

11 Exercise solutions – Construction of scoring matrix

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.

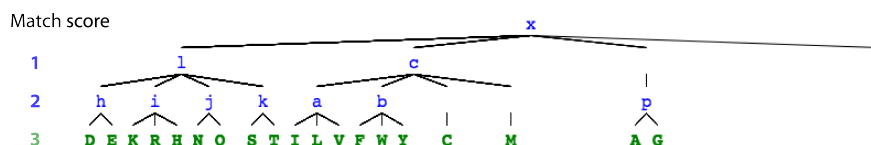
<i>First position</i>	<i>Second position</i>				<i>Third position</i>
	T	C	A	G	
T	F	S	Y	C	T
	F	S	Y	C	C
	L	S	<i>Stop</i>	<i>Stop</i>	A
	L	S	<i>Stop</i>	W	G
C	L	P	H	R	T
	L	P	H	R	C
	L	P	Q	R	A
	L	P	Q	R	G
A	I	T	N	S	T
	I	T	N	S	C
	I	T	K	R	A
	M	T	K	R	G
G	V	A	D	G	T
	V	A	D	G	C
	V	A	E	G	A
	V	A	E	G	G

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

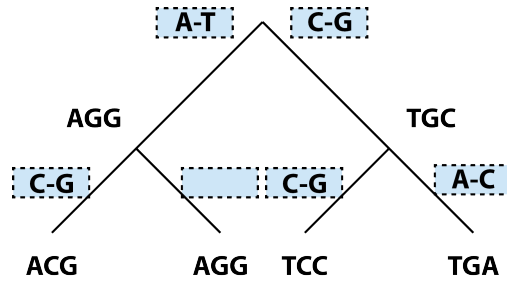
- (c) Use the AACH.



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	C	G	T
A		1		1
C	1		3	
G		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 mutation and background probabilities.

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

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

$$\begin{array}{l} f_A : 2, \quad f_G : 3, \quad f_C : 3, \quad f_T : 2 \\ f : 10 \end{array}$$

- 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 $\frac{f_a}{f}$.

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

- (b) Calculate $100p_a$.

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

- (c) Calculate the relative mutability m_a .

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

4. Mutation probabilities of PAM

Mutation probabilities are calculated from relative mutability.

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

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} .

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

- (b) Calculate M_{AA} .

$$\textbf{Solution: } 1 - 0.004 = 0.996$$

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} .

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

- (b) Calculate O_{CA} .

$$\textbf{Solution: } 0.005$$

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 $1/2wm(m-1)$.

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

$$e_{aa} : p_a p_a$$

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

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