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):
$\{(1,1),(4,2)\}$

für (a,c):
$\{(1,1),(2,2),(4,3)\}$

für (b,c):
$\{(1,2),(2,3)\}$

$$Pool = \begin{Bmatrix} \{(1,1),(4,2)\} \\ \{(1,1),(2,2),(4,3)\} \\ \{(1,2),(2,3)\} \end{Bmatrix}$$

2. Weight computation

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

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

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

Output (Computation: Extended Primary Library)

Hint: $L_{i,j}^{a,b} = L_{j,i}^{b,a}$ or it would not make sense

(a triple like three T in a column should be recognized irrelevant of order)

else:

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

correct:

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

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

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

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

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

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

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

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

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

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

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

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

$$= \frac{200}{3} + \min(0,50) + 0$$

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

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

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

$$= \frac{350}{3} \approx 116.67$$

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

$$= 50 + \min\left(L_{1,1}^{b,a}, L_{1,2}^{a,c}\right) + \min\left(L_{1,2}^{b,a}, L_{2,2}^{a,c}\right) + \min\left(L_{1,3}^{b,a}, L_{3,2}^{a,c}\right) + \min\left(L_{1,4}^{b,a}, L_{4,2}^{a,c}\right)$$

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

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

$$= 50 + \min\left(L_{2,1}^{b,a}, L_{1,3}^{a,c}\right) + \min\left(L_{2,2}^{b,a}, L_{2,3}^{a,c}\right) + \min\left(L_{2,3}^{b,a}, L_{3,3}^{a,c}\right) + \min\left(L_{2,4}^{b,a}, L_{4,3}^{a,c}\right)$$

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

$$= \frac{350}{3}$$

Output (Distances)

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

$$S_{a,c}^{rand} = \frac{1}{4}\begin{pmatrix} s(A_a,G_b)\cdot N_A(a)\cdot N_G(b) + s(A_a,C_b)\cdot N_A(a)\cdot N_C(b) + s(A_a,T_b)\cdot N_A(a)\cdot N_T(b) \\ +s(C_a,G_b)\cdot N_C(a)\cdot N_G(b) + s(C_a,C_b)\cdot N_C(a)\cdot N_C(b) + s(C_a,T_b)\cdot N_C(a)\cdot N_T(b) \\ +s(G_a,G_b)\cdot N_G(a)\cdot N_G(b) + s(G_a,C_b)\cdot N_G(a)\cdot N_C(b) + s(G_a,T_b)\cdot N_G(a)\cdot N_T(b) \\ +s(T_a,G_b)\cdot N_T(a)\cdot N_G(b) + s(T_a,C_b)\cdot N_T(a)\cdot N_C(b) + s(T_a,T_b)\cdot N_T(a)\cdot N_T(b) \end{pmatrix} + 1\cdot enlarge$$

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

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

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

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

$$S_{b,c}^{rand} = \frac{1}{3}\cdot\begin{pmatrix} s(A_a,G_b)\cdot N_A(a)\cdot N_G(b) + s(A_a,C_b)\cdot N_A(a)\cdot N_C(b) + s(A_a,T_b)\cdot N_A(a)\cdot N_T(b) \\ +s(T_a,G_b)\cdot N_T(a)\cdot N_G(b) + s(T_a,C_b)\cdot N_T(a)\cdot N_C(b) + s(T_a,T_b)\cdot N_T(a)\cdot N_T(b) \end{pmatrix} + 1\cdot enlarge$$

$$= \frac{1}{3}\cdot\begin{pmatrix} (-1)+(-1)+(-1) \\ +(-1)+(-1)+1 \end{pmatrix} - 2 = \frac{-4}{3} - 2 = -\frac{10}{3}$$

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

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

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

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

1.

$d_{min} = 1$

	a	b	c
a	0	1	1
b		0	1.5
c			0

2.

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

	a	b	c	d
a	0	1	1	
b		0	1.5	
c			0	1.25
d				0

3.

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

4.

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

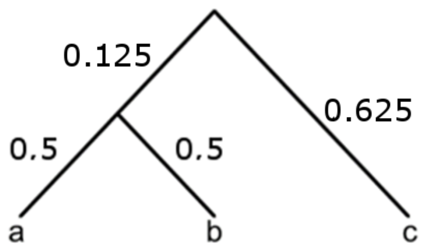
---

1) $d_{min} = 1.25$

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

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

	a	b	c	d	e
a	0	1	1		
b		0	1.5		
c			0	1.25	
d				0	
e					0



Output (Joinment)

```
Gap opening:     0     → Gotoh not needed for calculation
Enlargement:     0
```

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

1. a~b:

		A_1	T_2
	0	0	0
A_1	0	100	100
C_2	0	100	100
G_3	0	100	100
T_4	0	100	250

ACGT
A##T

Score 250

⋮

2.

A C G T G C T
A # # T and

ab~c: (every char with every other char, so A_a with G_c and A_b with G_c → 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
G_3	#	0	100/3	200/3	200/3
T_4	T_2	0	100/3	200/3	550/3

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

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

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

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

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

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

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

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

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

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

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

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

Output (Final)
ACGT
A__T
GC_T
`SoP-Score -5`