Algorithms for pairwise sequence alignments

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What is needed to define an optimal pairwise alignment?

- A **scoring function**, $d(x, y)$, giving the score of a column of any letter x and y. A typical scoring function could be

$$d(x,y) = \begin{cases} p & \text{if } x = y \\ g & \text{if } x = - \text{ or } y = - \\ n & \text{otherwise} \end{cases}.$$

Here, p, is called a match score, n, a mismatch score, and g a gap penalty.

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  Here, p, is called a match score, n, a mismatch score, and g a gap penalty.
- An **alignment approach.** If we want to find an optimal alignment of the full length sequences, we are searching a *global* alignment approach. If we search the highest scoring stretch of an alignment, you should use a *local* alignment approach.You can also use a semi-global alignment, searching for an optimal alignment, with the exception for any overshooting sequence terminals.

Needleman-Wunsch (global alignment)

Given two sequences $a_1, \ldots, a_N$ and $b_1, \ldots, b_M$, a scoring function d(x,y), we can find an optimal *global* alignment by investigating the dynamic programming matrix of size (N+1,M+1), defined by

$$
\begin{aligned}
S_{0,0} &= 0, \\
S_{i,0} &= d(x, -) \cdot i \text{ for all } i, \\
S_{0,j} &= d(-, y) \cdot j \text{ for all } j
\end{aligned}
$$

$$
S_{i,j} = \max \begin{cases} S_{i-1,j-1} & + d(a_i, b_j) \\ S_{i-1,j} & + d(a_i, -) \\ S_{i,j-1} & + d(-, b_j) \end{cases}
$$

The score of an optimal alignment is $S_{N,M}$.

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$$S_{i,j} = \max \begin{cases} S_{i-1,j-1} & + d(a_i, b_j) \\ S_{i-1,j} & + d(a_i, -) \\ S_{i,j-1} & + d(-, b_j) \end{cases}$$

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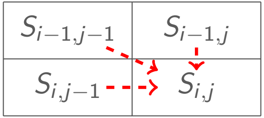

Example of Needleman-Wunsch (global alignment)

Align a =GAC, b =ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

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

$$S_{0,0} = 0,$$
$$S_{i,0} = -1 \cdot i \text{ for all } i,$$
$$S_{0,j} = -1 \cdot j \text{ for all } j$$

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

$$S_{1,1} = \max \begin{cases} S_{0,0} + d(G, A) & = 0 + -1 = -1 \\ S_{0,1} + d(G, -) & = -1 + -1 = -2 \\ S_{1,0} + d(-, A) & = -1 + -1 = -2 \end{cases}$$

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Align a =GAC, b =ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

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

$$S_{1,2} = \max \begin{cases} S_{0,1} + d(G, C) & = -1 + -1 = -2 \\ S_{0,2} + d(G, -) & = -2 + -1 = -3 \\ S_{1,1} + d(-, C) & = -1 + -1 = -2 \end{cases}$$

Example of Needleman-Wunsch (global alignment)

Align $a =$GAC, $b =$ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}.$

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

$$S_{1,3} = \max \begin{cases} S_{0,2} + d(G,G) & = -2 + 1 = -1 \\ S_{0,3} + d(G,-) & = -3 + -1 = -4 \\ S_{1,2} + d(-,G) & = -2 + -1 = -3 \end{cases}$$

Example of Needleman-Wunsch (global alignment)

Align a =GAC, b =ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

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

$$S_{2,1} = \max \begin{cases} S_{1,0} + d(A,A) & = -1 + 1 = 0 \\ S_{1,1} + d(A,-) & = -1 + -1 = -2 \\ S_{2,0} + d(-,A) & = -2 + -1 = -3 \end{cases}$$

Example of Needleman-Wunsch (global alignment)

Align a =GAC, b =ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

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

$$S_{2,2} = \max \begin{cases} S_{1,1} + d(A, C) & = -1 + -1 = -2 \\ S_{1,2} + d(A, -) & = -2 + -1 = -3 \\ S_{2,1} + d(-, C) & = 0 + -1 = -1 \end{cases}$$

Example of Needleman-Wunsch (global alignment)

Align $a =$GAC, $b =$ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

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

$$S_{2,3} = \max \begin{cases} S_{1,2} + d(A, G) & = -2 + -1 = -3 \\ S_{1,3} + d(A, -) & = -1 + -1 = -2 \\ S_{2,2} + d(-, G) & = -1 + -1 = -2 \end{cases}$$

Example of Needleman-Wunsch (global alignment)

Align a =GAC, b =ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

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

$$S_{3,1} = \max \begin{cases} S_{2,0} + d(C,A) & = -2 + -1 = -3 \\ S_{2,1} + d(C,-) & = 0 + -1 = -1 \\ S_{3,0} + d(-,A) & = -3 + -1 = -4 \end{cases}$$

Example of Needleman-Wunsch (global alignment)

Align $a =$GAC, $b =$ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

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

$$S_{3,2} = \max \begin{cases} S_{2,1} + d(C,C) & = 0 + 1 = +1 \\ S_{2,2} + d(C,-) & = -1 + -1 = -2 \\ S_{3,1} + d(-,C) & = -1 + -1 = -2 \end{cases}$$

Example of Needleman-Wunsch (global alignment)

Align a =GAC, b =ACG, using $d(x, y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

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

$$S_{3,3} = \max \begin{cases} S_{2,2} + d(C, G) & = -1 + -1 = -2 \\ S_{2,3} + d(C, -) & = -2 + -1 = -3 \\ S_{3,2} + d(-, G) & = 1 + -1 = 0 \end{cases}$$

Example of Needleman-Wunsch (global alignment)

Align a =GAC, b =ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

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

Optimal score given by $S_{3,3} = 0$.

An optimal alignment can be found by back tracing (-,G), (C,C), (A,A), (G,-) i.e.

```
GAC-
-ACG
```

Smith-Waterman (local alignment)

Given two sequences $a_1, \ldots, a_N$ and $b_1, \ldots, b_M$, a scoring function d(x,y), we can find an optimal *local* alignment by investigating the dynamic programming matrix of size (N+1,M+1), defined by

$$
\begin{aligned}
S_{0,0} &= 0, \\
S_{i,0} &= 0 \text{ for all } i, \\
S_{0,j} &= 0 \text{ for all } j
\end{aligned}
$$

$$
S_{i,j} = \max \begin{cases} S_{i-1,j-1} & +d(a_i, b_j) \\ S_{i-1,j} & +d(a_i, -) \\ S_{i,j-1} & +d(-, b_j) \\ 0 \end{cases}
$$

The score of an optimal alignment is $\max_{i,j} S_{i,j}$

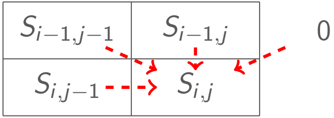
Smith-Waterman (local alignment)

Given two sequences $a_1, \dots, a_N$ and $b_1, \dots, b_M$, a scoring function d(x,y), we can find an optimal *local* alignment by investigating the dynamic programming matrix of size (N+1,M+1), defined by

$$
\begin{aligned}
S_{0,0} &= 0, \\
S_{i,0} &= 0 \text{ for all } i, \\
S_{0,j} &= 0 \text{ for all } j
\end{aligned}
$$

$$
S_{i,j} = \max \begin{cases} S_{i-1,j-1} & +d(a_i, b_j) \\ S_{i-1,j} & +d(a_i, -) \\ S_{i,j-1} & +d(-, b_j) \\ 0 & \end{cases}
$$

The score of an optimal alignment is $\max_{i,j} S_{i,j}$



Example of Smith-Waterman (local alignment)

Align a =GAC, b =ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

	-	A	C	G
-	0	0	0	0
G	0			
A	0			
C	0			

$S_{0,0} = 0,$

$S_{i,0} = 0 \text{ for all } i,$

$S_{0,j} = 0 \cdot j \text{ for all } j$

Example of Smith-Waterman (local alignment)

Align $a=$GAC, $b=$ACG, using $d(x,y)=\begin{cases}1 & \text{if } x=y\\ -1 & \text{otherwise}\end{cases}$.

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

$$S_{3,3}=\max\begin{cases}S_{2,2}+d(C,G) & =0+-1=-1\\ S_{2,3}+d(C,-) & =0+-1=-1\\ S_{3,2}+d(-,G) & =2+-1=1\\ 0\end{cases}$$

Example of Smith-Waterman (local alignment)

Align a =GAC, b =ACG, using $d(x,y) = \begin{cases} 1 & \text{if } x = y \\ -1 & \text{otherwise} \end{cases}$.

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

Optimal score given by $\max_{i,j} S_{i,j} = 2$.

An optimal alignment can be found by back tracing (C,C), (A,A) i.e.

```
AC
AC
```

Semi-global alignment

Given two sequences $a_1, \dots, a_N$ and $b_1, \dots, b_M$, a scoring function d(x,y), we can find an optimal *semi-global* alignment by investigating the dynamic programming matrix of size (N+1,M+1), defined by

$$
\begin{aligned}
S_{0,0} &= 0, \\
S_{i,0} &= 0 \text{ for all } i, \\
S_{0,j} &= 0 \text{ for all } j
\end{aligned}
$$

$$
S_{i,j} = \max \begin{cases} S_{i-1,j-1} & + d(a_i, b_j) \\ S_{i-1,j} & + d(a_i, -) \\ S_{i,j-1} & + d(-, b_j) \end{cases}
$$

The score of an optimal alignment is $\max(\max_i S_{i,M}, \max_j S_{N,j})$

Thanks!