Alignment

Sept 14, 2015

ANNOUNCEMENTS

PAIRWISE ALIGNMENT

What is alignment?

PAIRWISE ALIGNMENT

What is aligner actually doing?

SCORING MATRICES

DAYHOFF MATRIX

DAYHOFF MATRIX

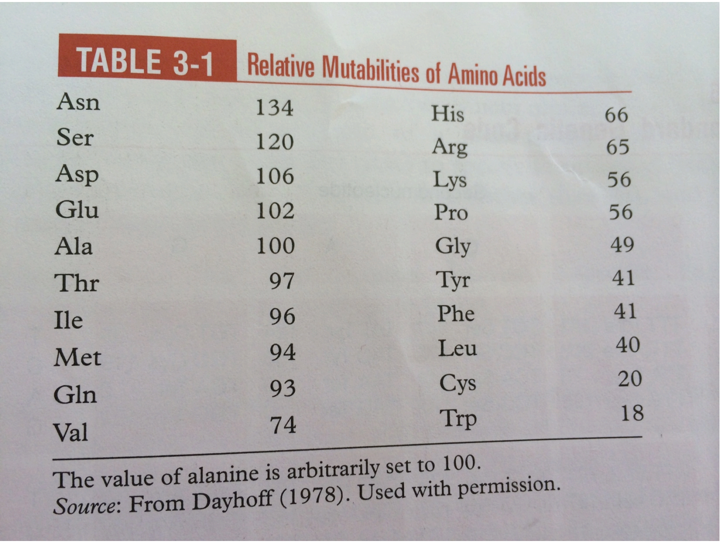


TABLE 3-1 Relative Mutabilities of Amino Acids

Asn	134	His	66
Ser	120	Arg	65
Asp	106	Lys	56
Glu	102	Pro	56
Ala	100	Gly	49
Thr	97	Tyr	41
Ile	96	Phe	41
Met	94	Leu	40
Gln	93	Cys	20
Val	74	Trp	18

The value of alanine is arbitrarily set to 100.
Source: From Dayhoff (1978). Used with permission.

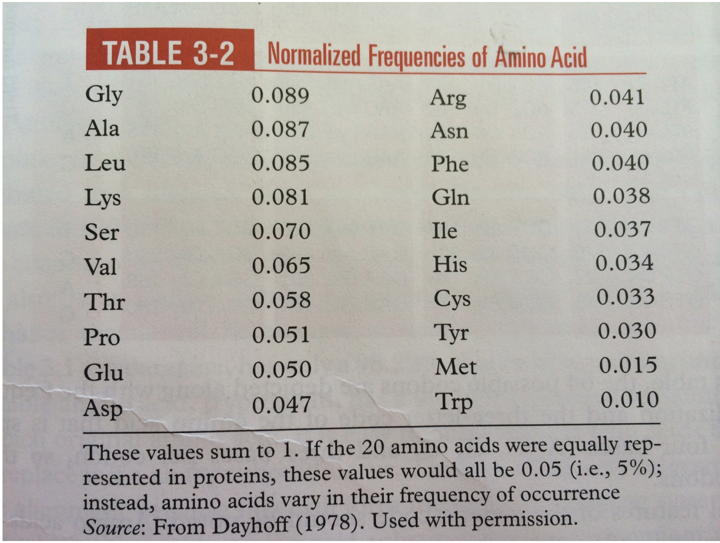
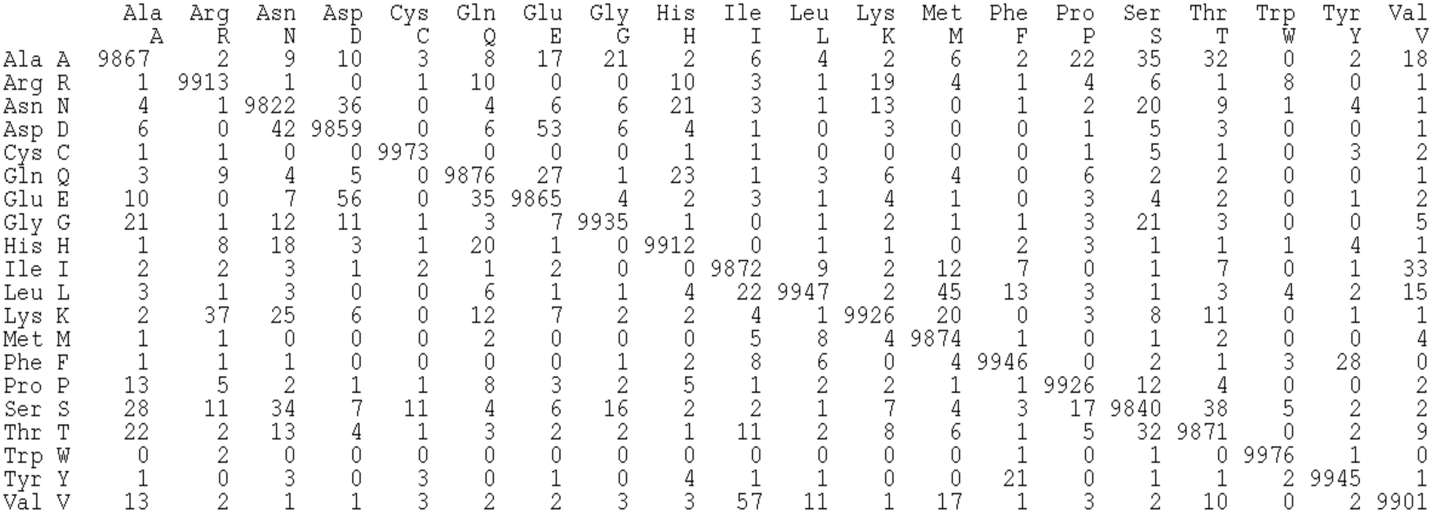


TABLE 3-2 Normalized Frequencies of Amino Acid

Gly	0.089	Arg	0.041
Ala	0.087	Asn	0.040
Leu	0.085	Phe	0.040
Lys	0.081	Gln	0.038
Ser	0.070	Ile	0.037
Val	0.065	His	0.034
Thr	0.058	Cys	0.033
Pro	0.051	Tyr	0.030
Glu	0.050	Met	0.015
Asp	0.047	Trp	0.010

These values sum to 1. If the 20 amino acids were equally represented in proteins, these values would all be 0.05 (i.e., 5%); instead, amino acids vary in their frequency of occurrence.
Source: From Dayhoff (1978). Used with permission.

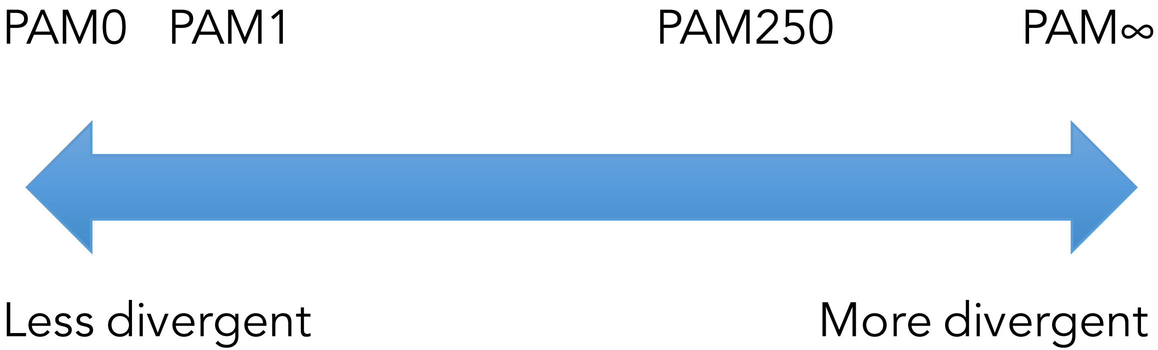
PAM1 MATRIX



	Ala A	Arg R	Asn N	Asp D	Cys C	Gln Q	Glu E	Gly G	His H	Ile I	Leu L	Lys K	Met M	Phe F	Pro P	Ser S	Thr T	Trp W	Tyr Y	Val V
Ala A	9867	2	9	10	3	8	17	21	2	6	4	2	6	2	22	35	32	0	2	18
Arg R	1	9913	1	0	1	10	0	0	10	3	1	19	4	1	4	6	1	8	0	1
Asn N	4	1	9822	36	0	4	6	6	21	3	1	13	0	1	2	20	9	1	4	1
Asp D	6	0	42	9859	0	6	53	6	4	1	0	3	0	0	1	5	3	0	0	1
Cys C	1	1	0	0	9973	0	0	0	1	1	0	0	0	0	1	5	1	0	3	2
Gln Q	3	9	4	5	0	9876	27	1	23	1	3	6	4	0	6	2	2	0	0	1
Glu E	10	0	7	56	0	35	9865	4	2	3	1	4	1	0	3	4	2	0	1	2
Gly G	21	1	12	11	1	3	7	9935	1	0	1	2	1	1	3	21	3	0	0	5
His H	1	8	18	3	1	20	1	0	9912	0	1	1	0	2	3	1	1	1	4	1
Ile I	2	2	3	1	2	1	2	0	0	9872	9	2	12	7	0	1	7	0	1	33
Leu L	3	1	3	0	0	6	1	1	4	22	9947	2	45	13	3	1	3	4	2	15
Lys K	2	37	25	6	0	12	7	2	2	4	1	9926	20	0	3	8	11	0	1	1
Met M	1	1	0	0	0	2	0	0	0	5	8	4	9874	1	0	1	2	0	0	4
Phe F	1	1	1	0	0	0	0	1	2	8	6	0	4	9946	0	2	1	3	28	0
Pro P	13	5	2	1	1	8	3	2	5	1	2	2	1	1	9926	12	4	0	0	2
Ser S	28	11	34	7	11	4	6	16	2	2	1	7	4	3	17	9840	38	5	2	2
Thr T	22	2	13	4	1	3	2	2	1	11	2	8	6	1	5	32	9871	0	2	9
Trp W	0	2	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	9976	1	0
Tyr Y	1	0	3	0	3	0	1	0	4	1	1	0	0	21	0	1	1	2	9945	1
Val V	13	2	1	1	3	2	2	3	3	57	11	1	17	1	3	2	10	0	2	9901

OTHER PAM MATRIX

PAM VERSUS DIVERGENCE

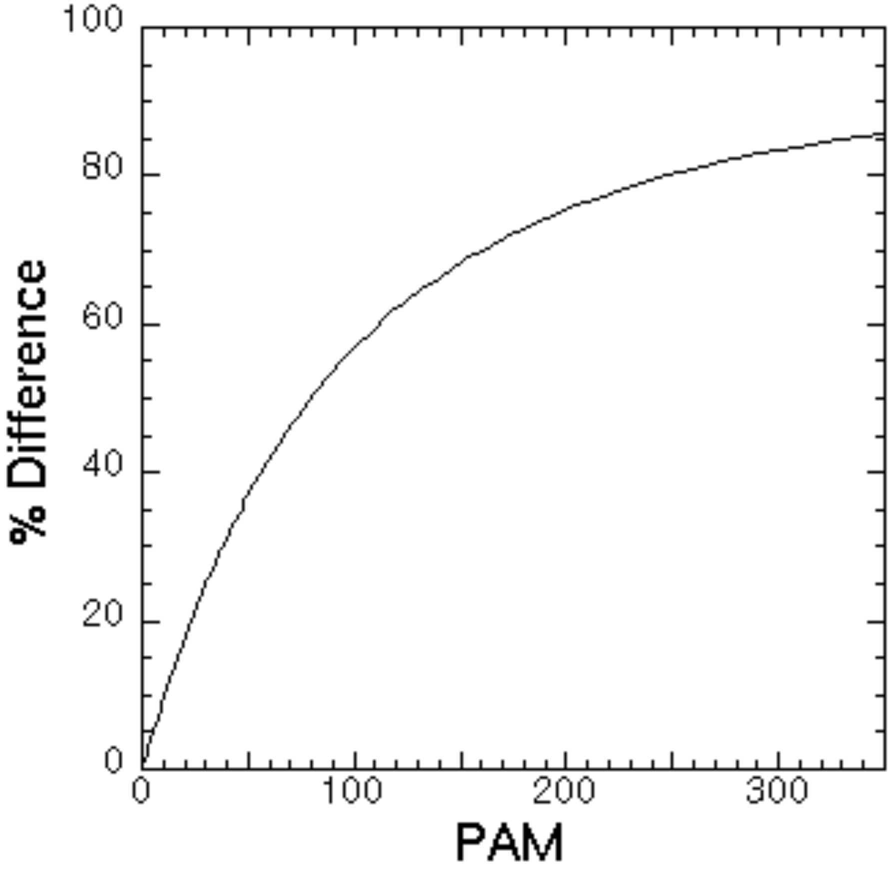


PAM0 PAM1 PAM250 PAM∞

Less divergent More divergent

http://blast.ncbi.nlm.nih.gov/Blast.cgi?PROGRAM=blastp

PAM VERSUS DIVERGENCE



PAM250

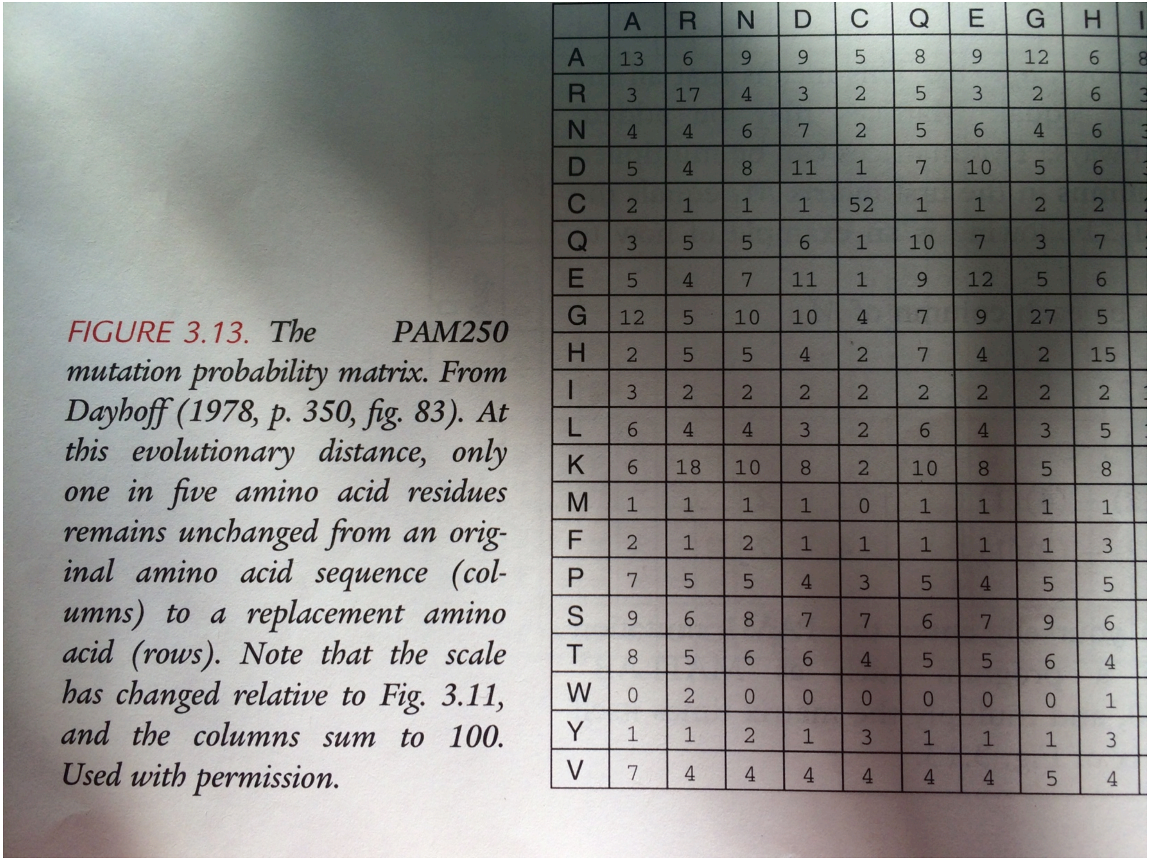


FIGURE 3.13. *The PAM250 mutation probability matrix. From Dayhoff (1978, p. 350, fig. 83). At this evolutionary distance, only one in five amino acid residues remains unchanged from an original amino acid sequence (columns) to a replacement amino acid (rows). Note that the scale has changed relative to Fig. 3.11, and the columns sum to 100. Used with permission.*

	A	R	N	D	C	Q	E	G	H
A	13	6	9	9	5	8	9	12	6
R	3	17	4	3	2	5	3	2	6
N	4	4	6	7	2	5	6	4	6
D	5	4	8	11	1	7	10	5	6
C	2	1	1	1	52	1	1	2	2
Q	3	5	5	6	1	10	7	3	7
E	5	4	7	11	1	9	12	5	6
G	12	5	10	10	4	7	9	27	5
H	2	5	5	4	2	7	4	2	15
I	3	2	2	2	2	2	2	2	2
L	6	4	4	3	2	6	4	3	5
K	6	18	10	8	2	10	8	5	8
M	1	1	1	1	0	1	1	1	1
F	2	1	2	1	1	1	1	1	3
P	7	5	5	4	3	5	4	5	5
S	9	6	8	7	7	6	7	9	6
T	8	5	6	6	4	5	5	6	4
W	0	2	0	0	0	0	0	0	1
Y	1	1	2	1	3	1	1	1	3
V	7	4	4	4	4	4	4	5	4

FROM MUTATIONAL PROBABILITY TO SCORING MATRICES

$$s_{i,j} = 10 * \log_{10}\left(\frac{q_{i,j}}{p_i}\right)$$

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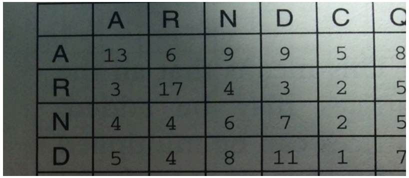
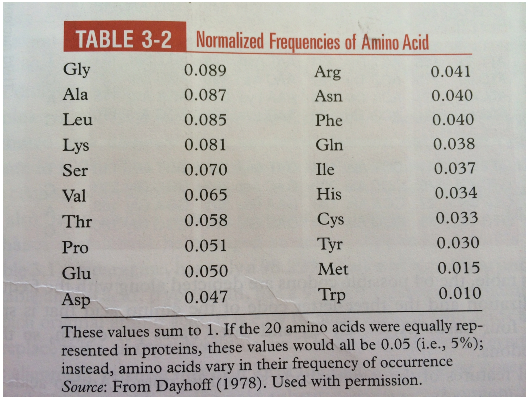


	A	R	N	D	C	Q
A	13	6	9	9	5	8
R	3	17	4	3	2	5
N	4	4	6	7	2	5
D	5	4	8	11	1	7



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WHAT DO THESE SCORES MEAN?

ALIGNMENT – THINK BLAST

Q	ANCQE	versus	ANCQE
D	ANCGE		ANCHE

BLOSUM MATRIX