INF281 Exercise 08 solutions

1. **Scoring schemes for protein alignments**

   Calculate the score of the alignment by using different scoring schemes.

```
Seq1 R-HIC
Seq2 RDDCC
```

   (a) Use the identity with a simple scoring scheme as match: 1, mismatch: 0, and gap penalty: 0.

   Solution: 2

   (b) Use the genetic code.

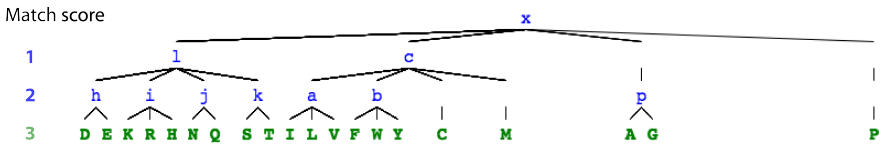
First position	*Second position* T	C	A	G	*Third position*
T	F	S	Y	C	T
	F	S	Y	C	C
	L	S	*Stop*	*Stop*	A
	L	S	*Stop*	W	G
C	L	P	H	R	T
	L	P	H	R	C
	L	P	Q	R	A
	L	P	Q	R	G
A	I	T	N	S	T
	I	T	N	S	C
	I	T	K	R	A
	M	T	K	R	G
G	V	A	D	G	T
	V	A	D	G	C
	V	A	E	G	A
	V	A	E	G	G

A	Ala	Alanine
C	Cys	Cysteine
D	Asp	Aspartic acid
E	Glu	Glutamic acid
F	Phe	Phenylalanine
G	Gly	Glycine
H	His	Histidine
I	Ile	Isoleucine
K	Lys	Lysine
L	Leu	Leucine
M	Met	Methionine
N	Asn	Asparagine
P	Pro	Proline
Q	Gln	Glutamine
R	Arg	Arginine
S	Ser	Serine
T	Thr	Threonine
V	Val	Valine
W	Trp	Tryptophan
Y	Tyr	Tyrosine

   Solution: 9

```
CGU --- CAU AUU UGU
CGU GAU GAU UGU UGU
```

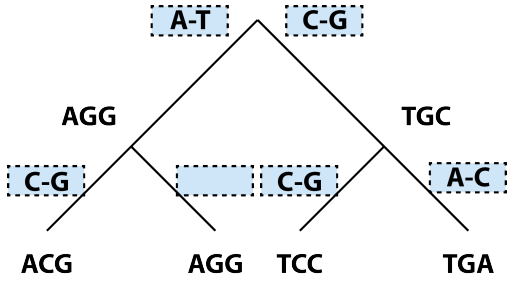
   (c) Use the AACH.



   Solution: $3 + 0 + 1 + 1 + 3 = 8$

2. **Probabilities of accepted mutations**

Use a phylogenetic tree below to calculate the probabilities of accepted mutations. The tree contains sequences of four OTUs.



(a) Estimate the mutations and fill them in the boxes next to the edges.

(b) Count the occurrences of mutations and fill them in the matrix. Note that a mutation A $\rightarrow$ B is equivalent with a mutation B $\rightarrow$ A.

	A	G	C	T
A			1	1
G			3	
C	1	3		
T	1			

(c) Use the following definitions and calculate f_{CG}, f_C and f.

f_{ab} : The number of mutations from a to b or from b to a
f_a : Total number of mutations in which a takes part
f : Twice the total number of mutations

f_{CG} : 3
f_C : $1 + 3 = 4$
f : $2\ (1 + 1 + 3) = 10$

(d) Use the following definition and calculate p_C.

p_a : The relative occurrence of a in the observed sequences

p_C : $3/12$

3. **Relative mutability of PAM**

Relative mutability is calculated from frequencies of estimated mutilation and background probabilities.

$$m_a : \frac{1}{100 p_a} \times \frac{f_a}{f}$$

f_a : Total number of point mutations in which a takes part
f : Twice the total number of point mutations

p_a : Relative occurrence of a in the observed sequences

Assume that the frequencies are pre-calculated as follows.

- Frequencies of estimated mutations

  $f_A : 2, \quad f_G : 3, \quad f_C : 3, \quad f_T : 2$
  $f : 10$

- Background probabilities

  $p_A : 3/10, \quad p_G : 2/10, \quad p_C : 4/10, \quad p_T : 1/10$

(a) Calculate the probabilities of point mutations by $\frac{f_a}{f}$.

$\frac{f_A}{f}$: 2/10 $\frac{f_G}{f}$: 3/10 $\frac{f_C}{f}$: 3/10 $\frac{f_T}{f}$: 2/10

(b) Calculate $100 p_a$.

$100 p_A$: 30 $100 p_G$: 20 $100 p_C$: 40 $100 p_T$: 10

(c) Calculate the relative mutability m_a.

m_A : 2/300 m_G : 3/200 m_C : 3/400 m_T : 2/100

4. **Mutation probabilities of PAM**

Mutation probabilities are calculated from relative mutability.

$$m_{ab} : m_a \times \frac{f_{ab}}{f_a}, \qquad m_{aa} : 1 - m_a$$

f_{ab} : Total number of point mutations in which a takes part
f_a : Twice the total number of point mutations
m_a : Relative mutability of a

Assume that the frequencies are pre-calculated as follows.

- Frequencies of estimated mutations

  $f_{AC} : 8, \quad f_A : 32$

- Relative mutability

  $m_A : 0.004$

(a) Calculate M_{AC}.

Solution: $0.004 \times \frac{8}{32} = 0.001$

(b) Calculate M_{AA}.

Solution: $1 - 0.004 = 0.996$

5. **Odds ratios of PAM**

Odds ratios are calculated from mutation probabilities and background probabilities.

$$O_{ab} = \frac{M_{ab}}{p_b} = m_a \times \frac{f_{ab}}{f_a} \times \frac{1}{f_b} = \frac{1}{100} \times \frac{f_{ab}}{f} \times \frac{1}{p_a p_b}$$

Assume that the frequencies are pre-calculated as follows.

$$f_{AC} : 16, \quad f : 400, \quad p_A : 0.2, \quad p_c : 0.4$$

(a) Calculate O_{AC}.

Solution: $(1/100) \times (16/400) \times (1/(0.2 \times 0.4)) = 0.005$

(b) Calculate O_{CA}.

Solution: 0.005

6. **BLOSUM**

BLOSUM uses several thousand blocks to calculate the probabilities of accepted mutation. Use the following definitions and Block1 & Block2 to solve the problems.

f_{ab} : Frequencies of an observed pair a and b.

T : Total number of pairs from all blocks.

The number of pairs can be calculated as $1/2wm(m-1)$.

$p_a : p_a = f_{aa} + \sum_{e \neq a} f_{ae}/2$

$e_{aa} : p_a p_a$

$e_{ab} : p_a p_b + p_b p_a = 2 p_a p_b$

Block1	Block2
CAGC	GGA
GTAC	GTA
CAGC	

(a) Count the occurrences of all pairs.

	A	G	C	T
A	2	2	0	2
G	2	2	2	1
C	0	2	4	0
T	2	1	0	0

(b) Calculate T.

Solution: $(1/2 \times 4 \times 3 \times 2) + (1/2 \times 3 \times 2 \times 1) = 12 + 3 = 15$

(c) Calculate f_{AA} and f_{AG}.

Solution: $f_{AA} : 2/15, \quad f_{AG} : 2/15$

(d) Calculate p_A and p_G.

Solution: $p_A : 8/30, \quad p_G : 9/30$

(e) Calculate e_{AA} and e_{AG}.

Solution: $e_{AA} : 64/900, \quad e_{AG} : 144/900$

(f) Calculate f_{AA}/e_{AA} and f_{AG}/e_{AG}.

Solution: $f_{AA}/e_{AA} : 1.875, \quad f_{AG}/e_{AG} : 0.833$

7. **PPM (Position probability matrix)**

PWM (position weight matrix) is a popular method to find sequenced patterns. It can be generated from PPM (position probability matrix) and PFM (position frequency matrix).

```
Seq1 CAA
Seq2 CAG
Seq3 GAC
Seq4 ATT
```

(a) Create a PFM from Seq1, Seq2, Seq3, and Seq4.

	1	2	3
A	1	3	1
G	1	0	1
C	2	0	1
T	0	1	1

(b) Create a PPM from Seq1, Seq2, Seq3, and Seq4.

	1	2	3
A	0.25	0.75	0.25
G	0.25	0	0.25
C	0.5	0	0.25
T	0	0.25	0.25

8. **Sequence profile**

A sequence profile is similar to PWM, but it uses a scoring scheme. Use the following definitions to calculate the profile values.

$$Prof_{ra} : \frac{1}{m_r} \sum_{b \in M} R_{ba} F_{rb}$$

F_{rb} : The number of occurrences of b at position r

R_{ba} : Pairwise score between b and a

m_r : The number of residues without gaps at position r

Scoring matrix:

	A	G	C	T
A	2	1	-3	-2
G	1	3	-2	-1
C	-3	-2	4	1
T	-2	-1	1	2

MSA

```
Seq1 GT
Seq2 -G
Seq3 CA
```

(a) Calculate the profile values of position 1.

A1: $(1/2) \times ((2 \times 0) + (1 \times 1) + (-3 \times 1) + (-2 \times 0)) = -1$

G1: $(1/2) \times ((1 \times 0) + (3 \times 1) + (-2 \times 1) + (-1 \times 0)) = 1/2$

C1: $(1/2) \times ((-3 \times 0) + (-2 \times 1) + (4 \times 1) + (1 \times 0)) = 1$

T1: $(1/2) \times ((-2 \times 0) + (-1 \times 1) + (1 \times 1) + (2 \times 0)) = 0$

(b) Calculate the profile values of position 2.

A2: $(1/3) \times ((2 \times 1) + (1 \times 1) + (-3 \times 0) + (-2 \times 1)) = 1/3$

G2: $(1/3) \times ((1 \times 1) + (3 \times 1) + (-2 \times 0) + (-1 \times 1)) = 1$

C2: $(1/3) \times ((-3 \times 1) + (-2 \times 1) + (4 \times 0) + (1 \times 1)) = -4/3$

T2: $(1/3) \times ((-2 \times 1) + (-1 \times 1) + (1 \times 0) + (2 \times 1)) = -1/3$

(c) Make a profile matrix.

	1	2
A	-1	1/3
G	1/2	1
C	1	-4/3
T	0	-1/3