

Global and local alignments

Needleman-Wunsch algorithm, mathematical form

$$\mathbf{M}(0, j) = j \times p \quad \text{first row, } p = \text{gap penalty}$$

$$\mathbf{M}(i, 0) = i \times p \quad \text{first column}$$

$$\mathbf{M}(i, j) = \max \left(\begin{array}{l} \mathbf{M}(i-1, j) + p \\ \mathbf{M}(i, j-1) + p \\ \mathbf{M}(i-1, j-1) + s(a_j, b_i) \end{array} \right) \begin{array}{l} \text{top} \\ \text{left} \\ \text{diagonal} \end{array}$$

$s(a_j, b_i)$ = match/mismatch score for sites j and i
in sequences a and b

Needleman-Wunsch in Python

```
# Fill in the first row
for j in range(0, n + 1):
    score[0][j] = gap_penalty * j

# Fill in the first column
for i in range(0, m + 1):
    score[i][0] = gap_penalty * i

# Fill in all other values in the score matrix
for i in range(1, m + 1):      # loop over all rows
    for j in range(1, n + 1):  # loop over all columns
        # Calculate the score by checking the top, left, and diagonal cells
        insert = score[i - 1][j] + gap_penalty      # top
        delete = score[i][j - 1] + gap_penalty     # left
        match = score[i - 1][j - 1] + \           # diagonal
                match_score(seq1[j-1], seq2[i-1])

        # Record the maximum score from the three possible ones
        score[i][j] = max(match, delete, insert)
```

Global vs. local alignments

- Global: align all nucleotides
- Local: align subsequences with best score

Align these sequences: GCAT, GCT
(match = 1, mismatch = -1, gap = -1)

global alignment:

GCAT

GC-T

local alignment:

?

We can make local alignments using the Smith-Waterman algorithm

Like Needleman-Wunsch, with 2 changes:

- Don't allow negative scores, set them to 0
- Backtrack from cell with highest score, stop at 0

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Needleman-Wunsch

	-	G	C	A	T
-	0	-1	-2	-3	-4
G	-1	1	0	-1	-2
C	-2	0	2	1	0
T	-3	-1	1	1	2

GCAT

GC-T

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GCAT
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Smith-Waterman

	-	G	C	A	T
-	0	0	0	0	0
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C	0	0	2	1	0
T	0	0	1	1	2

GC
GC

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Needleman-Wunsch

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GCAT
GC-T

Smith-Waterman

	-	G	C	A	T
-	0	0	0	0	0
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GC GCAT
GC GC-T
 or

Smith-Waterman algorithm, mathematical form

$$\mathbf{M}(0, j) = 0 \quad \text{first row}$$

$$\mathbf{M}(i, 0) = 0 \quad \text{first column}$$

$$\mathbf{M}(i, j) = \max \left(\begin{array}{l} 0 \\ \mathbf{M}(i-1, j) + p \\ \mathbf{M}(i, j-1) + p \\ \mathbf{M}(i-1, j-1) + s(a_j, b_i) \end{array} \right) \begin{array}{l} \text{top} \\ \text{left} \\ \text{diagonal} \end{array}$$

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in sequences a and b

BLAST

(Basic Local Alignment Search Tool)

BLAST is the primary method to find sequences in modern sequence data bases



Stephen Altschul

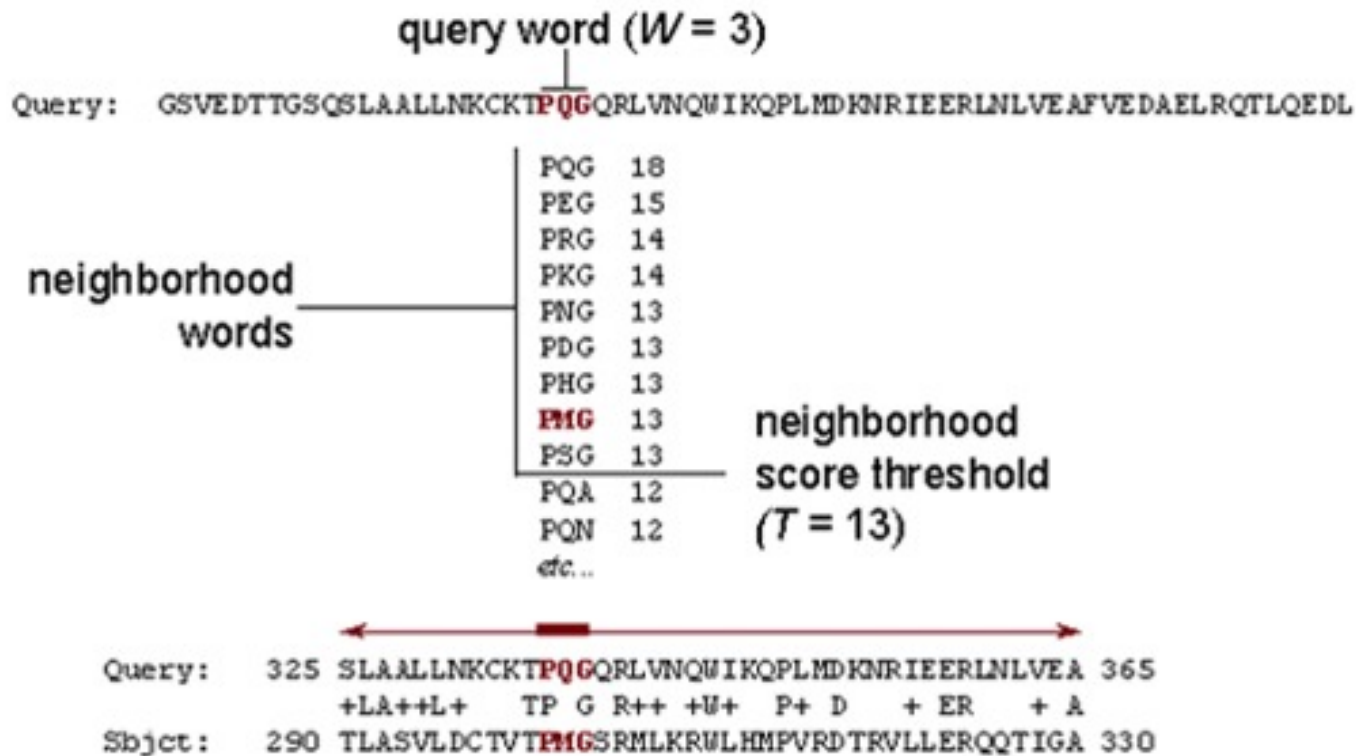
NCBI, NLM, NIH

[Bioinformatics](#)

Verified email at nih.gov

Title	1–20	Cited by	Year
Basic local alignment search tool	SF Altschul, W Gish, W Miller, EW Myers, DJ Lipman Journal of molecular biology 215 (3), 403-410	54882	1990
Gapped BLAST and PSI-BLAST: a new generation of protein database search programs	SF Altschul, TL Madden, AA Schäffer, J Zhang, Z Zhang, W Miller, ... Nucleic acids research 25 (17), 3389-3402	54781	1997
Identification of FAP locus genes from chromosome 5q21.	KW Kinzler, MC Nilbert, LK Su, B Vogelstein, TM Bryan, DB Levy, ... Science (New York, NY) 253 (5020), 661	2060	1991
Detecting subtle sequence signals: a Gibbs sampling strategy for multiple alignment	CF Lawrence, SF Altschul, MS Boguski, JS Liu, AF Neuwald, JC Wootton	1963	1993

The BLAST Search Algorithm



High-scoring Segment Pair (HSP)

Primary BLAST quality metric: E value

The **Expectation value** or **E value** represents the number of different alignments with scores equivalent to or better than the one observed that are expected to occur in a database search by chance.

The lower the E value, the more significant the score and the alignment.

Anatomy of a BLAST result

glycoprotein precursor [Junin virus]

Sequence ID: [gb|ABI51595.1|](#) Length: 485 Number of Matches: 1

Range 1: 1 to 241 [GenPept](#) [Graphics](#)

▼ Next Match ▲ Previous Match

Score	Expect	Method	Identities	Positives	Gaps
278 bits(710)	1e-86	Compositional matrix adjust.	137/252(54%)	168/252(66%)	11/252(4%)
Query	1	MGQLISFFQEIPVFLQEALNIALVAVSLIAVIKGIINLYKSGLFQFIFFLFLAGRSCSDG			60
		MGQ ISF QEIP FLQEALNIALVAVSLIA+IKGI+NLYKSGLFQF FL LAGRSC++			
Sbjct	1	MGQFISFMQEIPTFLQEALNIALVAVSLIAIIKGIIVNLYKSGLFQFFVFLALAGRSCTEE			60
Query	61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSLCMLNNSFYMKGGANIFLIRVSDVSVLMK			120
		FKIGLHTEFQ+V+F+M L +N+ ++LP LC LN S Y+KGG F+I D++VL+			
Sbjct	61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP			120
Query	121	EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS			180
		+YDV + P D+ C D W WF A+GHDW +DPP LCRN+TK EG Q N S			
Sbjct	121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDP PFLCRNRTKTEGFIFQVNTS			180
Query	181	KADES RVYGKKIRNGMRHLFRGFYDPCEEKVCYVTINQCGDPSSF EYCGTNYLSKCQFD			240
		K + Y KK + GM HL+R + D C GK+C + P+S+ +C D			
Sbjct	181	KTGVNENYAKKFKTGMHHL YREYPDSCLNGKLCLMK-----AQPTSWPL-----QCPLD			229
Query	241	HVNTLHFLVRSK 252			
		HVNTLHFL R K			
Sbjct	230	HVNTLHFLTRGK 241			

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sequence we found
(subject sequence)

Range 1: 1 to 241 [GenPept](#) [Graphics](#)

Score	Expect	Method	Identities	Positives	Gaps
278 bits(710)	1e-86	Compositional matrix adjust.	137/252(54%)	168/252(66%)	11/252(4%)
Query 1	MGQLISFFQEIPVFLQEALNIALVAVSLIAVIKGIINLYKSGLFQFIFFLFLAGRSCSDG				60
	MGQ ISF QEIP FLQEALNIALVAVSLIA+IKGI+NLYKSGLFQF FL LAGRSC++				
Sbjct 1	MGQFISFMQEIPTFLQEALNIALVAVSLIAI IKGIVNLYKSGLFQFFVFLALAGRSCTEE				60
Query 61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSLCMLNNSFYMKGGANIFLIRVSDVSVLMK				120
	FKIGLHTEFQ+V+F+M L +N+ ++LP LC LN S Y+KGG F+I D++VL+				
Sbjct 61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP				120
Query 121	EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS				180
	+YDV + P D+ C D W WF A+GHDW +DPP LCRN+TK EG Q N S				
Sbjct 121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDP PFLCRNRTKTEGFIFQVNTS				180
Query 181	KADESRVYGKKIRNGMRHLFRGFYDPCEEKVCYVTINQCGDPSSF EYCGTNYLSKCQFD				240
	K + Y KK + GM HL+R + D C GK+C + P+S+ +C D				
Sbjct 181	KTGVNENYAKKFKTGMHHL YREYPDSCLNGKLCLMK-----AQPTSWPL-----QCPLD				229
Query 241	HVNTLHFLVRSK 252				
	HVNTLHFL R K				
Sbjct 230	HVNTLHFLTRGK 241				

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Score	Expect	E value	Identities	Positives	Gaps
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Query 1	MGQLISFFQEIPVFLQEALNIALVAVSLIAVIKGIINLYKSGLFQFIFFLFLAGRSCSDG	60	MGQ ISF QEIP FLQEALNIALVAVSLIA+IKGI+NLYKSGLFQF FL LAGRSC++		
Sbjct 1	MGQFISFMQEIPTFLQEALNIALVAVSLIAI IKGIVNLYKSGLFQFFVFLALAGRSCTEE	60			
Query 61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSLCMLNNSFYMKGGANIFLIRVSDVSVLMK	120	FKIGLHTEFQ+V+F+M L +N+ ++LP LC LN S Y+KGG F+I D++VL+		
Sbjct 61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP	120			
Query 121	EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLMDPPMLCRNKTKEGSNIQFNIS	180	+YDV + P D+ C D W WF A+GHDW +DPP LCRN+TK EG Q N S		
Sbjct 121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDPFLCRNRTKTEGFIFQVNTS	180			
Query 181	KADES RVY GKKIRNGMRHLFRGFYDPCEEKVCYVTINQCGDPSSF EYCGTNYLSKCQFD	240	K + Y KK + GM HL+R + D C GK+C + P+S+ +C D		
Sbjct 181	KTGVNENYAKKFKTGMHHL YREYPDSCLNGKLCLMK-----AQPTSWPL-----QCPLD	229			
Query 241	HVNTLHFLVRSK 252				
	HVNTLHFL R K				
Sbjct 230	HVNTLHFLTRGK 241				

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Score	Expect	Method	Identities	Positives	Gaps
278 bits(710)	1e-86	Compositional matrix adjust.	137/252(54%)	168/252(66%)	11/252(4%)

Query	1	MGQLISFFQEIPVFLQEALNIALVAVSLIAV	number and % of exact	50
Sbjct	1	MGQ ISF QEIP FLQEALNIALVAVSLIA+IKGI+NLYKSGLFQF FL LAGRSC++	matches, near matches,	60
Query	61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSI	and no matches	120
Sbjct	61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP		120
Query	121	EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS		180
Sbjct	121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDP PFLCRNRTKTEGFIFQVNTS		180
Query	181	KADESRVYGKKIRNGMRHLFRGFYDPCEEKVCYVTINQCGDPSSF EYCGTNYLSKCQFD		240
Sbjct	181	KTGVNENYAKKFKTGMHHL YREYPDSCLNGKLCLMK----AQPTSWPL-----QCPLD		229
Query	241	HVNTLHFLVRSK		252
Sbjct	230	HVNTLHFLTRGK		241

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Query	1	MGQLISFFQEIPVFLQEALNIALVAVSLIAV	number and % of exact
Sbjct	1	MGQ ISF QEIP FLQEALNIALVAVSLIA+IKGI+NLYKSGLFQF FL LAGRSC++	matches, near matches,
Query	61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSI	and no matches
Sbjct	61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP	
Query	121	EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS	
Sbjct	121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHWDHLDPPFLCRNRTKTEGFIFQVNTS	
Query	181	KADES RVYGKKIRNGMRHLFRGFYDPCEEKVCYVTINQCGDPSSF EYCGTNYLSKCQFD	
Sbjct	181	KTGVNENYAKKFKTGMHLYREYPDSC LNGKLCLMK----AQPTSWPL-----QCPLD	
Query	241	HVNTLHFLVRSK 252	
Sbjct	230	HVNTLHFL R K 241	exact match

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glycoprotein precursor [Junin virus]

Sequence ID: [gb|ABI51595.1](#) Length: 485 Number of Matches: 1

Range 1: 1 to 241 [GenPept](#) [Graphics](#)

▼ Next Match ▲ Previous Match

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Query	1	MGQLISFFQEIPVFLQEALNIALVAVSLIAV	number and % of exact
Sbjct	1	MGQ ISF QEIP FLQEALNIALVAVSLIA+IKGI+NLYKSGLFQF FL LAGRSC++	matches, near matches,
Query	61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSI	and no matches
Sbjct	61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP	
Query	121	EYDVSVYEPEDLGNCNLNKS DSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS	
Sbjct	121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDP PFLCRNRTKTEGFIFQVNTS	
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Sbjct	181	KTGVNENYAKKFKTGMHHL YREYPDSCLNGKLCLMK----AQPTSWPL-----QCPLD	
Query	241	HVNTLHFLVRSK 252	
Sbjct	230	HVNTLHFLTRGK 241	near match (positive)

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Query	61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSI	and no matches	120
Sbjct	61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP		120
Query	121	EYDVSVYEPEDLGNCCLNKSDSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS		180
Sbjct	121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDP PFLCRNRTKTEGFIFQVNTS		180
Query	181	KADES RVYGKKIRNGMRHLFRGFYDPCEE GKVCYVTINQCGDPSSFEYCGTNYLSKCQFD		240
Sbjct	181	KTGVNENYAKKFKTGMHHLRYRYPD SCLNGKLC LMK----AQPTSWPL-----QCPLD		229
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Sbjct	230	HVNTLHFLTRGK 241	no match	

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Query	61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSLCMLNNSFYMKGGANIFLIRVSDVSVLMK			120
		FKIGLHTEFQ+V+F+M L +N+ ++LP LC LN S Y+KGG F+I D++VL+			
Sbjct	61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP			120
Query	121	EYDVSVYEPEDLGNCNLNKS DSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS			180
		+YDV + P D+ C D W WF A+GHDW +DPP LCRN+TK EG Q N S			
Sbjct	121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDP PFLCRNRTKTEGFIFQVNTS			180
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		K + Y KK + GM HL+R + D C GK+C + P+S+ +C D			
Sbjct	181	KTGVNENYAKKFKTGMHHL YREYPDSCLNGKLCLMK----AQPTSWPL-----QCPLD			229
Query	241	HVNTLHFLVRSK 252			
		HVNTLHFL R K			
Sbjct	230	HVNTLHFLTRGK 241			