Global alignment
vs
Local alignment

Group 1

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Background

- Why alignment?

  “Nothing in Biology Makes Sense Except in the Light of Evolution”

  ——T.Dobzhansky,1973

- Why computer arithmetic?

- Why dynamic programming?

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A													
J													
C													
J													
N													
R													
C													
K													
C													
R													
B													
P													

(modified from fig.1 of Needleman&Wunsch,1970)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	1	0	0	0	0	0	0	0	0	0	0	0	0
J	0	0	0	0	1	0	0	0	0	0	0	0	0
C	0	0	1	0	0	0	0	1	0	1	0	0	0
J	0	0	0	0	1	0	0	0	0	0	0	0	0
N	0	0	0	1	0	0	0	0	0	0	0	0	0
R	0	0	0	0	0	1	0	0	0	0	1	0	0
C	0	0	1	0	0	0	0	1	0	1	0	0	0
K	0	0	0	0	0	0	0	0	0	0	0	0	0
C	0	0	1	0	0	0	0	1	0	1	0	0	0
R	0	0	0	0	0	1	0	0	0	0	1	0	0
B	0	1	0	0	0	0	0	0	0	0	0	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	1												
J					1								
C			1					1		1			
J					1								
N				1									
R						1					1		
C			1					1		1			
K													
C			1					1		1			
R						1					1		
B		1											
P												1	

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	1												
J					1								
C			1					1		1			
J					1								
N				1									
R						1					1		
C			1					1		1			
K													
C			1					1		1			
R						1					1		
B		1											
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	1												
J					1								
C			1					1		1			
J					1								
N				1									
R						1					1		
C			1					1		1			
K													
C			1					1		1			
R						1					1		
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	1												
J					1								
C			1					1		1			
J					1								
N				1									
R						1	4	3	3	2	2	0	0
C	3	3	4	3	3	3	3	4	3	3	1	0	0
K	3	3	3	3	3	3	3	3	3	2	1	0	0
C	2	2	3	2	2	2	2	3	2	3	1	0	0
R	2	1	1	1	1	2	1	1	1	1	2	0	0
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	1												
J					1								
C			1					1		1			
J					1								
N				1									
R						1	4	3	3	2	2	0	0
C	3	3	4	3	3	3	3	4	3	3	1	0	0
K	3	3	3	3	3	3	3	3	3	2	1	0	0
C	2	2	3	2	2	2	2	3	2	3	1	0	0
R	2	1	1	1	1	2	1	1	1	1	2	0	0
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	1												
J					1								
C			1					1		1			
J					1								
N				1									
R						1	4	3	3	2	2	0	0
C	3	3	4	3	3	3	3	4	3	3	1	0	0
K	3	3	3	3	3	3	3	3	3	2	1	0	0
C	2	2	3	2	2	2	2	3	2	3	1	0	0
R	2	1	1	1	1	2	1	1	1	1	2	0	0
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	1												
J					1								
C			1					1		1			
J					1								
N				1									
R						5	4	3	3	2	2	0	0
C	3	3	4	3	3	3	3	4	3	3	1	0	0
K	3	3	3	3	3	3	3	3	3	2	1	0	0
C	2	2	3	2	2	2	2	3	2	3	1	0	0
R	2	1	1	1	1	2	1	1	1	1	2	0	0
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	8	7	6	6	5	4	4	3	3	2	1	0	0
J	7	7	6	6	6	4	4	3	3	2	1	0	0
C	6	6	7	6	5	4	4	4	3	3	1	0	0
J	6	6	6	5	6	4	4	3	3	2	1	0	0
N	5	5	5	6	5	4	4	3	3	2	1	0	0
R	4	4	4	4	4	5	4	3	3	2	2	0	0
C	3	3	4	3	3	3	3	4	3	3	1	0	0
K	3	3	3	3	3	3	3	3	3	2	1	0	0
C	2	2	3	2	2	2	2	3	2	3	1	0	0
R	2	1	1	1	1	2	1	1	1	1	2	0	0
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	8	7	6	6	5	4	4	3	3	2	1	0	0
J	7	7	6	6	6	4	4	3	3	2	1	0	0
C	6	6	7	6	5	4	4	4	3	3	1	0	0
J	6	6	6	5	6	4	4	3	3	2	1	0	0
N	5	5	5	6	5	4	4	3	3	2	1	0	0
R	4	4	4	4	4	5	4	3	3	2	2	0	0
C	3	3	4	3	3	3	3	4	3	3	1	0	0
K	3	3	3	3	3	3	3	3	3	2	1	0	0
C	2	2	3	2	2	2	2	3	2	3	1	0	0
R	2	1	1	1	1	2	1	1	1	1	2	0	0
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	8	7	6	6	5	4	4	3	3	2	1	0	0
J	7	7	6	6	6	4	4	3	3	2	1	0	0
C	6	6	7	6	5	4	4	4	3	3	1	0	0
J	6	6	6	5	6	4	4	3	3	2	1	0	0
N	5	5	5	6	5	4	4	3	3	2	1	0	0
R	4	4	4	4	4	5	4	3	3	2	2	0	0
C	3	3	4	3	3	3	3	4	3	3	1	0	0
K	3	3	3	3	3	3	3	3	3	2	1	0	0
C	2	2	3	2	2	2	2	3	2	3	1	0	0
R	2	1	1	1	1	2	1	1	1	1	2	0	0
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	8	7	6	6	5	4	4	3	3	2	1	0	0
J	7	7	6	6	6	4	4	3	3	2	1	0	0
C	6	6	7	6	5	4	4	4	3	3	1	0	0
J	6	6	6	5	6	4	4	3	3	2	1	0	0
N	5	5	5	6	5	4	4	3	3	2	1	0	0
R	4	4	4	4	4	5	4	3	3	2	2	0	0
C	3	3	4	3	3	3	3	4	3	3	1	0	0
K	3	3	3	3	3	3	3	3	3	2	1	0	0
C	2	2	3	2	2	2	2	3	2	3	1	0	0
R	2	1	1	1	1	2	1	1	1	1	2	0	0
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

	A	B	C	N	J	R	O	C	L	C	R	P	M
A	8	7	6	6	5	4	4	3	3	2	1	0	0
J	7	7	6	6	6	4	4	3	3	2	1	0	0
C	6	6	7	6	5	4	4	4	3	3	1	0	0
J	6	6	6	5	6	4	4	3	3	2	1	0	0
N	5	5	5	6	5	4	4	3	3	2	1	0	0
R	4	4	4	4	4	5	4	3	3	2	2	0	0
C	3	3	4	3	3	3	3	4	3	3	1	0	0
K	3	3	3	3	3	3	3	3	3	2	1	0	0
C	2	2	3	2	2	2	2	3	2	3	1	0	0
R	2	1	1	1	1	2	1	1	1	1	2	0	0
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Needleman-Wunsch Algorithm

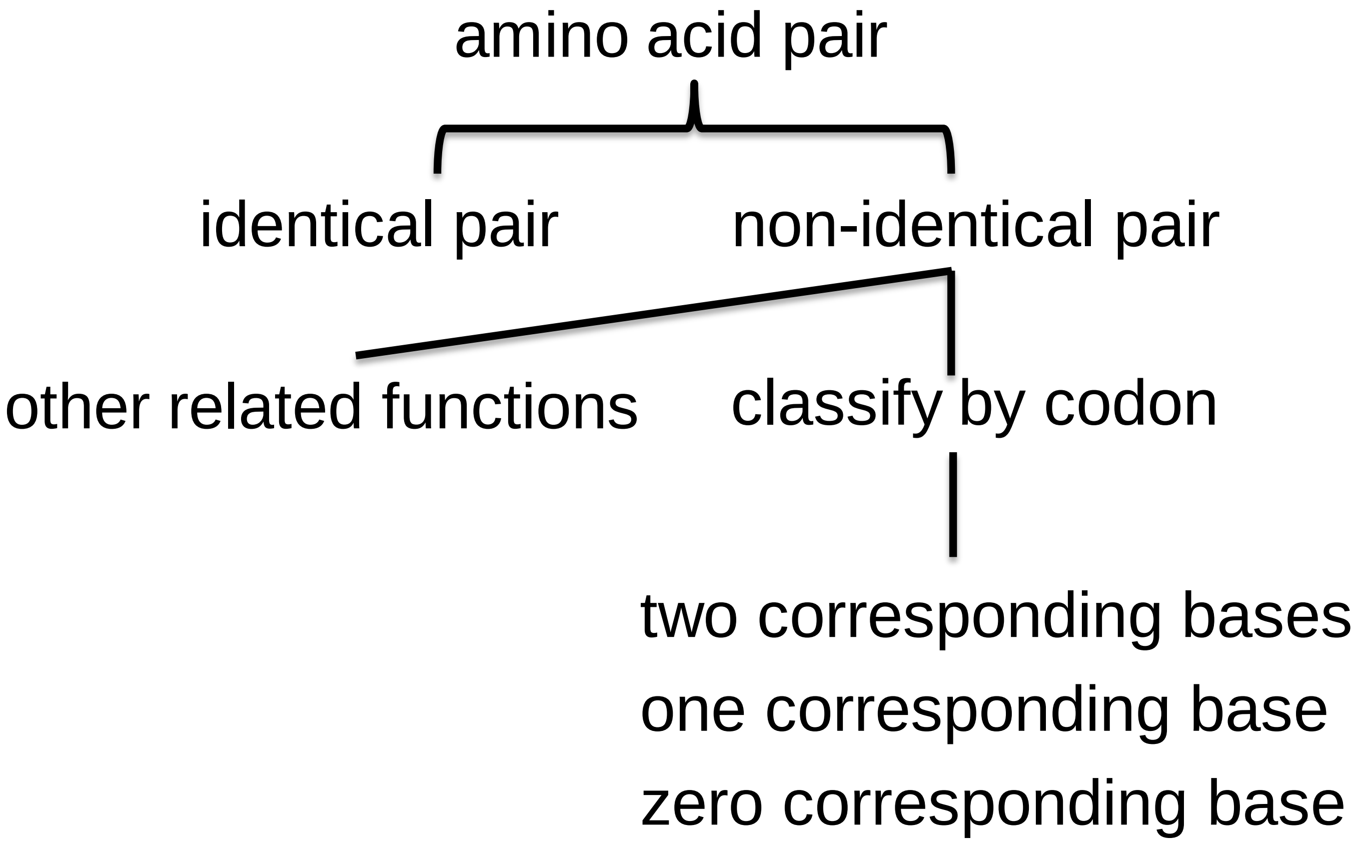
	A	B	C	N	J	R	O	C	L	C	R	P	M
A	8	7	6	6	5	4	4	3	3	2	1	0	0
J	7	7	6	6	6	4	4	3	3	2	1	0	0
C	6	6	7	6	5	4	4	4	3	3	1	0	0
J	6	6	6	5	6	4	4	3	3	2	1	0	0
N	5	5	5	6	5	4	4	3	3	2	1	0	0
R	4	4	4	4	4	5	4	3	3	2	2	0	0
C	3	3	4	3	3	3	3	4	3	3	1	0	0
K	3	3	3	3	3	3	3	3	3	2	1	0	0
C	2	2	3	2	2	2	2	3	2	3	1	0	0
R	2	1	1	1	1	2	1	1	1	1	2	0	0
B	1	2	1	1	1	1	1	1	1	1	1	0	0
P	0	0	0	0	0	0	0	0	0	0	0	1	0

(modified from fig.1 of Needleman&Wunsch,1970)

$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source:http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Scoring function and Gap Penalty



amino acid pair

identical pair

non-identical pair

other related functions

classify by codon

two corresponding bases

one corresponding base

zero corresponding base

Gap penalty: avoid too many gaps

Scoring function and Gap Penalty

- Needleman-Wunsch Algorithm

$$F_{i0} = d * i$$

$$F_{0j} = d * j$$

$$F_{ij} = \max(F_{i-1,j-1} + S(A_i, B_j),\ F_{i,j-1} + d,\ F_{i-1,j} + d)$$

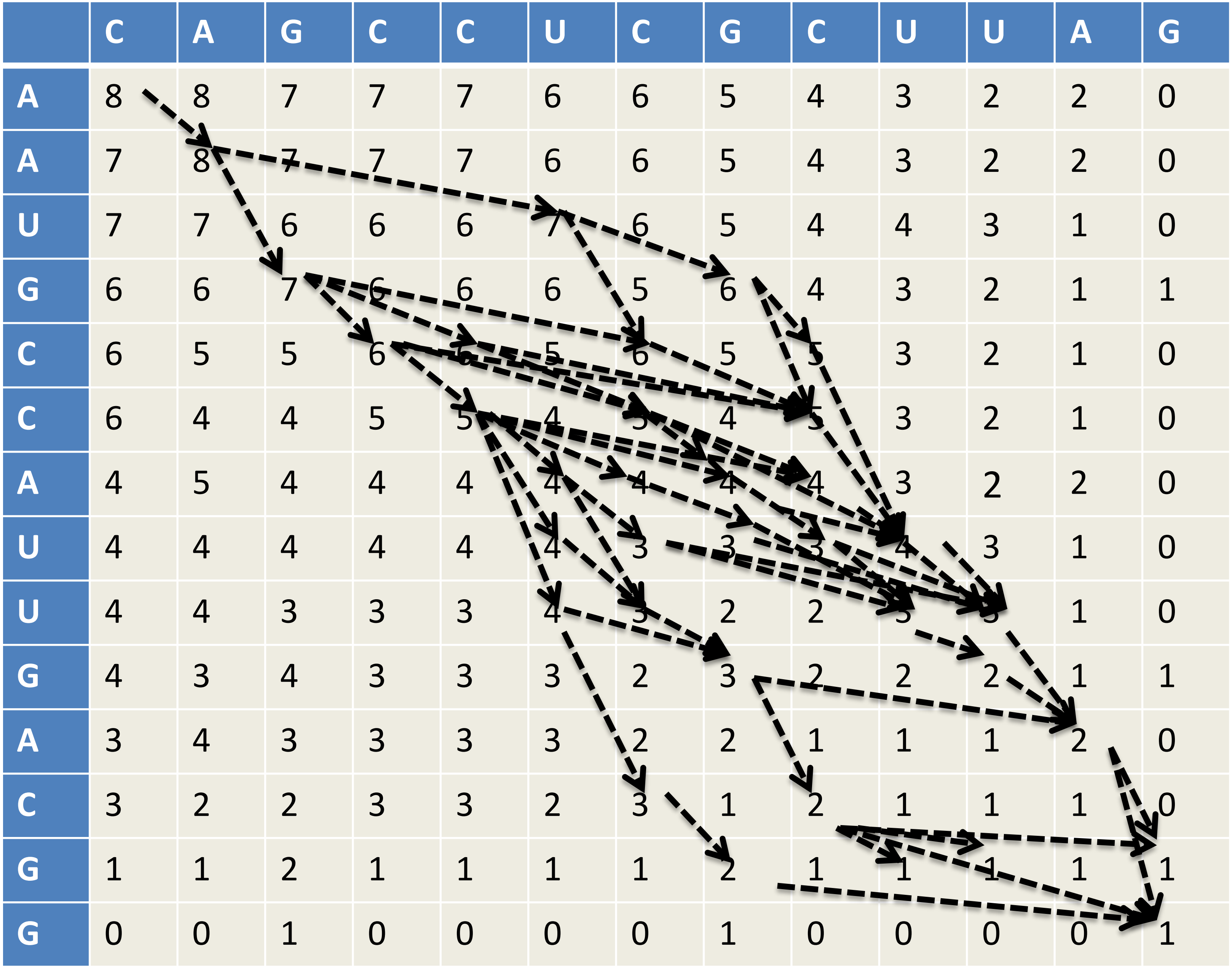
$$F_{ij} = \max_{h<i,k<j} \{F_{h,j-1} + S(A_i, B_j), F_{i-1,k} + S(A_i, B_j)\}$$

(source: http://en.wikipedia.org/wiki/Needleman–Wunsch_algorithm)

Scoring function and Gap Penalty

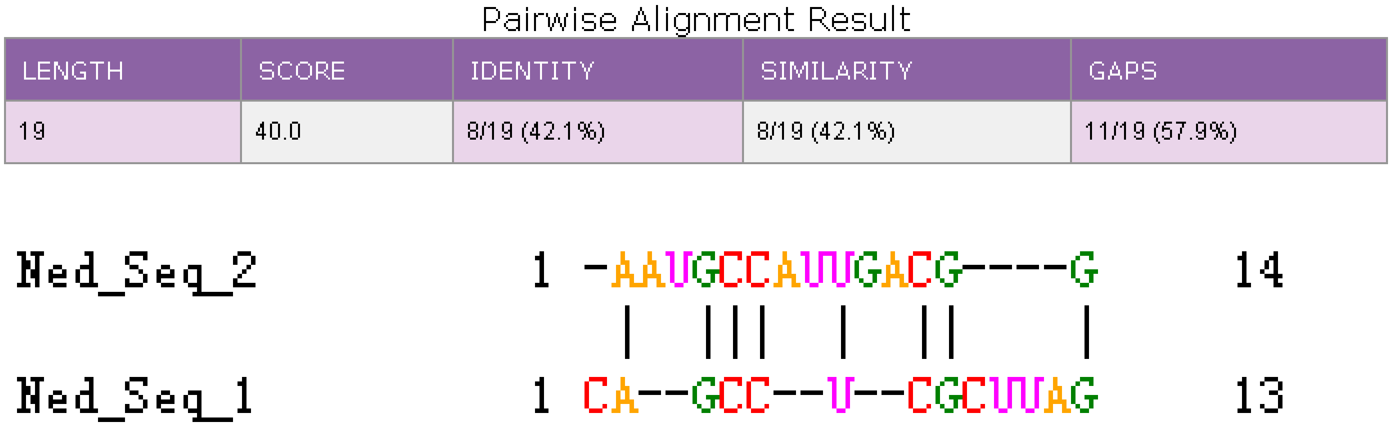
	C	A	G	C	C	U	C	G	C	U	U	A	G
A													
A													
U													
G													
C													
C													
A													
U													
U													
G													
A													
C													
G													
G													

Scoring function and Gap Penalty



	C	A	G	C	C	U	C	G	C	U	U	A	G
A	8	8	7	7	7	6	6	5	4	3	2	2	0
A	7	8	7	7	7	6	6	5	4	3	2	2	0
U	7	7	6	6	6	7	6	5	4	4	3	1	0
G	6	6	7	6	6	6	5	6	4	3	2	1	1
C	6	5	5	6	6	5	6	5	5	3	2	1	0
C	6	4	4	5	5	4	5	4	5	3	2	1	0
A	4	5	4	4	4	4	4	4	4	3	2	2	0
U	4	4	4	4	4	4	3	3	3	4	3	1	0
U	4	4	3	3	3	4	3	2	2	3	3	1	0
G	4	3	4	3	3	3	2	3	2	2	2	1	1
A	3	4	3	3	3	3	2	2	1	1	1	2	0
C	3	2	2	3	3	2	3	1	2	1	1	1	0
G	1	1	2	1	1	1	1	2	1	1	1	1	1
G	0	0	1	0	0	0	0	1	0	0	0	0	1

Scoring function and Gap Penalty

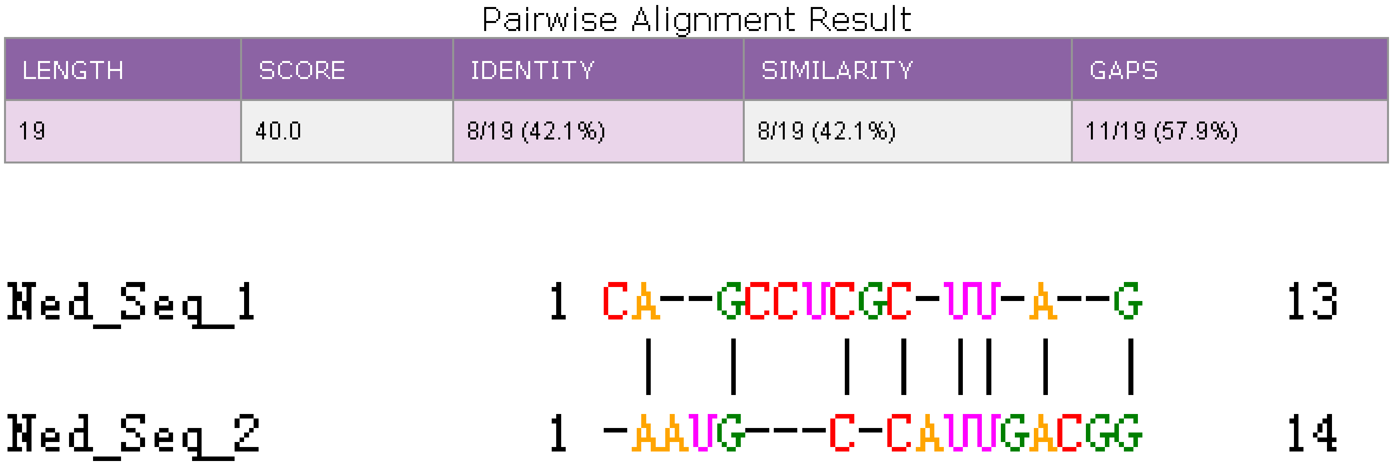


Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
19	40.0	8/19 (42.1%)	8/19 (42.1%)	11/19 (57.9%)

```
Ned_Seq_2      1 -AAUGCCAUUGACG----G     14
                  |  |||  |  ||    |
Ned_Seq_1      1 CA--GCC--U--CGCUUAG     13
```

a



Pairwise Alignment Result

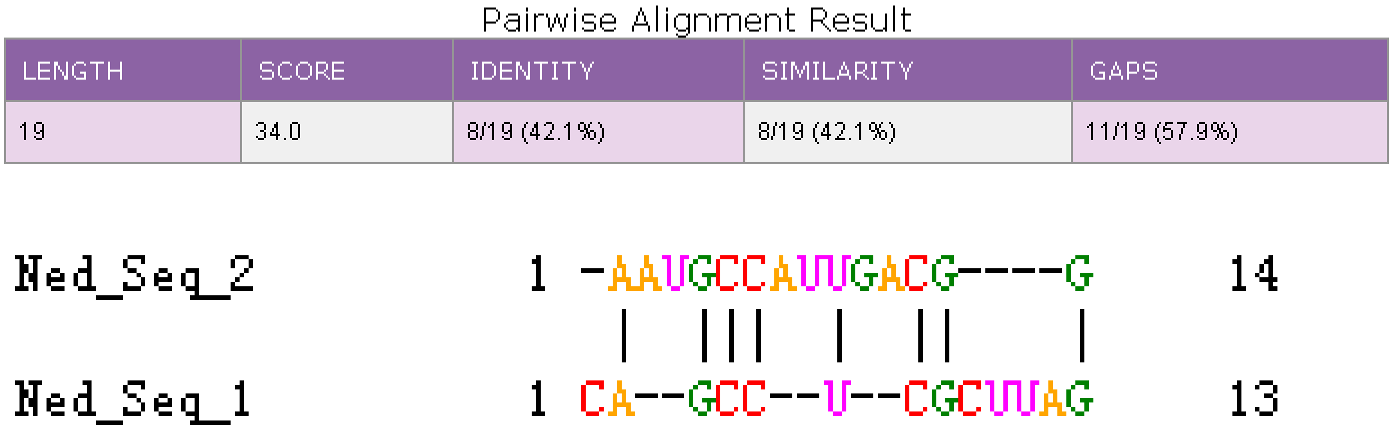
LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
19	40.0	8/19 (42.1%)	8/19 (42.1%)	11/19 (57.9%)

```
Ned_Seq_1      1 CA--GCCUCGC-UU-A--G     13
                  |  |   | | || |  |
Ned_Seq_2      1 -AAUG---C-CAUUGACGG     14
```

b

Needleman algorithm (simplified)

Scoring function and Gap Penalty

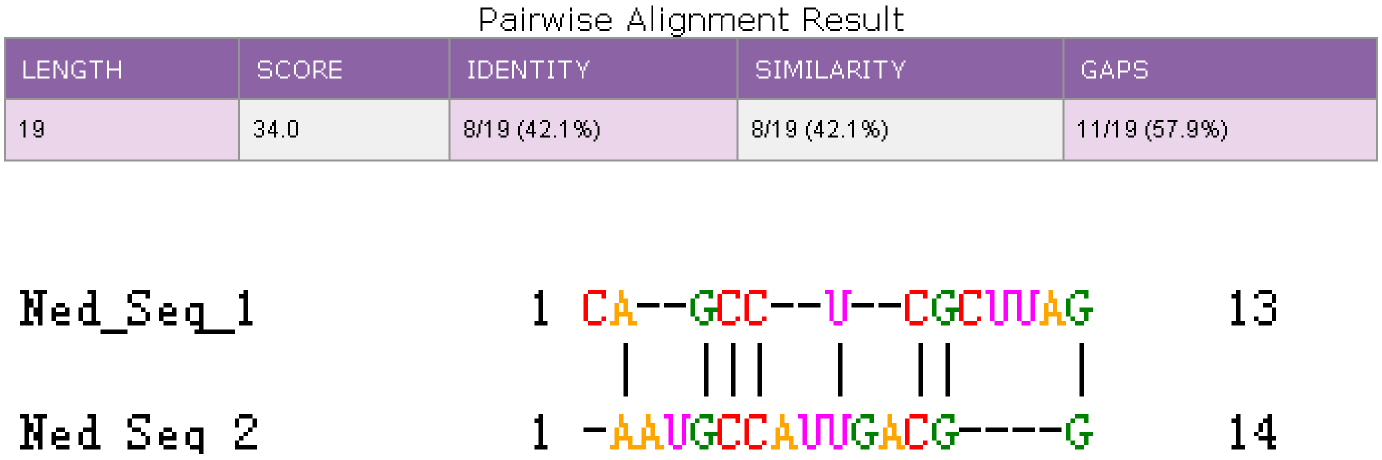


Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
19	34.0	8/19 (42.1%)	8/19 (42.1%)	11/19 (57.9%)

```
Ned_Seq_2      1 -AAUGCCAUUGACG----G      14
                  |  |||  |  ||    |
Ned_Seq_1      1 CA--GCC--U--CGCUUAG      13
```

c



Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
19	34.0	8/19 (42.1%)	8/19 (42.1%)	11/19 (57.9%)

```
Ned_Seq_1      1 CA--GCC--U--CGCUUAG      13
                  |  |||  |  ||    |
Ned Seq 2      1 -AAUGCCAUUGACG----G      14
```

d

Needleman algorithm

Alignment significance evaluation

- Question:

Whether a particular result differs significance from a fortuitous match between two random sequences ?

- To answer this question we can do:

  Sequence alignment between two sets of random sequences

  Or:

  Sequence alignment between one set of random sequences and a real sequence

Smith-Waterman Algorithm

$$H_{k0} = H_{0l} = 0 \text{ for } 0 \le k \le n \text{ and } 0 \le l \le m.$$

$$H_{ij} = \max\{H_{i-1,j-1} + s(a_i,b_j), \max_{k \ge 1}\{H_{i-k,j} - W_k\}, \max_{l \ge 1}\{H_{i,j-l} - W_l\}, 0\}. \quad (1)$$

$1 \le i \le n$ and $1 \le j \le m$.

$$W_k = 1.0 + 1/3*k.$$

(source: Smith & Waterman,1981)

	gap	a1	a2	a3	a4
gap	0	1 gap	2 gaps	3 gaps	4 gaps
b1	1 gap	A11	A21	A31	A41
b2	2 gaps	A12	A22	A32	A42
b3	3 gaps	A13	A23	A33	A43

(modified from Fig.3.9 of D.W.Mount
Bioinformatics Sequence and Gene
Analysis, Second Eition, P74)

Smith-Waterman Algorithm

$$H_{k0} = H_{0l} = 0 \text{ for } 0 \le k \le n \text{ and } 0 \le l \le m.$$

$$H_{ij} = \max\{H_{i-1,j-1} + s(a_i,b_j), \max_{k \ge 1}\{H_{i-k,j} - W_k\}, \max_{l \ge 1}\{H_{i,j-l} - W_l\}, 0\}. \quad (1)$$

$1 \le i \le n$ and $1 \le j \le m$.

$$W_k = 1.0 + 1/3 * k.$$

(source: Smith & Waterman,1981)

	gap	a1	a2	a3	a4
gap	0	1 gap	2 gaps	3 gaps	4 gaps
b1	1 gap	A11	A21	A31	A41
b2	2 gaps	A12	A22	A32	A42
b3	3 gaps	A13	A23	A33	A43

(modified from Fig.3.9 of D.W.Mount Bioinformatics Sequence and Gene Analysis, Second Eition, P74)

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O

(modified from Fig.3.9 of D.W.Mount Bioinformatics Sequence and Gene Analysis, Second Eition, P74)

Smith-Waterman Algorithm

$$H(i,0) = 0,\ 0 \le i \le m$$

$$H(0,j) = 0,\ 0 \le j \le n$$

if $a_i = b_j$ then $w(a_i, b_j) = w(\text{match})$ or if $a_i \ne b_j$ then $w(a_i, b_j) = w(\text{mismatch})$

$$H(i,j) = \max \left\{ \begin{array}{cc} & 0 \\ H(i-1, j-1) + \ w(a_i, b_j) & \text{Match/Mismatch} \\ H(i-1, j) + \ w(a_i, -) & \text{Deletion} \\ H(i, j-1) + \ w(-, b_j) & \text{Insertion} \end{array} \right\},\ 1 \le i \le m, 1 \le j \le n$$

(source: http://en.wikipedia.org/wiki/Smith-Waterman_algorithm)

	gap	a1	a2	a3	a4
gap	0	1 gap	2 gaps	3 gaps	4 gaps
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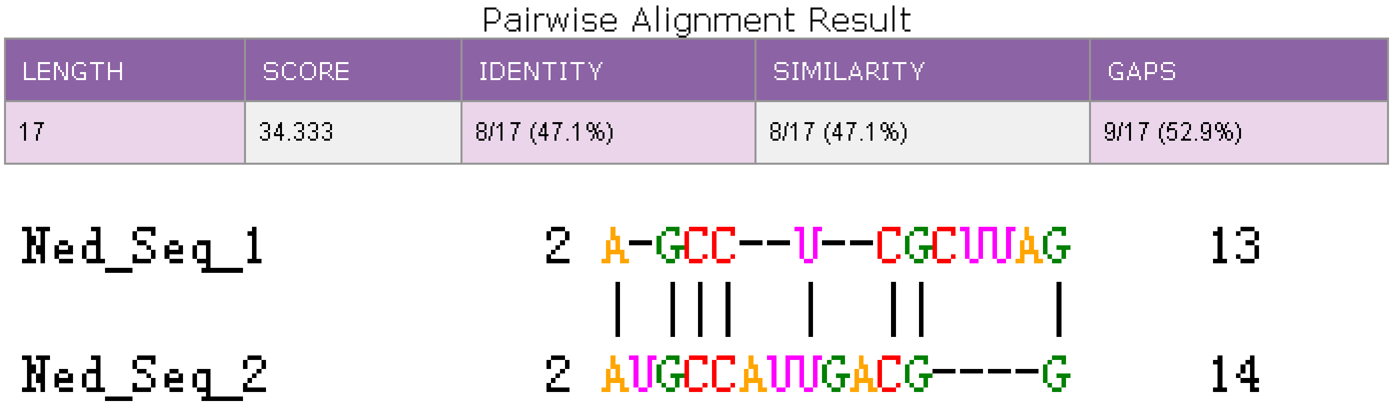
O

(modified from Fig.3.9 of D.W.Mount Bioinformatics Sequence and Gene Analysis, Second Eition, P74)

Smith-Waterman Algorithm

- Compared with global alignment：
  - Zero could terminate the current local alignment
  - Mismatch must be negative scored
- Other properties：
  - Suitable to identify conserved local sequence (substring)
  - Guaranteed to find the best local alignment
  - Perform poorly when dealing with separated regions within a long sequence

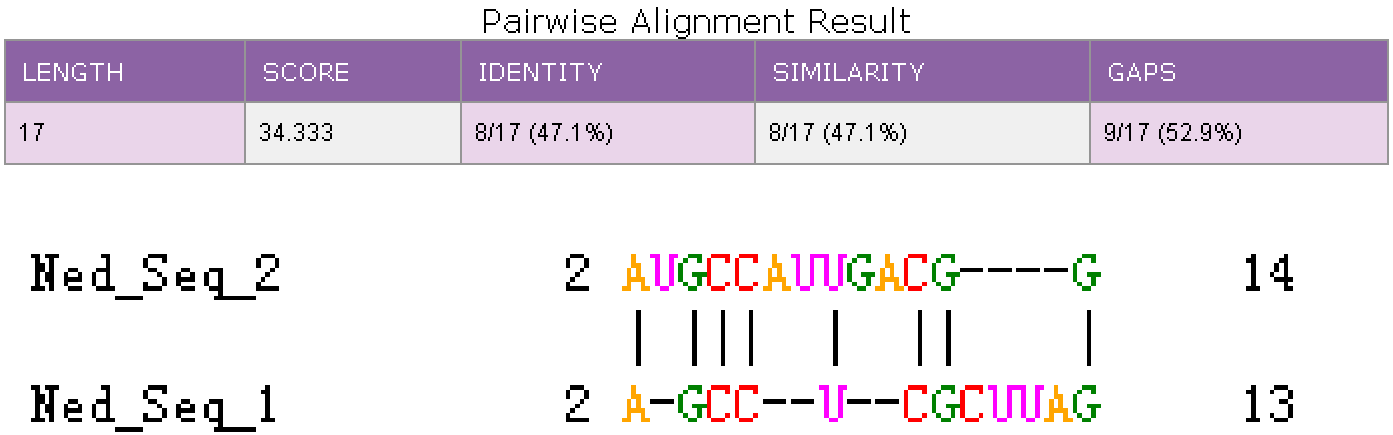
Smith-Waterman Algorithm



Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
17	34.333	8/17 (47.1%)	8/17 (47.1%)	9/17 (52.9%)

```
Ned_Seq_1          2 A-GCC--U--CGCUUAG      13
                     | |||  |  ||    |
Ned_Seq_2          2 AUGCCAUUGACG----G      14
```



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```
Ned_Seq_2          2 AUGCCAUUGACG----G      14
                     | |||  |  ||    |
Ned_Seq_1          2 A-GCC--U--CGCUUAG      13
```

Comparision

Match	1
Mismatch	0
Gap	0

	A	K	C	A	C	K
C	2	2	3	1	1	0
A	1	1	1	2	0	0
C	0	0	1	0	1	0

Needleman-Wunsch (Simplified)

Match	1
Mismatch	-1
Gap	-1

		A	K	C	A	C	K
	0	0	0	0	0	0	0
C	0	0	0	1	0	1	0
A	0	1	0	0	2	0	0
C	0	0	0	1	0	3	1

Needleman-Wunsch
Smith-Waterman

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8. http://en.wikipedia.org/wiki/Smith-Waterman_algorithm

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Thanks for your attention!