

## Exercise sheet 3: T-Coffee

### Exercise 1

You are given the sequences  $a$ ,  $b$  and  $c$

$$a = CACCGGb = ACCAAGc = AACACC$$

The pairwise optimal alignments of Pool  $P$  were calculated as:

|            |             |           |
|------------|-------------|-----------|
| a: CACCG_G | a: __CACCGG | b: ACCAAG |
| :          |             | :     : : |
| b: _ACCAAG | c: AACACC__ | c: AACACC |

**Question 1A** Calculate the primary library ( $L$ )

**Formulae** init:  $L_{j,j'}^{i,i'} = 0$

$\forall$  alignments  $A$  of sequence  $s^i$   $s^{i'}$  in pool  $P$

$$weight(A) = \frac{\text{number of matches}}{\min(\text{len}(s^i), \text{len}(s^{i'}))}$$

$\forall$  aligned positions  $i, j$

$$L_{j,j'}^{i,i'} = L_{j,j'}^{i,i'} + weight(A)$$

**Solution**  $L_{2,1}^{a,b} = L_{3,2}^{a,b} = L_{4,3}^{a,b} = L_{6,6}^{a,b} = 100 * \frac{4}{6} = 67$  and all other  $L_{i,j}^{a,b} = 0$

$L_{1,3}^{a,c} = L_{2,4}^{a,c} = L_{3,5}^{a,c} = L_{4,6}^{a,c} = 100 * \frac{4}{6} = 67$  and all other  $L_{i,j}^{a,c} = 0$

$L_{1,1}^{b,c} = L_{3,3}^{b,c} = L_{4,4}^{b,c} = 100 * \frac{3}{6} = 50$  and all other  $L_{i,j}^{b,c} = 0$

**Question 1B** Calculate the extended library ( $EL$ )

**Formulae**  $k :=$  number of entries in  $L$

$$EL_{j,j'}^{i,i'} = L_{j,j'}^{i,i'} + \sum_{i \neq (1 \leq i^* \leq k) \neq i'} \min(L_{j,j^*}^{i,i^*}, L_{j^*,j'}^{i^*,i'})$$

**Solution** The original Library doesn't change as there are no edges enforcing certain connections. Hence

$$EL_{j,j'}^{i,i'} = L_{j,j'}^{i,i'} \quad \forall L_{j,j'}^{i,i'} \neq 0$$

and the following weights are added:

```
a: CACCG_G
   |||: |
b: _ACCAAG
   |:|:::
c: AACACC
   * *
```

$$EL_{1,3}^{a,b} = EL_{2,4}^{a,b} = 50$$

```
a: __CACCGG
   ||||
c: AACACC__
   |:|:::
b: ACCAAG
   **
```

$$EL_{2,1}^{a,c} = EL_{4,3}^{a,c} = 50$$

```
b:   ACCAAG
   |||: |
a:   CACCG_G
   ||||
c: AACACC
   ***
```

$$EL_{1,4}^{b,c} = EL_{2,5}^{b,c} = EL_{3,6}^{b,c} = 67$$

**Question 1C** Realign the sequences  $b$  and  $c$  using EL for scoring and gap costs and mismatch costs of 0

**Solution**

| - | - | A  | C   | C   | A   | A   | G   |
|---|---|----|-----|-----|-----|-----|-----|
| - | 0 | 0  | 0   | 0   | 0   | 0   | 0   |
| A | 0 | 50 | 50  | 50  | 50  | 50  | 50  |
| A | 0 | 50 | 50  | 50  | 50  | 50  | 50  |
| C | 0 | 50 | 50  | 100 | 100 | 100 | 100 |
| A | 0 | 67 | 67  | 100 | 150 | 150 | 150 |
| C | 0 | 67 | 133 | 133 | 150 | 150 | 150 |
| C | 0 | 67 | 133 | 200 | 200 | 200 | 200 |

**Question 1C** Do the other alignments a-b and a-c change? Provide arguments, without calculating new alignments.

**Solution** No. The newly added alignment scores in  $EL$  represent edges that are incompatible with the current best alignments and can not score higher.

**Question 1E** Sketch the Guide Tree

**Solution**  $((a, c), b)$  or  $((a, b), c)$

**Question 1F** Perform a progressive alignment by aligning sequence b to the already existing alignment  $A(a, c)$ . To score a match between  $b$  and  $A(a, c)$  use the sum  $EL^{a,b} + EL^{b,c}$  with the correct indices. Show the resulting multiple sequence alignment.

**Solution**

| – | – | -A | -A | CC  | AA  | CC  | CC  | G-  | G-  |
|---|---|----|----|-----|-----|-----|-----|-----|-----|
| - | 0 | 0  | 0  | 0   | 0   | 0   | 0   | 0   | 0   |
| A | 0 | 50 | 50 | 50  | 133 | 133 | 133 | 133 | 133 |
| C | 0 | 50 | 50 | 50  | 133 | 267 | 267 | 267 | 267 |
| C | 0 | 50 | 50 | 150 | 150 | 267 | 400 | 400 | 400 |
| A | 0 | 50 | 50 | 150 | 250 | 267 | 400 | 400 | 400 |
| A | 0 | 50 | 50 | 150 | 250 | 267 | 400 | 400 | 400 |
| G | 0 | 50 | 50 | 150 | 250 | 267 | 400 | 400 | 467 |