

Exercise sheet 3: T-Coffee



Exercise 1

You are given the sequences a , b and c

$$a = CACCGG = ACCAAG = AACACC$$

The pairwise optimal alignments $A(x, y)$ of the set of sequences S were calculated as:

a: CACCG_G	a: _CACCGG	b: ACCAAG
:		: ::
b: _ACCAAG	c: AACACC__	c: AACACC

1a)

Calculate the primary library (L)

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Formulae init: $L_{i,j}^{x,y} = 0$

\forall alignments A of sequences x and y of the set S .

$$\text{weight}(A) = \frac{\text{number of matches}}{\min(\text{len}(x), \text{len}(y))} * 100$$

\forall aligned positions i, j with $1 \leq i \leq \text{len}(x)$ and $1 \leq j \leq \text{len}(y)$

$$L_{i,j}^{x,y} = L_{i,j}^{x,y} + \text{weight}(A)$$

Solution $L_{2,1}^{a,b} = L_{3,2}^{a,b} = L_{4,3}^{a,b} = L_{6,6}^{a,b} = 100 * \frac{4}{6} = 66.6\bar{6} \approx 67$ and all other $L_{i,j}^{a,b} = 0$

$L_{1,3}^{a,c} = L_{2,4}^{a,c} = L_{3,5}^{a,c} = L_{4,6}^{a,c} = 100 * \frac{4}{6} = 66.6\bar{6} \approx 67$ 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 $L_{i,j}^{b,c} = 0$

1b)

Calculate the extended library (EL)

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$$\text{Formulae } EL_{i,j}^{x,y} = L_{i,j}^{x,y} + \sum_{z \in S \setminus \{x, y\}} \sum_{1 \leq k \leq \text{len}(z)} \min(L_{i,k}^{x,z}, L_{k,j}^{z,y})$$

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

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

and the following weights are added:

a: __CACCGG

|||||

c: AACACC__

|:||::

b: ACCAAG

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

a: CACCG_G

|||: |

b: _ACCAAG

|:||::

c: AACACC

* *

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

b: ACCAAG

|||: |

a: CACCG_G

|||||

c: AACACC

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

1c)

Realign the sequences b and c using EL for scoring and gap costs and mismatch costs of 0

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Formulae

$$\begin{aligned}
i &\in [1, |x|] \\
j &\in [1, |y|] \\
L(0, 0) &= 0 \\
L(i, 0) &= w(x_i, -) * i \quad \text{or} = L(i - 1, 0) + w(x_i, -) \\
L(0, j) &= w(-, y_j) * j \quad \text{or} = L(0, j - 1) + w(-, y_j) \\
L(i, j) &= \max \begin{cases} L(i - 1, j) + w(x_i, -) \\ L(i, j - 1) + w(-, y_j) \\ L(i - 1, j - 1) + w(x_i, y_j) \end{cases} \\
w(x_i, y_j) &= \begin{cases} EL_{i,j}^{x,y} & \text{match-score if } (x_i = y_j) \\ 0 & \text{insert/deletion-score if } (x_i = - \vee y_j = -) \\ 0 & \text{mismatch-score else } (x_i \neq y_j) \end{cases}
\end{aligned}$$

Solution

-1	-	A1	C2	C3	A4	A5	G6
-	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

Alignment:

b: ___ACCAAG
 |||
 c: AACACC___

1d)

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

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

1e)

Sketch a Guide Tree (either Sketch or Newick format)

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Solution Newick: $((a, c), b)$ or $((a, b), c)$ or $((b, c), a)$

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.

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

Solution

One Possible Alignment:

a: __CACC_GG
 ||||
 c: AACACC__
 |||
 b: ___ACCAAG

