4 Local alignment

4.1 Local alignments

Local pairwise alignments are aligned pairs of sub–sequences that have certain level of similarities.

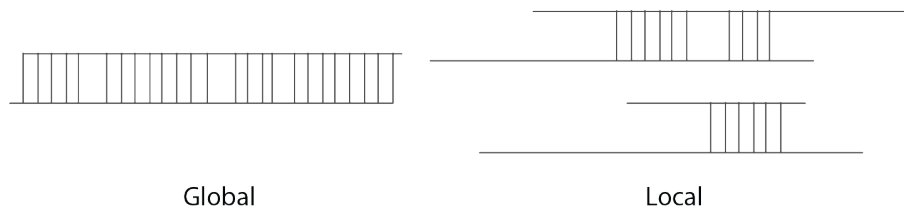**Deiffrence between global and local alignments**

Global   Local

Figure 4.1: Global and local alignments

Elements of local alignment

- Segment: a substring of a sequence

- Segment pair: a pair of segments

- Local alignment: an alignment of a segment pair

Elements of local alignment

- Dynamic programming (Smith–Waterman)

- Dot matrix

Applications

- Sequence motifs

- Conserved regions

- Inverted repeats

4.2 Local alignment with DP

Dynamic programming can be used to find local alignments.

Requirements

- Find all local alignments between two sequences

- Assign scores to all local alignments

Modification of DP for local alignments

- The minimum alignment score must be 0

- Some entries of the score matrix should be negative

- Backtracking also needs to be modified

Update rule of DP cells

$$H_{i,j}^{(0)} = H_{i-1,j} - g \qquad\qquad (vertical)$$
$$H_{i,j}^{(1)} = H_{i,j-1} - g \qquad\qquad (horizontal)$$
$$H_{i,j}^{(2)} = H_{i-1,j-1} + R_{a,b} \qquad\qquad (diagonal)$$
$$H_{i,j}^{(2)} = 0 \qquad\qquad (minimum\ score)$$

Example of cell update

	A	C
C	0.1	0.4
T	0.2	0

Scoring scheme:
  Match: 0.5
  Mismatch: -0.3
  Gap penalty: 0.5

$$H_{i,j}^{(0)} = -0.1 \qquad\qquad (vertical)$$
$$H_{i,j}^{(1)} = -0.3 \qquad\qquad (horizontal)$$
$$H_{i,j}^{(2)} = -0.2 \qquad\qquad (diagonal)$$
$$H_{i,j}^{(2)} = 0 \qquad\qquad \checkmark (minimum\ score)$$

Backtracking for local alignments

It starts from the cells with the maximum score instead of the right bottom cell.

- Start cells: cells with the maximum score

- End cells: cells with 0

N.B. the end cell with score 0 should not be included in the alignment.

Example of backtracking

	A	C	G	C
	0	0	0	0	0
C	0	0	0.5	0	0.5
G	0	0	0	1	0.5
A	0	0.5	0	0.5	0.7

Local alignment
```
q: 2 CG 3
d: 2 CG 3
```

Pseudo-code of updating DP table for local alignment

The cells in the first row and the first column are initialized with 0.

Algorithm 4.1: Update dynamic programming table for global alignment

$H_{i,j}$: Dynamic programming table
$R_{a,b}$: Match/mismatch scores
g   : Gap penalty

```
// Initialization
```
for $i \leftarrow 0$ **to** m **do**
| $H_{i,0} \leftarrow \mathbf{0}$;
end
for $j \leftarrow 1$ **to** n **do**
| $H_{0,j} \leftarrow \mathbf{0}$;
end

```
// Main loop for table update
```
for $i \leftarrow 1$ **to** m **do**
| **for** $j \leftarrow 1$ **to** n **do**
| | $H_{i,j} \leftarrow max(\mathbf{0}, H_{i-1,j} - g, H_{i,j-1} - g, H_{i-1,j-1} + R_{a,b})$;
| **end**
end

Exercise 4.1

Use DP to find a local alignment.

q/d		A	G	C	C
A					
G					
C					

Scoring scheme:
   Match: 0.2
   Mismatch: -0.2
   Gap penalty: 0.2

4.3   Dot matrix

Using a dot matrix is an effective and easy way to find local similarities.

Basic concept

It uses an $m \times n$ binary matrix from two sequences.

- A dot: match

- Empty: mismatch

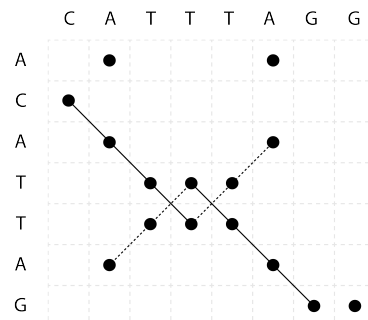## Example of dot matrix

    q: ACATTAG, d: CATTTAGG

Figure 4.2: Dot matrix of 7×8

It is easy to find segment pairs with a dot matrix. Contiguous dots along diagonals indicate local alignments. It is also easy to find other similarities. For instance, contiguous dots along anti-diagonals indicate reversed substrings.

Filtering of dot matrix

Dot matrices usually get noisy with too many dots. Overlapping windows are usually applied to reduce the noise.
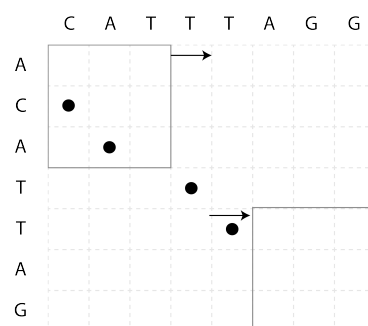
Example of filtering

Figure 4.3: Filtered dot matrix with window size 3 and threshold 3.

Exercise 4.2

Find local similarities between two DNA sequences, q: GATTACA and d: GGATTTAC.

1. Create a dot matrix for the two sequences.

2. Filter dots with overlapping windows size 3 and threshold 3.