Notredame-Higgins-Heringa (T-Coffee)

Unit Tests

Hint: Many test values are taken from project Algorithms for Bioninformatics of Alexander Mattheis or the lectures.

Test 1 (Hint: Notation from original Feng-Doolittle paper used!)

Input

Sequence a: ACGT Sequence b: AT Sequence c: GCT

Gap opening: 0 (easifies later visual proofment)

Enlargement: -2

Match: 1 (and 0 for placeholder #)

Mismatch: -1

Output (Computation: Global Primary Library)

	Alignment- Length	Gaps	Gap- starts	Score
(a,b)	4	2	1	-2
(a,c)	4	1	1	-1
(b,c)	3	1	1	-2

a: ACGT

b: A_T

a: ACGT

|* *

c: GC_T

b: _AT |*

c: GCT

Hint: More alignments exists, but only one is computed!

Output (Computation: Weight Primary Library)

1. Conversion (not used in implementation – only for visualization)

für (a,b): {(1,1),(4,2)}

((1,1), (1,2))

für (a,c): {(1,1),(2,2),(4,3)}

für (b,c): {(1,2),(2,3)}

$$Pool = \left\{ \begin{cases} \{(1,1), (4,2)\} \\ \{(1,1), (2,2), (4,3)\} \\ \{(1,2), (2,3)\} \end{cases} \right\}$$

$$L_{i,i}^{S_1,S_2} = 0$$

$$L_{i,j}^{S_1,S_2} = L_{i,j}^{S_1,S_2} + weight(A(a,b))$$
 where $weight(A(a,b)) = seq_{ID}(A(a,b))$

2. Weight computation
$$L_{i,j}^{s_1,s_2} = 0$$

$$L_{i,j}^{s_1,s_2} = L_{i,j}^{s_1,s_2} + weight(A(a,b)) \text{ where } weight(A(a,b)) = seq_{ID}(A(a,b))$$

$$PrimLib = \begin{cases} \{L_{1,1}^{a,b}, L_{4,2}^{a,b}\} \\ \{L_{1,1}^{a,c}, L_{2,2}^{a,c}, L_{4,3}^{a,c}\} \\ \{L_{1,2}^{b,c}, L_{2,3}^{b,c}\} \end{cases} = \begin{cases} \frac{2}{2} \cdot 100, \frac{2}{2} \cdot 100 \\ \frac{2}{3} \cdot 100, \frac{2}{3} \cdot 100, \frac{2}{3} \cdot 100 \\ \frac{2}{3} \cdot 100, \frac{2}{3} \cdot 100 \end{cases}$$

$$\left\{ \frac{200}{3}, \frac{$$

Output (Computation: Extended Primary Library)

 $L_{i,j}^{a,b} = L_{j,i}^{b,a}$ or it would not make sense (a triple like three T in a column should be recognized irrelevant of order)

$$ExtendedLib = \begin{cases} \left\{EL_{1,1}^{a,b}, EL_{4,2}^{a,b}\right\} \\ \left\{EL_{1,1}^{a,c}, EL_{2,2}^{a,c}, EL_{4,3}^{a,c}\right\} \\ \left\{EL_{1,2}^{b,c}, EL_{2,3}^{b,c}\right\} \end{cases} = \begin{cases} \left\{100, 100\right\} \\ \left\{\frac{200}{3}, \frac{200}{3}, \frac{350}{3}\right\} \\ \left\{50, 50\right\} \end{cases}$$

correct:

$$ExtendedLib = \begin{cases} \left\{EL_{1,1}^{a,b}, EL_{4,2}^{a,b}\right\} \\ \left\{EL_{1,1}^{a,c}, EL_{2,2}^{a,c}, EL_{4,3}^{a,c}\right\} \\ \left\{EL_{1,2}^{b,c}, EL_{2,3}^{b,c}\right\} \end{cases} = \begin{cases} \left\{100, 150\right\} \\ \left\{\frac{200}{3}, \frac{200}{3}, \frac{350}{3}\right\} \\ \left\{50, \frac{350}{2}\right\} \end{cases}$$
 Hint: because of Triple-Match $\frac{350}{3}$

$$EL_{1,1}^{a,b} = L_{1,1}^{a,b} + \sum_{x \in S \setminus \{a,b\}} \sum_{k \in Pos(x)} \min(L_{1,k}^{a,x}, L_{k,1}^{x,b})$$

$$=L_{1,1}^{a,b}+\sum_{x\in\{c\}}\sum_{k\in\{1,2,3\}}\min(L_{1,k}^{a,x},L_{k,1}^{x,b})$$

$$= 100 + \min(L_{1,1}^{a,c}, L_{1,1}^{c,b}) + \min(L_{1,2}^{a,c}, L_{2,1}^{c,b}) + \min(L_{1,3}^{a,c}, L_{3,1}^{c,b})$$

$$= 100 + \min\left(\frac{200}{3}, 0\right) + 0 + 0 = 100$$

$$EL_{4,2}^{a,b} = 100 + \min(L_{4,1}^{a,c}, L_{1,2}^{c,b}) + \min(L_{4,2}^{a,c}, L_{2,2}^{c,b}) + \min(L_{4,3}^{a,c}, L_{3,2}^{c,b})$$

$$= 100 + 0 + 0 + \min\left(\frac{200}{3}, 50\right) = 150$$

$$\begin{split} EL_{1,1}^{a,c} &= L_{1,1}^{a,c} + \sum_{x \in \{b\}} \sum_{k \in \{1,2\}} \min(L_{1,k}^{a,x}, L_{k,1}^{x,b}) \\ &= \frac{200}{3} + \min(L_{1,1}^{a,b}, L_{1,1}^{b,c}) + \min(L_{1,2}^{a,b}, L_{2,1}^{b,c}) \\ &= \frac{200}{3} + \min(100,0) + \min(0,50) \\ EL_{2,2}^{a,c} &= L_{2,2}^{a,c} + \sum_{x \in \{b\}} \sum_{k \in \{1,2\}} \min(L_{2,k}^{a,x}, L_{k,2}^{x,b}) \\ &= \frac{200}{3} + \min(L_{2,1}^{a,b}, L_{1,2}^{b,c}) + \min(L_{2,2}^{a,b}, L_{2,2}^{b,c}) \\ &= \frac{200}{3} + \min(0,50) + 0 \end{split}$$

$$\begin{split} EL_{4,3}^{a,c} &= L_{4,3}^{a,c} + \sum_{x \in \{b\}} \sum_{k \in \{1,2\}} \min(L_{4,k}^{a,x}, L_{k,3}^{x,c}) \\ &= \frac{200}{3} + \min(L_{4,1}^{a,b}, L_{1,3}^{b,c}) + \min(L_{4,2}^{a,b}, L_{2,3}^{b,c}) \\ &= \frac{200}{3} + 0 + \min(100,50) \\ &= \frac{350}{3} \approx 116.67 \end{split}$$

$$\begin{split} &EL_{1,2}^{b,c} = L_{1,2}^{b,c} + \sum_{x \in \{a\}} \sum_{k \in \{1,2,3,4\}} \min(L_{1,k}^{b,x}, L_{k,2}^{x,c}) \\ &= 50 + \min(L_{1,1}^{b,a}, L_{1,2}^{a,c}) + \min(L_{1,2}^{b,a}, L_{2,2}^{a,c}) + \min(L_{1,3}^{b,a}, L_{3,2}^{a,c}) + \min(L_{1,4}^{b,a}, L_{4,2}^{a,c}) \\ &= 50 + \min(100,0) + \min\left(0, \frac{100}{3}\right) + 0 + 0 \\ &EL_{2,3}^{b,c} = L_{2,3}^{b,c} + \sum_{x \in \{a\}} \sum_{k \in \{1,2,3,4\}} \min(L_{2,k}^{b,x}, L_{k,3}^{x,c}) \\ &= 50 + \min(L_{2,1}^{b,a}, L_{1,3}^{a,c}) + \min(L_{2,2}^{b,a}, L_{2,3}^{a,c}) + \min(L_{2,3}^{b,a}, L_{3,3}^{a,c}) + \min(L_{2,4}^{b,a}, L_{4,3}^{a,c}) \\ &= 50 + 0 + 0 + 0 + \min\left(100, \frac{200}{3}\right) \\ &= \frac{350}{3} \end{split}$$

Output (Distances)

 $D(a,b) = -\ln S_{a,b}^{eff} \approx 0.9808$ (look into Feng-Doolittle Unit-Tests)

$$S_{a,c}^{rand}$$

$$=\frac{1}{4}\begin{pmatrix} s(A_{a},G_{b})\cdot N_{A}(a)\cdot N_{G}(b)+s(A_{a},C_{b})\cdot N_{A}(a)\cdot N_{C}(b)+s(A_{a},T_{b})\cdot N_{A}(a)\cdot N_{T}(b)\\ +s(C_{a},G_{b})\cdot N_{C}(a)\cdot N_{G}(b)+s(C_{a},C_{b})\cdot N_{C}(a)\cdot N_{C}(b)+s(C_{a},T_{b})\cdot N_{C}(a)\cdot N_{T}(b)\\ +s(G_{a},G_{b})\cdot N_{G}(a)\cdot N_{G}(b)+s(G_{a},C_{b})\cdot N_{G}(a)\cdot N_{C}(b)+s(G_{a},T_{b})\cdot N_{G}(a)\cdot N_{T}(b)\\ +s(T_{a},G_{b})\cdot N_{T}(a)\cdot N_{G}(b)+s(T_{a},C_{b})\cdot N_{T}(a)\cdot N_{C}(b)+s(T_{a},T_{b})\cdot N_{T}(a)\cdot N_{T}(b) \end{pmatrix}$$

 $+1 \cdot enlarge$

$$= \frac{1}{4} \begin{pmatrix} (-1) + (-1) + (-1) \\ + (-1) + 1 + (-1) \\ + 1 + (-1) + (-1) \\ + (-1) + (-1) + 1 \end{pmatrix} + 1 \cdot (-2) = \frac{-6}{4} - 2 = -3.5$$

$$S_{a,c}^{max} = \frac{4+3}{2} = 3.5$$

$$S_{a,c}^{eff} = \frac{S(a,c) - S_{a,c}^{rand}}{S_{a,c}^{max} - S_{a,c}^{rand}} = \frac{-1 - (-3.5)}{3.5 - (-3.5)} = \frac{2.5}{7}$$

$$D(a,c) = -\ln(S_{a,c}^{eff}) \approx 1.0296$$

Shand

$$= \frac{1}{3} \cdot \left(\begin{array}{c} s(A_a, G_b) \cdot N_A(a) \cdot N_G(b) + s(A_a, C_b) \cdot N_A(a) \cdot N_C(b) + s(A_a, T_b) \cdot N_A(a) \cdot N_T(b) \\ + s(T_a, G_b) \cdot N_T(a) \cdot N_G(b) + s(T_a, C_b) \cdot N_T(a) \cdot N_C(b) + s(T_a, T_b) \cdot N_T(a) \cdot N_T(b) \end{array} \right) \\ + 1 \cdot enlarge \\ = \frac{1}{3} \cdot \left(\begin{array}{c} (-1) + (-1) + (-1) \\ + (-1) + (-1) + 1 \end{array} \right) - 2 = \frac{-4}{3} - 2 = -\frac{10}{3}$$

$$S_{b,c}^{max} = \frac{2+3}{2} = 2.5$$

$$S_{b,c}^{eff} = \frac{S(b,c) - S_{b,c}^{rand}}{S_{b,c}^{max} - S_{b,c}^{rand}} = \frac{-2 - \left(-\frac{10}{3}\right)}{2.5 - \left(-\frac{10}{3}\right)} = \frac{\frac{4}{3}}{\frac{35}{6}} = \frac{8}{35}$$

$$D(b,c) = -\ln(S_{b,c}^{eff}) \approx 1.4759$$

Output (Phylogenetic Tree : look into Feng-Doolittle Unit-Tests)

1.

$$\mathcal{C} = \big((\mathcal{C} - \{a\}) - \{b\}\big) \cup \{d\}$$

	;	1)	С	d	
					4		
а		′		-			
1.					1.5		
U			 	,	1.0		
С					0	1.25	
c d					0	1.25 0	

3.

$$dist(d, a) = dist(d, b) = \frac{1}{2} = 0.5$$

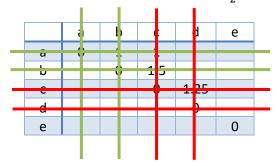
$$dist(c, d = \{a, b\}) = \frac{|a| \cdot dist(c, a) + |b| \cdot dist(c, b)}{|a| + |b|} = \frac{1 \cdot 1 + 1 \cdot 1.5}{1 + 1} = 1.25$$

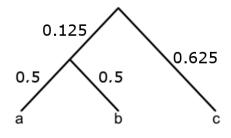
1)
$$d_{min} = 1.25$$

1)
$$d_{min} = 1.25$$

2) $C = ((C - \{c\}) - \{d\}) \cup \{e\}$

3)
$$dist(e,c) = dist(e,d) = \frac{d_{min}}{2} = 0.625$$





Output (Joinment)

Gap opening: 0 \rightarrow Gotoh not needed for calculation

Enlargement: 0

a

$$ExtendedLib = \left\{ \begin{cases} EL_{1,1}^{a,b}, EL_{4,2}^{a,b} \\ \{EL_{1,1}^{a,c}, EL_{2,2}^{a,c}, EL_{4,3}^{a,c} \} \\ \{EL_{1,2}^{b,c}, EL_{2,3}^{b,c} \} \end{cases} = \left\{ \begin{cases} \{100, 150\} \\ \frac{200}{3}, \frac{200}{3}, \frac{350}{3} \} \\ \{50, \frac{350}{3} \} \end{cases} \right\}$$

1. a~b:

		A ₁	T ₂
	0	0	0
A ₁	0	100	100
C ₂	0	100	100
G₃	0	100	100
T ₄	0	100	250

ACGT

A##T

Score 250

2.

A C

G T

and

G C T

ab~c: (every char with every other char, so A_a with G_c and A_b with $G_c \rightarrow$ and then average)

			G ₁	C ₂	T ₃
		0	0	0	0
A ₁	A_1	0	100/3	100/3	100/3
C ₂	#	0	100/3	200/3	200/3
G₃	#	0	100/3	200/3	200/3
T ₄	T ₂	0	100/3	200/3	550/3

$$\frac{EL_{1,1}^{a,c} + EL_{1,1}^{b,c}}{2} = \frac{\frac{200}{3} + 0}{2} = \frac{100}{3}$$

$$\frac{EL_{1,2}^{a,c} + EL_{1,2}^{b,c}}{2} = \frac{0+50}{2} = 25$$

$$\frac{EL_{1,3}^{a,c} + EL_{1,3}^{b,c}}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{2,1}^{a,c}+0}{2}=\frac{0+0}{2}=0$$

$$\frac{EL_{2,2}^{a,c}+0}{2} = \frac{\frac{200}{3}+0}{2} = 100/3$$

$$\frac{EL_{2,3}^{a,c} + 0}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{3,1}^{a,c}+0}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{3,2}^{a,c}+0}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{3,3}^{a,c}+0}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{4,1}^{a,c} + EL_{2,1}^{b,c}}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{4,2}^{a,c} + EL_{2,2}^{b,c}}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{4,3}^{a,c} + EL_{2,3}^{b,c}}{2} = \frac{\frac{350}{3} + \frac{350}{3}}{2} = \frac{350}{3}$$

Output (Final)

ACGT

A T

GC T

SoP-Score -5

Test 2

Input

Sequence a: ACGT Sequence b: AT Sequence c: GCT

Gap opening: 0 (easifies later visual proofment)

Enlargement: -2

Match: 1 (and 0 for placeholder #)

Mismatch: -1

Output (Computation: Local Primary Library)

Pos: 1
a: A
*
b: A
Pos: 1
Pos: 2
a: C

C: C
Pos: 2

Pos: 2 b: T * c: T Pos: 3

Hint: More alignments exists, but only one is computed!

Output (Computation: Weight Primary Library)

1. Conversion

(taken out)

2. Weight computation

$$\begin{split} PrimLib_{loc} &= \begin{cases} \{L_{1,1}^{a,b}\} \\ \{L_{2,2}^{a,c}\} \\ \{L_{2,3}^{b,c}\} \end{cases} = \begin{cases} \{100\} \\ \{100\} \\ \{100\} \end{cases} \\ \\ PrimLib_{glob} &= \begin{cases} \{L_{1,1}^{a,b}, L_{4,2}^{a,b}\} \\ \{L_{1,1}^{a,c}, L_{2,2}^{a,c}, L_{4,3}^{a,c}\} \\ \{L_{1,2}^{b,c}, L_{2,3}^{b,c}\} \end{cases} = \begin{cases} \{100, 100\} \\ \{\frac{200}{3}, \frac{200}{3}, \frac{200}{3} \} \\ \{50,50\} \end{cases} \end{split}$$

$$PrimLib = \begin{cases} \left\{ L_{1,1}^{a,b}, L_{4,2}^{a,b} \right\} \\ \left\{ L_{1,1}^{a,c}, L_{2,2}^{a,c}, L_{4,3}^{a,c} \right\} \\ \left\{ L_{1,2}^{b,c}, L_{2,3}^{b,c} \right\} \end{cases} = \begin{cases} \left\{ 200, 100 \right\} \\ \left\{ \frac{200}{3}, \frac{500}{3}, \frac{200}{3} \right\} \\ \left\{ 50, 150 \right\} \end{cases}$$

Output (Computation: Extended Primary Library)

$$ExtendedLib = \begin{cases} \left\{ EL_{1,1}^{a,b}, EL_{4,2}^{a,b} \right\} \\ \left\{ EL_{1,1}^{a,c}, EL_{2,2}^{a,c}, EL_{4,3}^{a,c} \right\} \\ \left\{ EL_{1,2}^{b,c}, EL_{2,3}^{b,c} \right\} \end{cases} = \begin{cases} \left\{ 200, \frac{500}{3} \right\} \\ \left\{ \frac{200}{3}, \frac{500}{3}, \frac{500}{3} \right\} \\ \left\{ 50, \frac{650}{3} \right\} \end{cases} \end{cases}$$

$$EL_{1,1}^{a,b} = L_{1,1}^{a,b} + \sum_{x \in S \setminus \{a,b\}} \sum_{k \in Pos(x)} \min(L_{1,k}^{a,x}, L_{k,1}^{x,b})$$

= 200 (because in last computation on page 2, it was 100)

$$\begin{split} EL_{4,2}^{a,b} &= 100 + \min\left(L_{4,1}^{a,c}, L_{1,2}^{c,b}\right) + \min\left(L_{4,2}^{a,c}, L_{2,2}^{c,b}\right) + \min\left(L_{4,3}^{a,c}, L_{3,2}^{c,b}\right) \\ &= 100 + 0 + 0 + \min\left(\frac{200}{3}, 150\right) = \frac{500}{3} \end{split}$$

$$EL_{1,1}^{a,c} = L_{1,1}^{a,c} + \sum_{x \in \{b\}} \sum_{k \in \{1,2\}} \min(L_{1,k}^{a,x}, L_{k,1}^{x,b})$$

$$= \frac{200}{3} + \min(L_{1,1}^{a,b}, L_{1,1}^{b,c}) + \min(L_{1,2}^{a,b}, L_{2,1}^{b,c})$$

$$= \frac{200}{3}$$

$$\begin{split} EL_{2,2}^{a,c} &= L_{2,2}^{a,c} + \sum_{x \in \{b\}} \sum_{k \in \{1,2\}} \min(L_{2,k}^{a,x}, L_{k,2}^{x,b}) \\ &= \frac{500}{3} + \min(L_{2,1}^{a,b}, L_{1,2}^{b,c}) + \min(L_{2,2}^{a,b}, L_{2,2}^{b,c}) \\ &= \frac{500}{3} \end{split}$$

$$EL_{4,3}^{a,c} = L_{4,3}^{a,c} + \sum_{x \in \{b\}} \sum_{k \in \{1,2\}} \min(L_{4,k}^{a,x}, L_{k,3}^{x,c})$$

$$= \frac{200}{3} + \min(L_{4,1}^{a,b}, L_{1,3}^{b,c}) + \min(L_{4,2}^{a,b}, L_{2,3}^{b,c})$$

$$= \frac{200}{3} + 0 + \min(100,150)$$

$$= \frac{500}{3} \approx 166.67$$

$$\begin{split} &EL_{1,2}^{b,c} = L_{1,2}^{b,c} + \sum_{x \in \{a\}} \sum_{k \in \{1,2,3,4\}} \min(L_{1,k}^{b,x}, L_{k,2}^{x,c}) \\ &= 50 + \min(L_{1,1}^{b,a}, L_{1,2}^{a,c}) + \min(L_{1,2}^{b,a}, L_{2,2}^{a,c}) + \min(L_{1,3}^{b,a}, L_{3,2}^{a,c}) + \min(L_{1,4}^{b,a}, L_{4,2}^{a,c}) \\ &= 50 \end{split}$$

$$&EL_{2,3}^{b,c} = L_{2,3}^{b,c} + \sum_{x \in \{a\}} \sum_{k \in \{1,2,3,4\}} \min(L_{2,k}^{b,x}, L_{k,3}^{x,c})$$

$$\begin{split} &EL_{2,3}^{b,c} = L_{2,3}^{b,c} + \sum_{x \in \{a\}} \sum_{k \in \{1,2,3,4\}} \min(L_{2,k}^{b,x}, L_{k,3}^{x,c}) \\ &= 50 + \min(L_{2,1}^{b,a}, L_{1,3}^{a,c}) + \min(L_{2,2}^{b,a}, L_{2,3}^{a,c}) + \min(L_{2,3}^{b,a}, L_{3,3}^{a,c}) + \min(L_{2,4}^{b,a}, L_{4,3}^{a,c}) \\ &= 150 + 0 + 0 + 0 + \min\left(200, \frac{200}{3}\right) \\ &= \frac{650}{3} \end{split}$$

Output (Joinment)

Gap opening: 0 \rightarrow Gotoh not needed for calculation Enlargement: 0

$$ExtendedLib = \begin{cases} \left\{EL_{1,1}^{a,b}, EL_{4,2}^{a,b}\right\} \\ \left\{EL_{1,1}^{a,c}, EL_{2,2}^{a,c}, EL_{4,3}^{a,c}\right\} \\ \left\{EL_{1,2}^{b,c}, EL_{2,3}^{b,c}\right\} \end{cases} = \begin{cases} \left\{200, \frac{500}{3}\right\} \\ \left\{\frac{200}{3}, \frac{500}{3}, \frac{500}{3}\right\} \\ \left\{50, \frac{650}{3}\right\} \end{cases}$$

1. a~b:

		A ₁	T ₂
	0	0	0
A ₁	0	200	200
C ₂	0	200	200
G₃	0	200	200
T ₄	0	200	1100/3

ACGT A##T

Score ~366.67

2. A

C G T # # T

and

G C T

ab~C: (every char with every other char, so A_a with G_c and A_b with $G_c \rightarrow$ and then average)

				G ₁	C ₂	T ₃
			0	0	0	0
	A_1	A_1	0	100/3	100/3	100/3
	C ₂	#	0	100/3	350/3	350/3
	G₃	#	0	100/3	350/3	350/3
	T ₄	T ₂	0	100/3	350/3	925/3

$$\frac{EL_{1,1}^{a,c} + EL_{1,1}^{b,c}}{2} = \frac{\frac{200}{3} + 0}{2} = \frac{100}{3}$$

$$\frac{EL_{1,2}^{a,c} + EL_{1,2}^{b,c}}{2} = \frac{0+50}{2} = 25$$

$$\frac{EL_{1,3}^{a,c} + EL_{1,3}^{b,c}}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{2,1}^{a,c} + 0}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{2,2}^{a,c}+0}{2} = \frac{\frac{500}{3}+0}{2} = 250/3$$

$$\frac{EL_{2,3}^{a,c}+0}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{3,1}^{a,c} + 0}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{3,2}^{a,c}+0}{2}=\frac{0+0}{2}=0$$

$$\frac{EL_{3,3}^{a,c}+0}{2} = \frac{0+0}{2} = 0$$

.....

$$\frac{EL_{4,1}^{a,c} + EL_{2,1}^{b,c}}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{4,2}^{a,c} + EL_{2,2}^{b,c}}{2} = \frac{0+0}{2} = 0$$

$$\frac{EL_{4,3}^{a,c} + EL_{2,3}^{b,c}}{2} = \frac{\frac{500}{3} + \frac{650}{3}}{2} = \frac{575}{3}$$

Output (Final)

ACGT

GC T

SoP-Score -5