Sequence Alignment: II

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Topics to be covered

- Sequence formats
- Dot Plot
- Global and Local alignment
- Scoring Matrices
- Needleman Wunsch Algorithm
- Smith Waterman Algorithm
- BLAST and FASTA
- HMM
- Multiple sequence alignment

Alignment of Sequences

1. Dot matrix analysis

2. The dynamic programming (or DP) algorithm

3. Word or *k-tuple methods, such as used by the programs FASTA and BLAST*

Dynamic Programming Algorithm

- Needleman and Wunsch (1970)
  - Global Alignment

- Smith and Waterman (1981)
  - Local Alignment

Needleman–Wunsch Algorithm

(1) Setting up a matrix

(2) Scoring the matrix

(3) Identifying the optimal alignment

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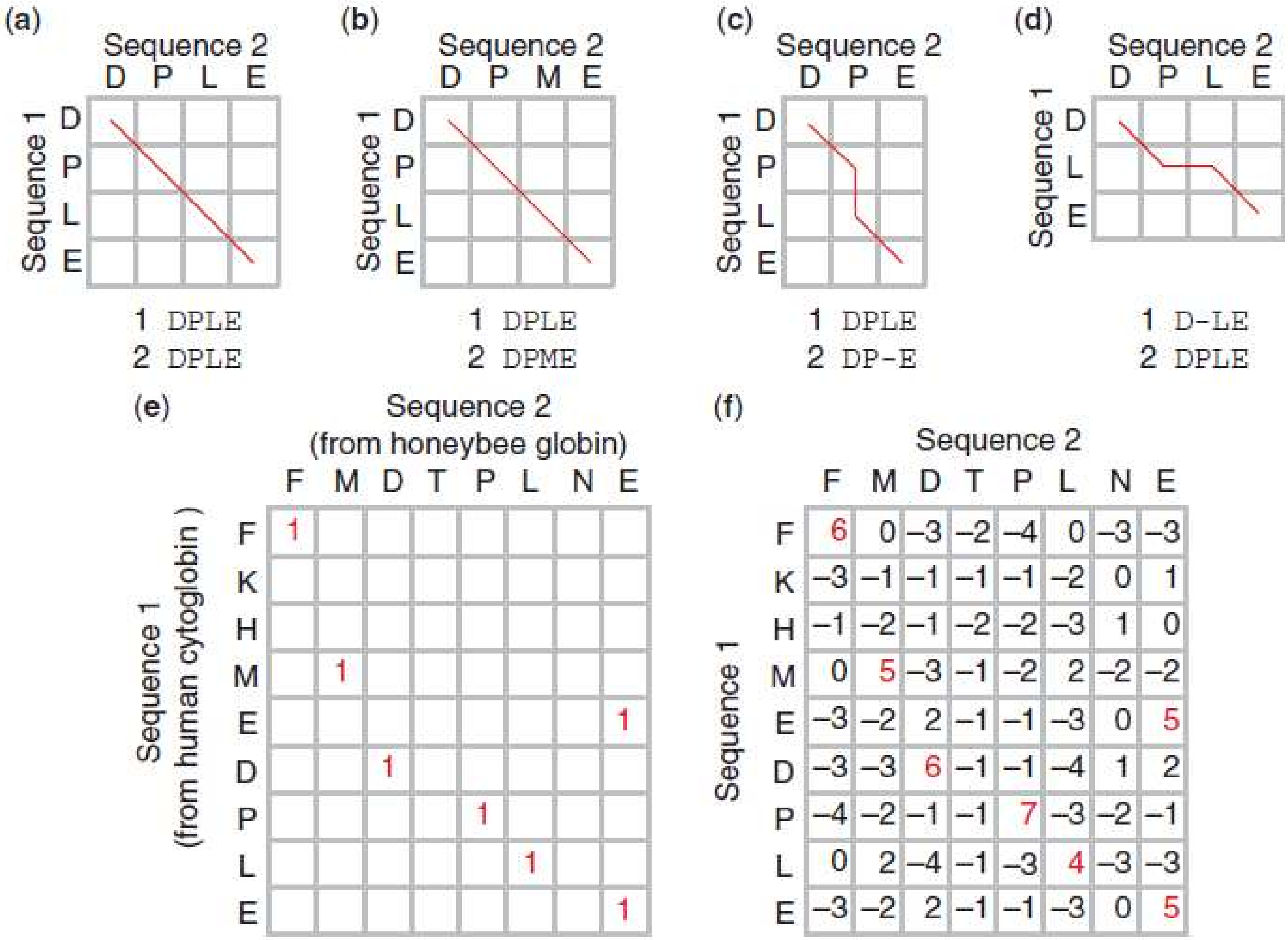
Setting up a matrix



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1. Two residues may be perfectly matched (i.e., identical)

2. They may be mismatched

3. A gap may be introduced from the first sequence

4. A gap may be introduced from the second sequence

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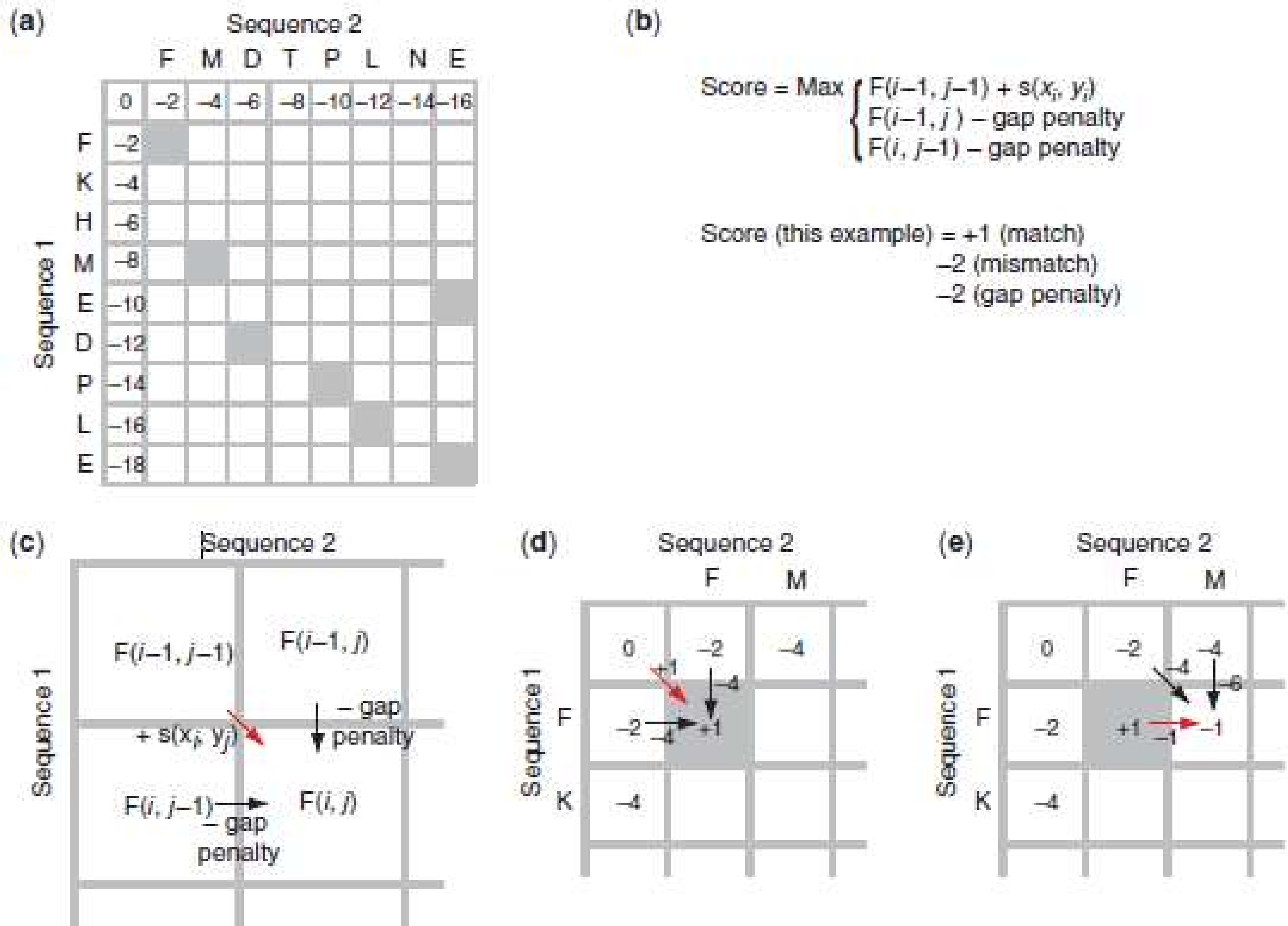
Scoring the Matrix



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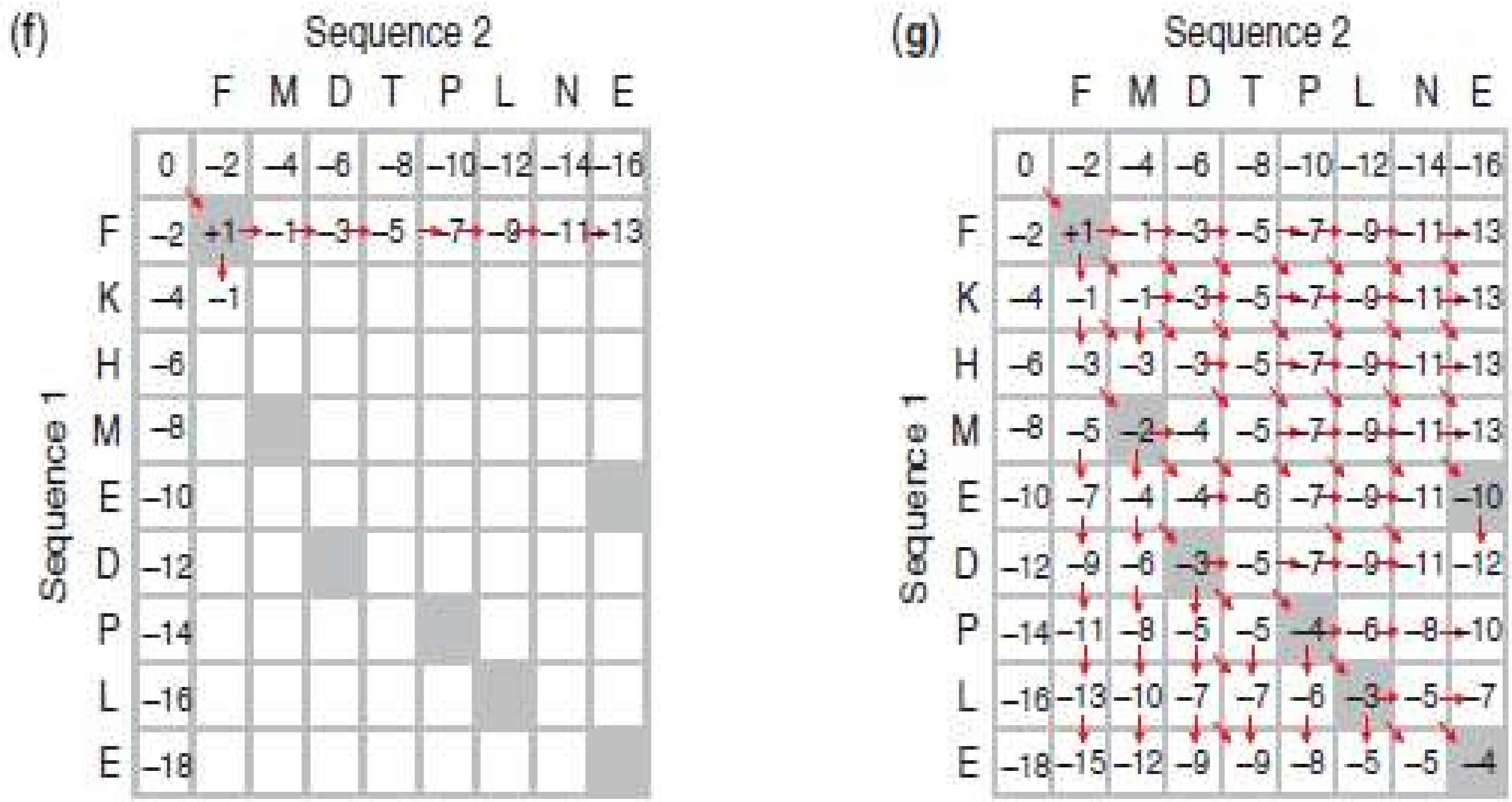

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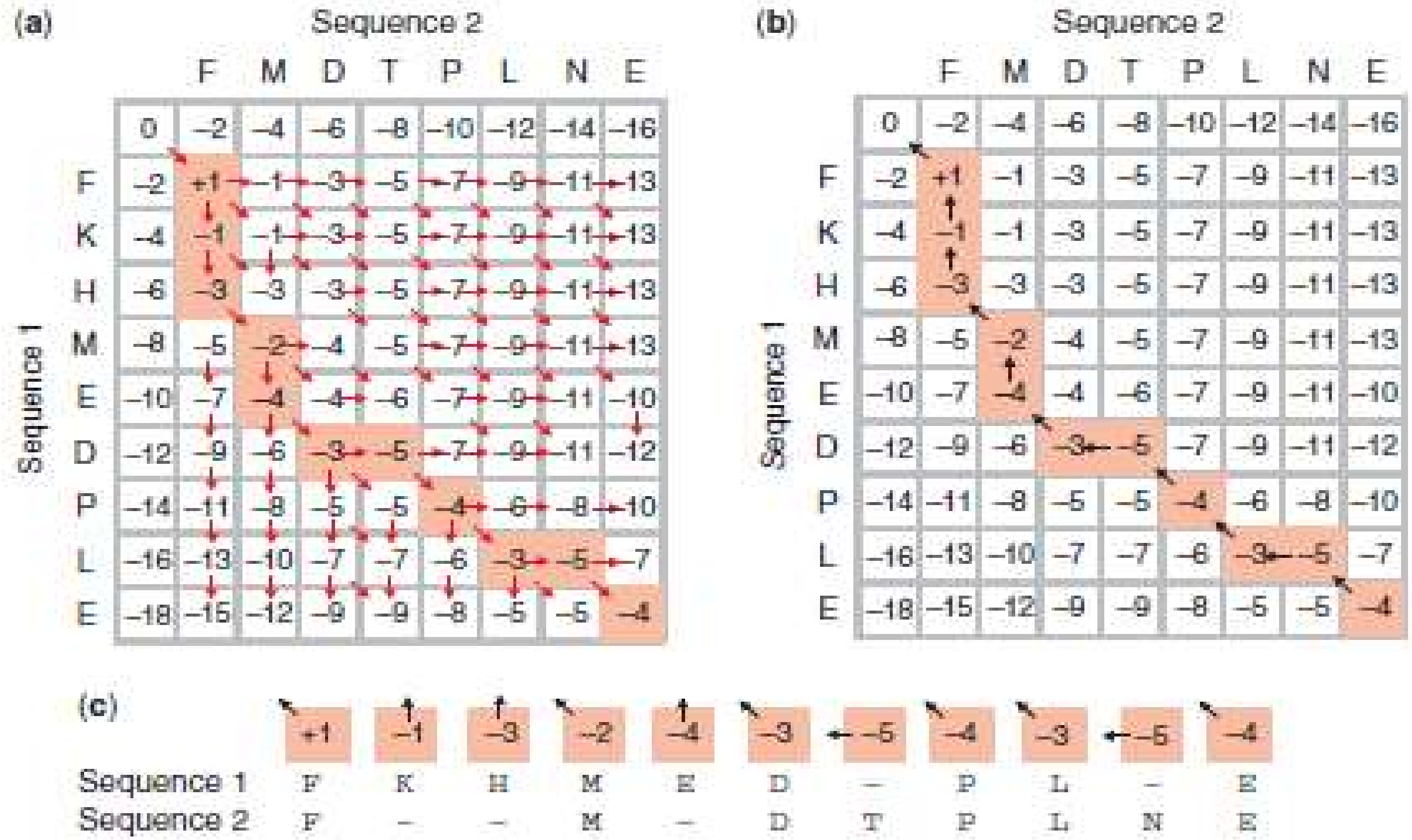
Identifying the Optimal Alignment



Note that the final score of -4 equals sum of matches (6) and gaps (-10)

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Smith and Waterman Algorithm

Sequence 1

Sequence 2		C	A	G	C	C	U	C	G	C	U	U	A	G
	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
A	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.0
A	0.0	0.0	1.0	0.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.7
U	0.0	0.0	0.0	0.7	0.3	0.0	1.0	0.0	0.0	0.0	1.0	1.0	0.0	0.7
G	0.0	0.0	0.0	1.0	0.3	0.0	0.0	0.7	1.0	0.0	0.0	0.7	0.7	1.0
C	0.0	1.0	0.0	0.0	2.0	1.3	0.3	1.0	0.3	2.0	0.7	0.3	0.3	0.3
C	0.0	1.0	0.7	0.0	1.0	3.0	1.7	1.3	1.0	1.3	1.7	0.3	0.0	0.0
A	0.0	0.0	2.0	0.7	0.3	1.7	2.7	1.3	1.0	0.7	1.0	1.3	1.3	0.0
U	0.0	0.0	0.7	1.7	0.3	1.3	2.7	2.3	1.0	0.7	1.7	2.0	1.0	1.0
U	0.0	0.0	0.3	0.3	1.3	1.0	2.3	2.3	2.0	0.7	1.7	2.7	1.7	1.0
G	0.0	0.0	0.0	1.3	0.0	1.0	1.0	2.0	3.3	2.0	1.7	1.3	2.3	2.7
A	0.0	0.0	1.0	0.0	1.0	0.3	0.7	0.7	2.0	3.0	1.7	1.3	2.3	2.0
C	0.0	1.0	0.0	0.7	1.0	2.0	0.7	1.7	1.7	3.0	2.7	1.3	1.0	2.0
G	0.0	0.0	0.7	1.0	0.3	0.7	1.7	0.3	2.7	1.7	2.7	2.3	1.0	2.0
G	0.0	0.0	0.0	1.7	0.7	0.3	0.3	1.3	1.3	2.3	1.3	2.3	2.0	2.0

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1. The score from the cell at position $i-1, j-1$; that is, the score diagonally up to the left. To this score, add the new score at position $s[i, j]$, which consists of either a match or a mismatch.
2. $s(i, j-1)$ (i.e., the score one cell to the left) minus a gap penalty.
3. $s(i-1, j)$ (i.e., the score immediately above the new cell) minus a gap penalty.
4. The number zero. This condition assures that there are no negative values in the matrix. In contrast negative numbers commonly occur in global alignments because of gap or mismatch penalties (note the log-odds matrices in this chapter).

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Global vs Local

(b)

```
sequence 1   GCC-UCG
sequence 2   GCCAUUG
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(c)

```
sequence 1   CAGCC-UCGCUUAG
sequence 2   AAUGCCAUUGACGG
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Thank You