

Global and local alignments

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

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GCAT

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Smith-Waterman

	-	G	C	A	T
-	0	0	0	0	0
G	0	1	0	0	0
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
G	0	1	0	0	0
C	0	0	2	1	0
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GC GCAT
GC GC-T
 or

Smith-Waterman algorithm, mathematical form

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

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

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

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

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	EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLMPPMLCRNKTKEGSNIQFNIS			180
		+YDV + P D+ C D W WF A+GHDW +DPP LCRN+TK EG Q N S			
Sbjct	121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDPFLCRNRTKTEGFIFQVNTS			180
Query	181	KADES RVYGKKIRNGMRHLFRGFYDPCEEGKVCYVTINQCGDPSSF 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)

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		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		EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLMPPMLCRNKTKEGSNIQFNIS			180
		+YDV + P D+ C D W WF A+GHDW +DPP LCRN+TK EG Q N S			
Sbjct 121		QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDPFLCRNRTKTEGFIFQVNTS			180
Query 181		KADESRVYGKKIRNGMRHLFRGFYDPCEEKVCYVTINQCGDPSSFYECGTNYLSKCQFD			240
		K + Y KK + GM HL+R + D C GK+C + P+S+ +C D			
Sbjct 181		KTGVNENYAKKFKTGMHHLREYPPDSCLNGLCLMK----AQPTSWPL-----QCPLD			229
Query 241		HVNTLHFLVRSK 252			
		HVNTLHFL R K			
Sbjct 230		HVNTLHFLTRGK 241			

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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	EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLMPPMLCRNKTKEGSNIQFNIS	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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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	KADES RVYGKKIRNGMRHLFRGFYDPCEE GKVCYVTINQCGDPSSF EYCGTNYLSKCQFD		240
Sbjct	181	KTGVNENYAKKFKTGMHHL YREYPDSCLNGKLCLMK----AQPTSWPL-----QCPLD		229
Query	241	HVNTLHFLVRSK	252	
Sbjct	230	HVNTLHFLTRGK	241	

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278 bits(710)	1e-86	Compositional matrix adjust.	137/252(54%)	168/252(66%)	11/252(4%)

Query	1	MGQLISFFQEIPVFLQEALNIALVAVSLIAV	number and % of exact	60
Sbjct	1	MGQ ISF QEIP FLQEALNIALVAVSLIA+IKGI+NLYKSGLFQF FL LAGRSC++	matches, near matches,	
Query	61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSI	and no matches	120
Sbjct	61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP		120
Query	121	EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS		180
Sbjct	121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDP PFLCRNRTKTEGFIFQVNTS		180
Query	181	KADES RVYGKKIRNGMRHLFRGFYDPCEE GKVCYVTINQCGDPSSF EYCGTNYLSKCQFD		240
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Query	241	HVNTLHFLVRSK 252		
Sbjct	230	HVNTLHFL R K 241	exact match	

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Query 61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSI				
Sbjct 61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP				
Query 121	EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS				
Sbjct 121	QYDVVIQHPADMSWCSKSDDQIWLSQWFMNAVGHDWHLDP PFLCRNRTKTEGFIFQVNTS				
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Query 241	HVNTLHFLVRSK 252				
Sbjct 230	HVNTLHFL R K 241				

number and % of exact matches, near matches, and no matches

near match (positive)

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Sbjct 1	MGQ ISF QEIP FLQEALNIALVAVSLIA+IKGI+NLYKSGLFQF FL LAGRSC++				
Query 61	TFKIGLHTEFQSVTFTMQRLLANHSNELPSI				
Sbjct 61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP				
Query 121	EYDVSVYEPEDLGNCLNKSDSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS				
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number and % of exact matches, near matches, and no matches

no match

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	FKIGLHTEFQ+V+F+M L +N+ ++LP LC LN S Y+KGG F+I D++VL+				
Sbjct 61	AFKIGLHTEFQTVSFSMVGLFSNNPHDLPLLCTLNKSHLYIKGGNASFMISFDDIAVLLP				120
Query 121	EYDVSVYEPEDLGNCCLNKSDSSWAIHWFSIALGHDWLM DPPMLCRNKTKEGSNIQFNIS				180
	+YDV + P D+ C D W WF A+GHDW +DPP LCRN+TK EG Q N S				
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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
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Sbjct 230	HVNTLHFLTRGK 241				