } x = y \\ 0 & \text{if } x \neq y \end{cases}$$

```
AGTCTT
A-TCT-
1+0+1+1+1+0 = 4
```

alignment score= 4

(4/6)%= 67% identical

scoring matrix

- Simple scoring scheme is **Identity score** which is defined by the following equation:

$$id(x, y) = \begin{cases} 1 & \text{if } x = y \\ 0 & \text{if } x \neq y \end{cases}$$

as a matrix

	x	y
x	1	0
y	0	1

If amino acids are used? RNA seq? DNA seq?

	A	C	G	T
A	1	0	0	0
C	0	1	0	0
G	0	0	1	0
T	0	0	0	1

Identity Score (problems)

```
ATCG
ATTG
```

```
ATCG
ATTG
```

alignment score= 3

```
AT-CG
ATT-G
```

alignment score= 3

```
ATCTA
ATTTTTA
```

```
ATC--TA
ATTTTTA
```

alignment score= 4

```
AT-C-TA
ATTTTTA
```

alignment score= 4

substitution matrix

	A	C	G	T
A	2	-1	1	-1
C	-1	2	-1	1
G	1	-1	2	-1
T	-1	1	-1	2

Purines

Pyrimidine

substitution matrix

- A protein substitution matrix can be based on any property of amino acids: size, polarity, charge, etc.

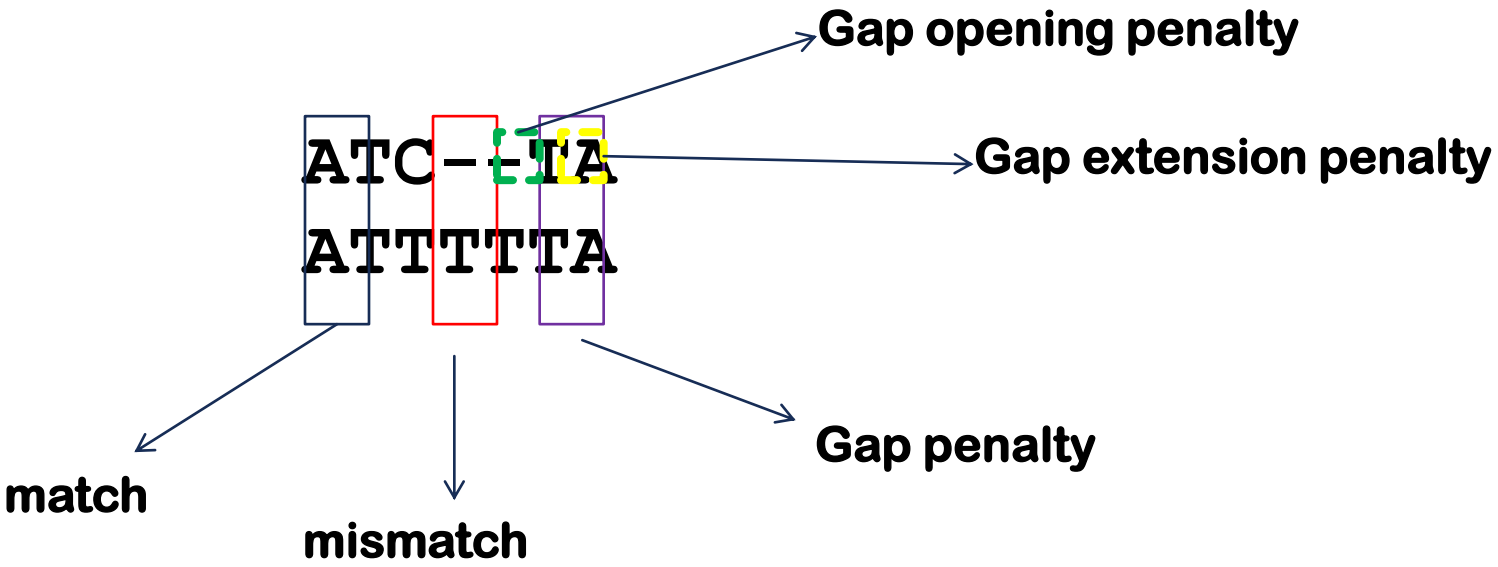
- In practice the most important are evolutionary substitution matrices:
  - PAM (”point accepted mutation”) family PAM250, PAM120, etc.
  - BLOSUM (”Blocks substitution matrix”) family BLOSUM62, BLOSUM50, etc.
  - The substitution scores of both PAM and BLOSUM matrices are derived from the analysis of known alignments of closely related proteins.

substitution matrix (blosum62)

	A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V	B	Z	X	*
A	4	-1	-2	-2	0	-1	-1	0	-2	-1	-1	-1	-1	-2	-1	1	0	-3	-2	0	-2	-1	0	-4
R	-1	5	0	-2	-3	1	0	-2	0	-3	-2	2	-1	-3	-2	-1	-1	-3	-2	-3	-1	0	-1	-4
N	-2	0	6	1	-3	0	0	0	1	-3	-3	0	-2	-3	-2	1	0	-4	-2	-3	3	0	-1	-4
D	-2	-2	1	6	-3	0	2	-1	-1	-3	-4	-1	-3	-3	-1	0	-1	-4	-3	-3	4	1	-1	-4
C	0	-3	-3	-3	9	-3	-4	-3	-3	-1	-1	-3	-1	-2	-3	-1	-1	-2	-2	-1	-3	-3	-2	-4
Q	-1	1	0	0	-3	5	2	-2	0	-3	-2	1	0	-3	-1	0	-1	-2	-1	-2	0	3	-1	-4
E	-1	0	0	2	-4	2	5	-2	0	-3	-3	1	-2	-3	-1	0	-1	-3	-2	-2	1	4	-1	-4
G	0	-2	0	-1	-3	-2	-2	6	-2	-4	-4	-2	-3	-3	-2	0	-2	-2	-3	-3	-1	-2	-1	-4
H	-2	0	1	-1	-3	0	0	-2	8	-3	-3	-1	-2	-1	-2	-1	-2	-2	2	-3	0	0	-1	-4
I	-1	-3	-3	-3	-1	-3	-3	-4	-3	4	2	-3	1	0	-3	-2	-1	-3	-1	3	-3	-3	-1	-4
L	-1	-2	-3	-4	-1	-2	-3	-4	-3	2	4	-2	2	0	-3	-2	-1	-2	-1	1	-4	-3	-1	-4
K	-1	2	0	-1	-3	1	1	-2	-1	-3	-2	5	-1	-3	-1	0	-1	-3	-2	-2	0	1	-1	-4
M	-1	-1	-2	-3	-1	0	-2	-3	-2	1	2	-1	5	0	-2	-1	-1	-1	-1	1	-3	-1	-1	-4
F	-2	-3	-3	-3	-2	-3	-3	-3	-1	0	0	-3	0	6	-4	-2	-2	1	3	-1	-3	-3	-1	-4
P	-1	-2	-2	-1	-3	-1	-1	-2	-2	-3	-3	-1	-2	-4	7	-1	-1	-4	-3	-2	-2	-1	-2	-4
S	1	-1	1	0	-1	0	0	0	-1	-2	-2	0	-1	-2	-1	4	1	-3	-2	-2	0	0	0	-4
T	0	-1	0	-1	-1	-1	-1	-2	-2	-1	-1	-1	-1	-2	-1	1	5	-2	-2	0	-1	-1	0	-4
W	-3	-3	-4	-4	-2	-2	-3	-2	-2	-3	-2	-3	-1	1	-4	-3	-2	11	2	-3	-4	-3	-2	-4
Y	-2	-2	-2	-3	-2	-1	-2	-3	2	-1	-1	-2	-1	3	-3	-2	-2	2	7	-1	-3	-2	-1	-4
V	0	-3	-3	-3	-1	-2	-2	-3	-3	3	1	-2	1	-1	-2	-2	0	-3	-1	4	-3	-2	-1	-4
B	-2	-1	3	4	-3	0	1	-1	0	-3	-4	0	-3	-3	-2	0	-1	-4	-3	-3	4	1	-1	-4
Z	-1	0	0	1	-3	3	4	-2	0	-3	-3	1	-1	-3	-1	0	-1	-3	-2	-2	1	4	-1	-4
X	0	-1	-1	-1	-2	-1	-1	-1	-1	-1	-1	-1	-1	-1	-2	0	0	-2	-1	-1	-1	-1	-1	-4
*	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	1

Image credit: https://www.ncbi.nlm.nih.gov/Class/FieldGuide/BLOSUM62.txt

scoring scheme updated!



Gap Scoring Scheme (Linear)

```
ATC---TA
ATTTTTTA
```

match(1), mismatch(-1), gap(-1)

gap penalty * gap length (L)

= -1 * 3 = - 3

Total similarity score:

= -3 +4 -1=0

Gap Scoring Scheme (Affine)

```
ATC---TA
ATTTTTTA
```

match(1), mismatch(-1),
gap opening (-2), gap extension (- 4)

gap opening penalty + (gap length (L)* gap extension penalty)

= -2 + (2*-4)= -2-8=-10

Total similarity score:

= 4 – 1 - 10= -7

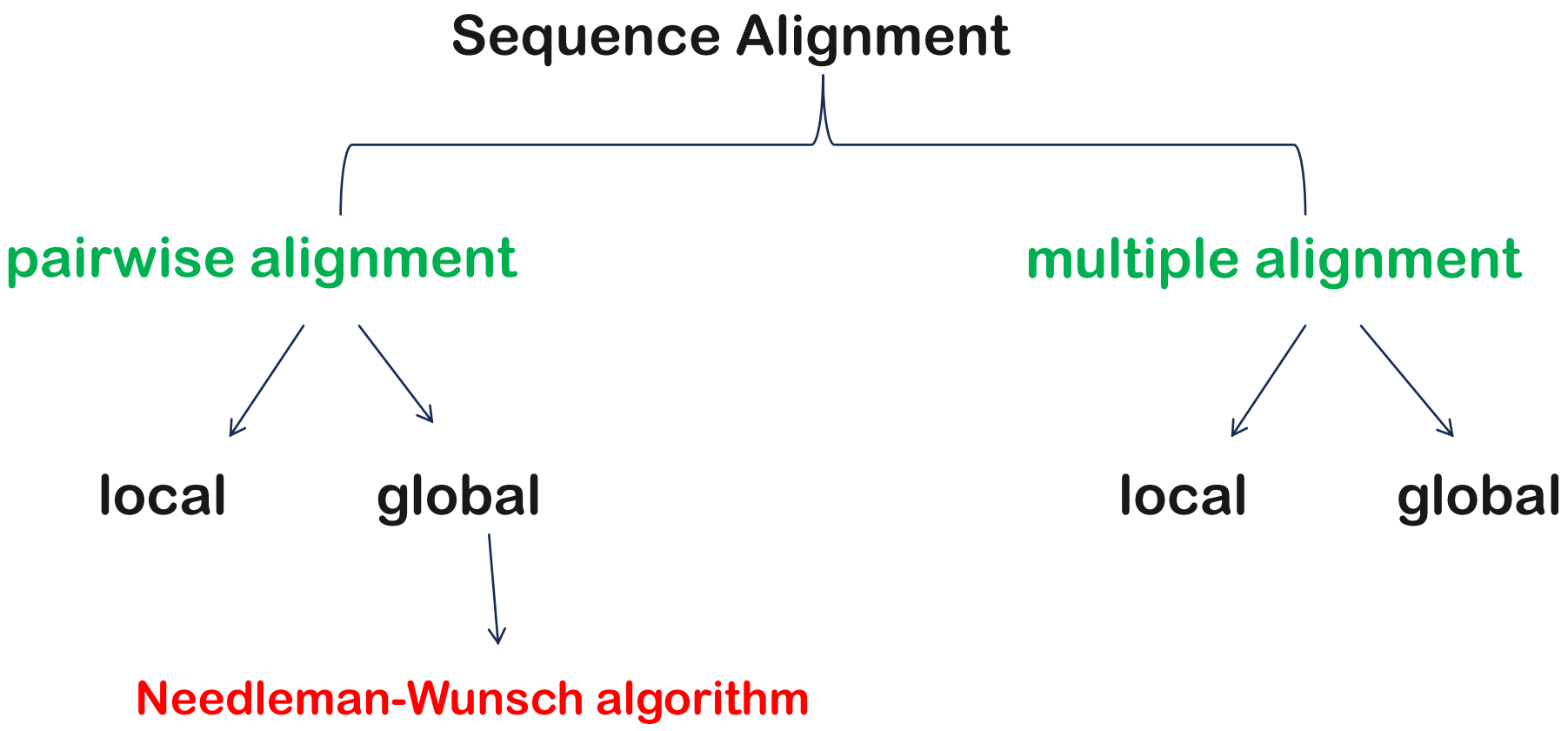
Gap Scoring Scheme (Affine : Q)

```
GAATTCCGTTA
GGAT-C-G--A
```

match(2), mismatch(-1),
gap opening (-2), gap extension (-3)

Total similarity score:
2-1+2+2-2+2-2+2-2-3+2= 2

Sequence alignment



Needleman Wunch algorithm

- It is global pairwise sequence alignment algorithm.

- You need to know:
  - Sequences that you will align.
  - Scoring scheme that you will use.

Needleman Wunch algorithm

- **Example**: Suppose you have two sequences:
  - S1=GATTACA
  - S2=GCATGCT
  - Match (+1), mismatch(-1), Linear Gap Model (-1)
    - **Length of S1=m=7chars.**
    - **Length of S2=n=7chars.**
    - **Create a matrix of rows (m+1) and columns (n+1)**

Needleman Wunch algorithm

S1=GATTACA
S2=GCATGCT

Match (+1), mismatch(-1), Linear Gap Model (-1)

column number

row number

S2, # n+1 columns

S1, # m+1 rows

		G	C	A	T	G	C	T
	i,j							
G								
A								
T								
T								
A								
C								
A								

Needleman Wunch algorithm

S1=GATTACA
S2=GCATGCT

Match (+1), mismatch(-1), Linear Gap Model (-1)

Step 1: Fill all (i,0) with i * Gap score

		G	C	A	T	G	C	T
	0,0	0,1	0,2	0,3	0,4	0,5	0,6	0,7
G	1,0 −1							
A	2,0 −2							
T	3,0 −3							
T	4,0 −4							
A	5,0 −5							
C	6,0 −6							
A	7,0 −7							

Needleman Wunch algorithm

S1=GATTACA
S2=GCATGCT

Match (+1), mismatch(-1), Linear Gap Model (-1)

Step 2: Fill all (0,j) with j * Gap score

		G	C	A	T	G	C	T
	0,0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1							
A	2,0 −2							
T	3,0 −3							
T	4,0 −4							
A	5,0 −5							
C	6,0 −6							
A	7,0 −7							

Needleman Wunch algorithm

S1=GATTACA
S2=GCATGCT

Match (+1), mismatch(-1), Linear Gap Model (-1)

Step 3: Fill (0,0) with 0

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1							
A	2,0 −2							
T	3,0 −3							
T	4,0 −4							
A	5,0 −5							
C	6,0 −6							
A	7,0 −7							

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1, j-1) + score(ch1, ch2) \\ (i, j-1) + gap\ score \\ (i-1, j) + gap\ score \end{Bmatrix}$$

$$cell\ (1,1) = max\begin{Bmatrix} (0,0) + score(G, G) \\ (1,0) + -1 \\ (0,1) + -1 \end{Bmatrix}$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1						
A	2,0 −2							
T	3,0 −3							
T	4,0 −4							
A	5,0 −5							
C	6,0 −6							
A	7,0 −7							

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$cell\ (1,1) = max\begin{Bmatrix} (0,0) + score(G,G) \\ (1,0) + -1 \\ (0,1) + -1 \end{Bmatrix}$$

$$cell\ (1,1) = max\begin{Bmatrix} 0 + 1 \\ -1 + -1 \\ -1 + -1 \end{Bmatrix} = 1$$

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

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$cell\ (1,1) = max\begin{Bmatrix} (0,0) + score(G,G) \\ (1,0) + -1 \\ (0,1) + -1 \end{Bmatrix}$$

$$cell\ (1,1) = max\begin{Bmatrix} 0 + 1 \\ -1 + -1 \\ -1 + -1 \end{Bmatrix} = 1$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1						
A	2,0 −2							
T	3,0 −3							
T	4,0 −4							
A	5,0 −5							
C	6,0 −6							
A	7,0 −7							

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix}(i-1,j-1) + score(ch1,ch2)\\ (i,j-1) + gap\ score\\ (i-1,j) + gap\ score\end{Bmatrix}$$

$$cell\ (1,2) = max\begin{Bmatrix}(0,1) + score(G,C)\\ (1,1) + -1\\ (0,2) + -1\end{Bmatrix}$$

$$cell\ (1,2) = max\begin{Bmatrix}-1 + -1\\ 1 + -1\\ -2 + -1\end{Bmatrix} = 0$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0					
A	2,0 −2							
T	3,0 −3							
T	4,0 −4							
A	5,0 −5							
C	6,0 −6							
A	7,0 −7							

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix}(i-1,j-1) + score(ch1,ch2)\\ (i,j-1) + gap\ score\\ (i-1,j) + gap\ score\end{Bmatrix}$$

$$cell\ (1,2) = max\begin{Bmatrix}-2 + -1\\ 0 + -1\\ -3 + -1\end{Bmatrix} = -1$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1				
A	2,0 −2							
T	3,0 −3							
T	4,0 −4							
A	5,0 −5							
C	6,0 −6							
A	7,0 −7							

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1,j-1) + score(ch1,ch2) \\ (i,j-1) + gap\ score \\ (i-1,j) + gap\ score \end{Bmatrix}$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	−3	−4	−5
A	2,0 −2							
T	3,0 −3							
T	4,0 −4							
A	5,0 −5							
C	6,0 −6							
A	7,0 −7							

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1,j-1) + score(ch1,ch2) \\ (i,j-1) + gap\ score \\ (i-1,j) + gap\ score \end{Bmatrix}$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3							
T	4,0 −4							
A	5,0 −5							
C	6,0 −6							
A	7,0 −7							

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1,j-1) + score(ch1,ch2) \\ (i,j-1) + gap\ score \\ (i-1,j) + gap\ score \end{Bmatrix}$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1						
T	4,0 −4	−2						
A	5,0 −5	−3						
C	6,0 −6	−4						
A	7,0 −7	−5						

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1,j-1) + score(ch1,ch2) \\ (i,j-1) + gap\ score \\ (i-1,j) + gap\ score \end{Bmatrix}$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1					
T	4,0 −4	−2	−2					
A	5,0 −5	−3	−3					
C	6,0 −6	−4	−2					
A	7,0 −7	−5	−3					

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1,j-1) + score(ch1,ch2) \\ (i,j-1) + gap\ score \\ (i-1,j) + gap\ score \end{Bmatrix}$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2					
A	5,0 −5	−3	−3					
C	6,0 −6	−4	−2					
A	7,0 −7	−5	−3					

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1,j-1) + score(ch1,ch2) \\ (i,j-1) + gap\ score \\ (i-1,j) + gap\ score \end{Bmatrix}$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1				
A	5,0 −5	−3	−3	−1				
C	6,0 −6	−4	−2	−2				
A	7,0 −7	−5	−3	−1				

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1,j-1) + score(ch1,ch2) \\ (i,j-1) + gap\ score \\ (i-1,j) + gap\ score \end{Bmatrix}$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1			
A	5,0 −5	−3	−3	−1	0			
C	6,0 −6	−4	−2	−2	−1			
A	7,0 −7	−5	−3	−1	−2			

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1,j-1) + score(ch1,ch2) \\ (i,j-1) + gap\ score \\ (i-1,j) + gap\ score \end{Bmatrix}$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	
A	5,0 −5	−3	−3	−1	0	0	0	
C	6,0 −6	−4	−2	−2	−1	−1	1	
A	7,0 −7	−5	−3	−1	−2	−2	0	

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1,j-1) + score(ch1,ch2) \\ (i,j-1) + gap\ score \\ (i-1,j) + gap\ score \end{Bmatrix}$$

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	1
A	5,0 −5	−3	−3	−1	0	0	0	0
C	6,0 −6	−4	−2	−2	−1	−1	1	0
A	7,0 −7	−5	−3	−1	−2	−2	0	0

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

$$for\ cell\ (i,j) = max\begin{Bmatrix} (i-1,j-1) + score(ch1,ch2) \\ (i,j-1) + gap\ score \\ (i-1,j) + gap\ score \end{Bmatrix}$$

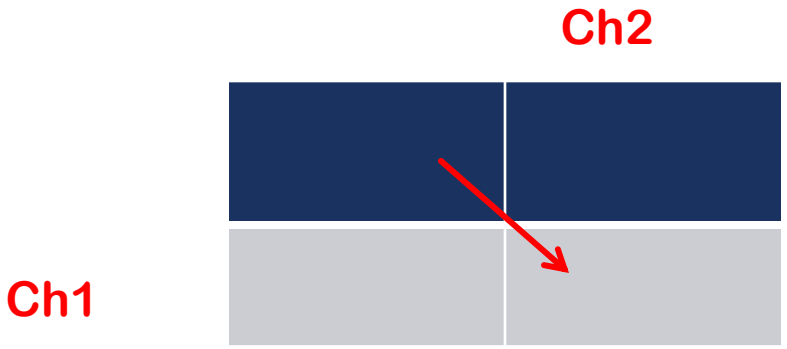
Similarity Score will be 0

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	1
A	5,0 −5	−3	−3	−1	0	0	0	0
C	6,0 −6	−4	−2	−2	−1	−1	1	0
A	7,0 −7	−5	−3	−1	−2	−2	0	0

Match (+1), mismatch(-1), Linear Gap Model (-1)

Needleman Wunch algorithm

- To compute the global alignment, we need to trace back the matrix.
- Start from the bottom right corner and follow the arrows back.



Needleman Wunch algorithm

- To compute the global alignment, we need to trace back the matrix.
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Needleman Wunch algorithm

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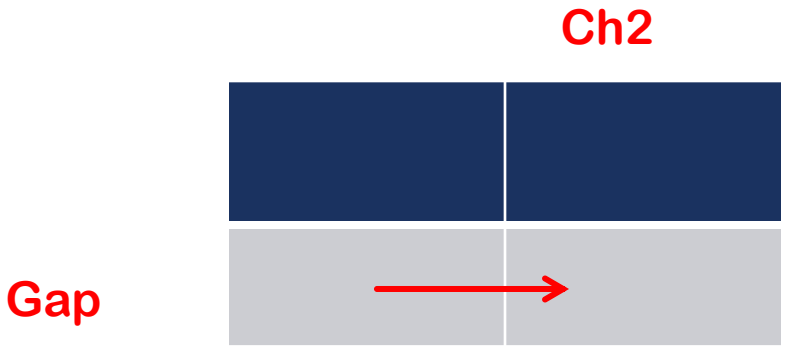
- Start from the bottom right corner and follow the arrows back.



Needleman Wunch algorithm

A

T

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	1
A	5,0 −5	−3	−3	−1	0	0	0	0
C	6,0 −6	−4	−2	−2	−1	−1	1	0
A	7,0 −7	−5	−3	−1	−2	−2	0	0

Needleman Wunch algorithm

CA

CT

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	1
A	5,0 −5	−3	−3	−1	0	0	0	0
C	6,0 −6	−4	−2	−2	−1	−1	1	0
A	7,0 −7	−5	−3	−1	−2	−2	0	0

Needleman Wunch algorithm

ACA

GCT

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	1
A	5,0 −5	−3	−3	−1	0	0	0	0
C	6,0 −6	−4	−2	−2	−1	−1	1	0
A	7,0 −7	−5	−3	−1	−2	−2	0	0

Needleman Wunch algorithm

TACA

TGCT

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	1
A	5,0 −5	−3	−3	−1	0	0	0	0
C	6,0 −6	−4	−2	−2	−1	−1	1	0
A	7,0 −7	−5	−3	−1	−2	−2	0	0

Needleman Wunch algorithm

TTACA

-TGCT

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	1
A	5,0 −5	−3	−3	−1	0	0	0	0
C	6,0 −6	−4	−2	−2	−1	−1	1	0
A	7,0 −7	−5	−3	−1	−2	−2	0	0

Needleman Wunch algorithm

ATTACA

A-TGCT

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	1
A	5,0 −5	−3	−3	−1	0	0	0	0
C	6,0 −6	−4	−2	−2	−1	−1	1	0
A	7,0 −7	−5	−3	−1	−2	−2	0	0

Needleman Wunch algorithm

-ATTACA

CA-TGCT

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	1
A	5,0 −5	−3	−3	−1	0	0	0	0
C	6,0 −6	−4	−2	−2	−1	−1	1	0
A	7,0 −7	−5	−3	−1	−2	−2	0	0

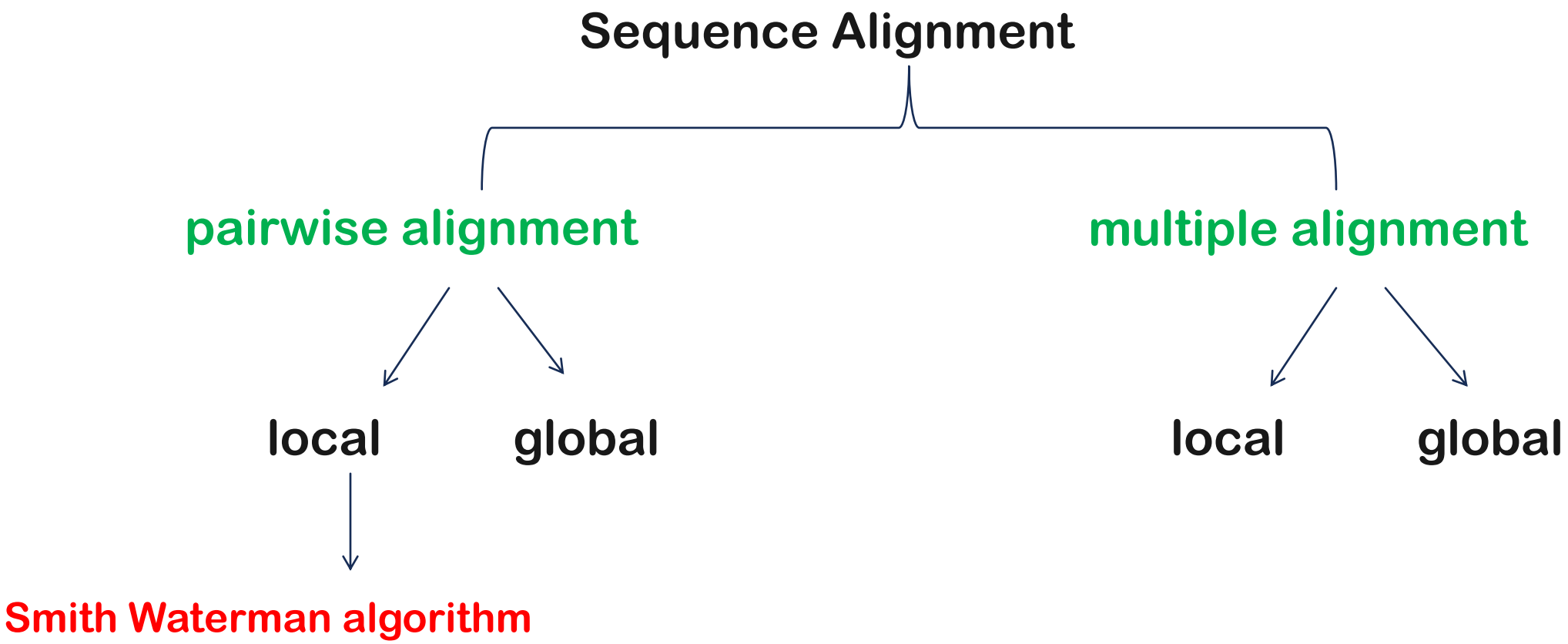
Needleman Wunch algorithm

G-ATTACA

GCA-TGCT

		G	C	A	T	G	C	T
	0,0 0	0,1 −1	0,2 −2	0,3 −3	0,4 −4	0,5 −5	0,6 −6	0,7 −7
G	1,0 −1	1,1 1	1,2 0	−1	−2	3	−4	−5
A	2,0 −2	0	0	1	0	−1	−2	−3
T	3,0 −3	−1	−1	0	2	1	0	−1
T	4,0 −4	−2	−2	−1	1	1	0	1
A	5,0 −5	−3	−3	−1	0	0	0	0
C	6,0 −6	−4	−2	−2	−1	−1	1	0
A	7,0 −7	−5	−3	−1	−2	−2	0	0

Sequence alignment



Smith Waterman algorithm

- **Example**: Suppose you have two sequences:
  - S1=GGTTGACTA
  - S2=TGTTACGG
  - Match (+3), mismatch(-3), Linear Gap Model (-2)
    - **Length of S1=m=9chars.**
    - **Length of S2=n=8chars.**
    - **Create a matrix of rows (m+1) and columns (n+1)**

Smith Waterman algorithm

S1=GGTTGACTA
S2=TGTTACGG
Match (+3), mismatch(-3), Linear Gap Model (-2)

Step 1: Fill all (i,0) with 0

		T	G	T	T	A	C	G	G
	0,0	0,1	0,2	0,3	0,4	0,5	0,6	0,7	0,8
G	1,0 0								
G	2,0 0								
T	3,0 0								
T	4,0 0								
G	5,0 0								
A	6,0 0								
C	7,0 0								
T	8,0 0								
A	9,0 0								

Smith Waterman algorithm

S1=GGTTGACTA
S2=TGTTACGG
Match (+3), mismatch(-3), Linear Gap Model (-2)

Step 1: Fill all (0,j) with 0

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0								
G	2,0 0								
T	3,0 0								
T	4,0 0								
G	5,0 0								
A	6,0 0								
C	7,0 0								
T	8,0 0								
A	9,0 0								

Smith Waterman algorithm

Match (+3), mismatch(-3), Linear Gap Model (-2)

$$cell(i,j) = max \begin{Bmatrix} (i-1, j-1) + score(ch1, ch2) \\ (i, j-1) + Gap\ Score \\ (i-1, j) + Gap\ Score \\ 0 \end{Bmatrix}$$

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0								
G	2,0 0								
T	3,0 0								
T	4,0 0								
G	5,0 0								
A	6,0 0								
C	7,0 0								
T	8,0 0								
A	9,0 0								

Smith Waterman algorithm

Match (+3), mismatch(-3), Linear Gap Model (-2)

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0	0							
G	2,0 0								
T	3,0 0								
T	4,0 0								
G	5,0 0								
A	6,0 0								
C	7,0 0								
T	8,0 0								
A	9,0 0								

Smith Waterman algorithm

Match (+3), mismatch(-3), Linear Gap Model (-2)

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0	0	3	1	0	0	0	3	3
G	2,0 0	0	3	1					
T	3,0 0								
T	4,0 0								
G	5,0 0								
A	6,0 0								
C	7,0 0								
T	8,0 0								
A	9,0 0								

Smith Waterman algorithm

Match (+3), mismatch(-3), Linear Gap Model (-2)

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0	0	3	1	0	0	0	3	3
G	2,0 0	0	3	1	0	0	0	3	6
T	3,0 0	3	1	6	4	2	0	1	4
T	4,0 0	3	1	4	9	7	5	3	2
G	5,0 0	1	6	4	7	6	4	8	6
A	6,0 0	0	4	3	5	10	8	6	5
C	7,0 0	0	2	1	3	8	13	11	9
T	8,0 0	3	1	5	4	6	11	10	8
A	9,0 0	1	0	3	2	7	9	8	7

Smith Waterman algorithm

Match (+3), mismatch(-3), Linear Gap Model (-2)

C

C

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0	0	3	1	0	0	0	3	3
G	2,0 0	0	3	1	0	0	0	3	6
T	3,0 0	3	1	6	4	2	0	1	4
T	4,0 0	3	1	4	9	7	5	3	2
G	5,0 0	1	6	4	7	6	4	8	6
A	6,0 0	0	4	3	5	10	8	6	5
C	7,0 0	0	2	1	3	8	13	11	9
T	8,0 0	3	1	5	4	6	11	10	8
A	9,0 0	1	0	3	2	7	9	8	7

Smith Waterman algorithm

Match (+3), mismatch(-3), Linear Gap Model (-2)

AC

AC

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0	0	3	1	0	0	0	3	3
G	2,0 0	0	3	1	0	0	0	3	6
T	3,0 0	3	1	6	4	2	0	1	4
T	4,0 0	3	1	4	9	7	5	3	2
G	5,0 0	1	6	4	7	6	4	8	6
A	6,0 0	0	4	3	5	10	8	6	5
C	7,0 0	0	2	1	3	8	13	11	9
T	8,0 0	3	1	5	4	6	11	10	8
A	9,0 0	1	0	3	2	7	9	8	7

Smith Waterman algorithm

Match (+3), mismatch(-3), Linear Gap Model (-2)

GAC

-AC

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0	0	3	1	0	0	0	3	3
G	2,0 0	0	3	1	0	0	0	3	6
T	3,0 0	3	1	6	4	2	0	1	4
T	4,0 0	3	1	4	9	7	5	3	2
G	5,0 0	1	6	4	7	6	4	8	6
A	6,0 0	0	4	3	5	10	8	6	5
C	7,0 0	0	2	1	3	8	13	11	9
T	8,0 0	3	1	5	4	6	11	10	8
A	9,0 0	1	0	3	2	7	9	8	7

Smith Waterman algorithm

Match (+3), mismatch(-3), Linear Gap Model (-2)

TGAC

T-AC

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0	0	3	1	0	0	0	3	3
G	2,0 0	0	3	1	0	0	0	3	6
T	3,0 0	3	1	6	4	2	0	1	4
T	4,0 0	3	1	4	9	7	5	3	2
G	5,0 0	1	6	4	7	6	4	8	6
A	6,0 0	0	4	3	5	10	8	6	5
C	7,0 0	0	2	1	3	8	13	11	9
T	8,0 0	3	1	5	4	6	11	10	8
A	9,0 0	1	0	3	2	7	9	8	7

Smith Waterman algorithm

Match (+3), mismatch(-3), Linear Gap Model (-2)

TTGAC

TT-AC

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0	0	3	1	0	0	0	3	3
G	2,0 0	0	3	1	0	0	0	3	6
T	3,0 0	3	1	6	4	2	0	1	4
T	4,0 0	3	1	4	9	7	5	3	2
G	5,0 0	1	6	4	7	6	4	8	6
A	6,0 0	0	4	3	5	10	8	6	5
C	7,0 0	0	2	1	3	8	13	11	9
T	8,0 0	3	1	5	4	6	11	10	8
A	9,0 0	1	0	3	2	7	9	8	7

Smith Waterman algorithm

Match (+3), mismatch(-3), Linear Gap Model (-2)

GTTGAC

GTT-AC

		T	G	T	T	A	C	G	G
	0,0 0	0,1 0	0,2 0	0,3 0	0,4 0	0,5 0	0,6 0	0,7 0	0,8 0
G	1,0 0	0	3	1	0	0	0	3	3
G	2,0 0	0	3	1	0	0	0	3	6
T	3,0 0	3	1	6	4	2	0	1	4
T	4,0 0	3	1	4	9	7	5	3	2
G	5,0 0	1	6	4	7	6	4	8	6
A	6,0 0	0	4	3	5	10	8	6	5
C	7,0 0	0	2	1	3	8	13	11	9
T	8,0 0	3	1	5	4	6	11	10	8
A	9,0 0	1	0	3	2	7	9	8	7

Thank you!