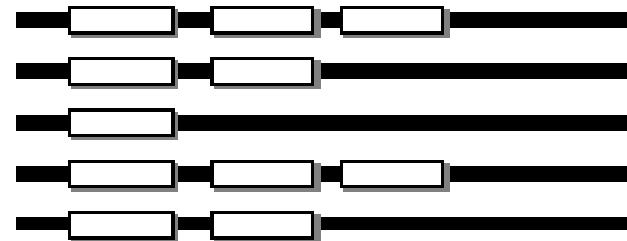


3. Çoklu dizi hızalama

Human beta	-----VHLTPEEKSAVTALWGRVN--VDEVGGEALGRLLVVYPWTQRFFESFGDLST
Horse beta	-----VQLSGEEKAAVLALWDKVN--EEEVGGEALGRLLVVYPWTQRFFDSFGDLSN
Human alpha	-----VLSPADKTNVKAAMGKVGGAHAGEYGAEALERMFLSPTTTKTYFPHF-DLS-
Horse alpha	-----VLSAADKTNVKAANSKVGGHAGEYGAEALERMFGLGFPPTTKTYFPHF-DLS-
Whale myoglobin	-----VLSEGEWQLVLHVWAKVEADVAHGQDILIRLFKSHPETLEKFDRFKHLKT
Lamprey globin	PIVDTGSVAPLSSAAEKTKIRSAWAPVYSTYETSGVDILVKFFTSTPAAQEFFPKFKGLTT
Lupin globin	-----GALTESQAALVKSSWEENANIPKHTHRFFILVLEIAAAKDLFSFLKGTE
	* : ; : ; * . : : * : * : .
Human beta	PDAVMGNPKVKAHGKKVLGAFSDGLAHLDN-----LKGTFAATLSELHCDKLHVDPENFRL
Horse beta	PGAVMGNPKVKAHGKKVLHSFGEGVHHLDN-----LKGTFAALSELHCDKLHVDPENFRL
Human alpha	---HGSAQVKGHGKKVADALTNAVAHVD----MPNALSALSDLHAHKLRVDPVNFKL
Horse alpha	---HGSAQVKAHGKKVGDALTAVGHLD----LPGALSNLSDLHAHKLRVDPVNFKL
Whale myoglobin	EAEMKASEDLKKHGVTVLTLGAILKKKGH----HEAEELKPLAQSHATKHKIPIKYLEF
Lamprey globin	ADQLKKSADVRWHAERIINAVNDAVASMDT--EKMSMKLRDLSGKHAKSFQVD PQYFKV
Lupin globin	VP--QNNPELQAHAGKVFKLVYEAAIQLQVTGVVVTDATLKNLGSVHSKGVAD-AHFPV
	. . : : * . : . : * . * . : .
Human beta	LGNVLVCVLAHHFGKEFTPPVQAAAYQKVVAGVANALAHKYH-----
Horse beta	LGNVLVVVLARHFGKDFTPELQASYQKVVAGVANALAHKYH-----
Human alpha	LSHCLLVTLAAHLPAEFTPASVHASLDKFLASVSTVLTSKYR-----
Horse alpha	LSHCLLSTLAVHLPNDFTPASVHASLDKFLSSVSTVLTSKYR-----
Whale myoglobin	ISEAIIHVLHSRHPGDFGADAQGAMMNKALELFRKDIAAKYKELGYQG
Lamprey globin	LAAVIADTVAAAG---D---AGFEKLMMSMICILLRSAY-----
Lupin globin	VKEAILKTIKEVVGAKWSEELNSANTIAYDELAIVIKKEMNDAA---
	: : : : . : . : . : :

(a)

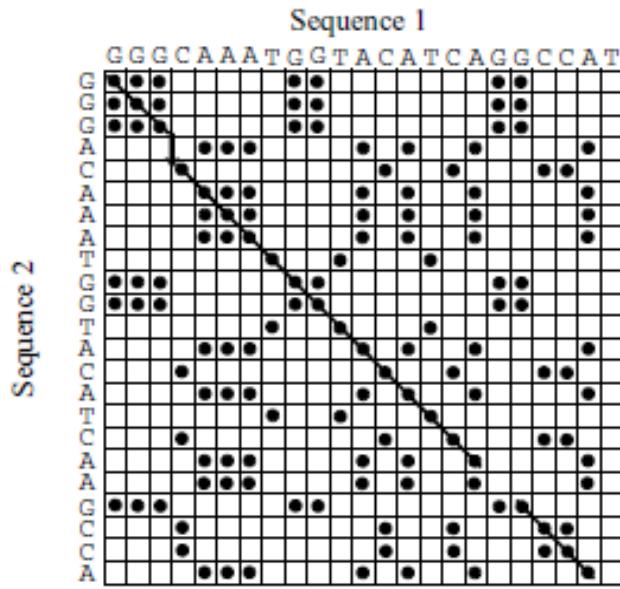


(b)

```

accgtaccc--gtaccgt
accgtaccccgataccgt
accgtaccc--gtaccgt
accgtaccc--gtaccgt
***** ***** *

```



```

GGG-CAAATGGTACATCAGGCCATA
      *           *   **
GGGACAAATGGTACATCAAGCCA--
```

(b)

Sequence X

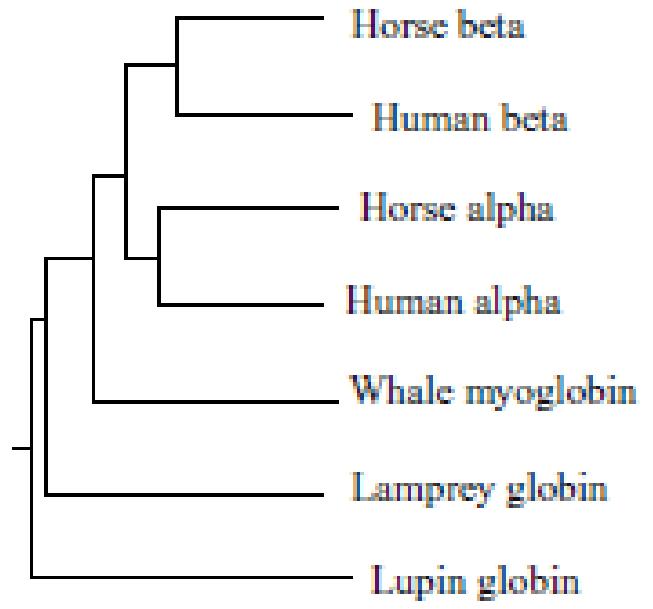
<i>j</i>	<i>i</i>	*	G	R	Q	T	A	G	L	
1	1	*	0	-8	-8	-8	-8	-8	-8	
2	2	G	-8	6	-2	-2	-2	0	6	-4
3	3	T	-8	-2	-1	-1	5	0	-2	-1
4	4	A	-8	0	5	-1	0	4	0	-1
5	5	Y	-8	-3	-2	-1	-2	-2	-3	-1
6	6	D	-8	-1	-2	0	-1	-2	-1	-4
7	7	L	-8	-4	-2	-2	-1	-1	-4	4

Sequence Y

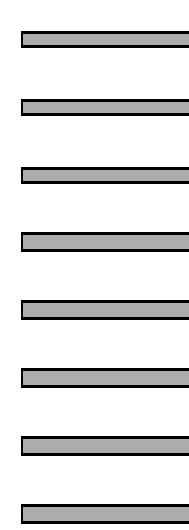
$$F(i, j) = \max \begin{cases} F(i - 1, j - 1) + s(X_i, Y_j), \\ F(i - 1, j) - g, \\ F(i, j - 1) - g \end{cases}$$

		Sequence X									
		i	1	2	3	4	5	6	7	8	
		j	*	G	R	Q	T	A	G	L	
Sequence Y	1	*	0	-8	-16	-24	-32	-40	-48	-56	
	2	G	-8	6	-2	-10	-18	-26	-34	-42	
	3	T	-16	-2	5	-3	-5	-13	-21	-29	
	4	A	-24	-10	-3	4	-3	-1	-9	-17	
	5	Y	-32	-18	-11	-4	2	-5	-4	-10	
	6	D	-40	-26	-19	-11	-3	0	-6	-8	
	7	L	-48	-34	-27	-19	-11	-4	-4	-2	

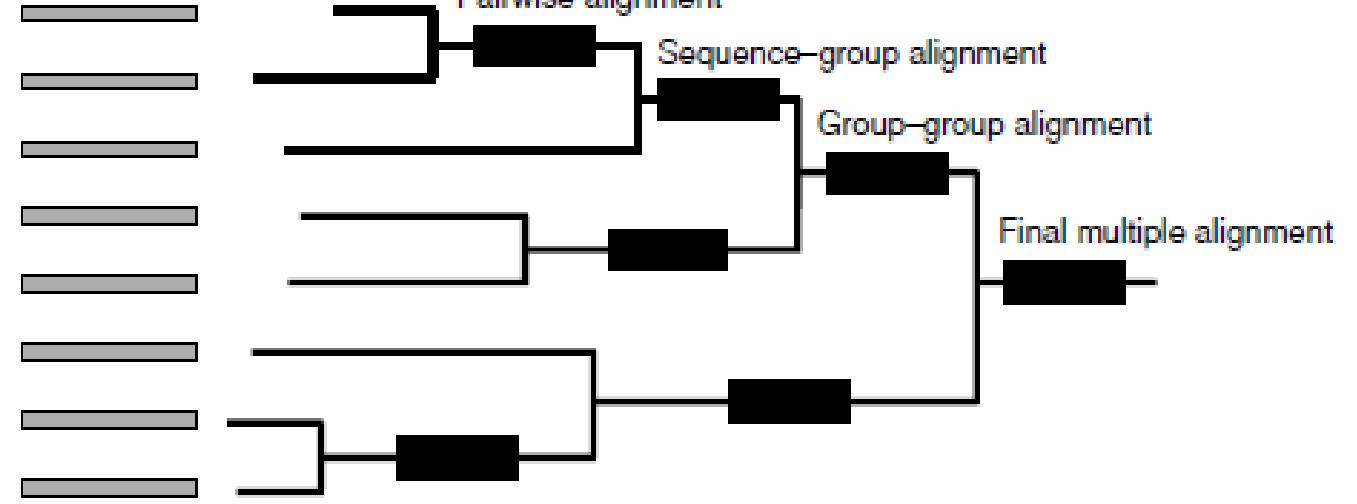
		Sequence X									
		i	1	2	3	4	5	6	7	8	
		j	*	G	R	Q	T	A	G	L	
Sequence Y	1	*	0	-8	-10	-12	-14	-16	-18	-20	
	2	G	-8	6	-2	-4	-6	-8	-10	-12	
	3	T	-10	-2	5	-3	1	-6	-10	-11	
	4	A	-12	-4	-3	4	-3	5	-3	-11	
	5	Y	-14	-6	-5	-4	2	-3	2	-4	
	6	D	-16	-8	-7	-5	-3	0	-4	-2	
	7	L	-18	-10	-9	-9	-6	-4	-4	0	



Sequences



Pairwise alignment

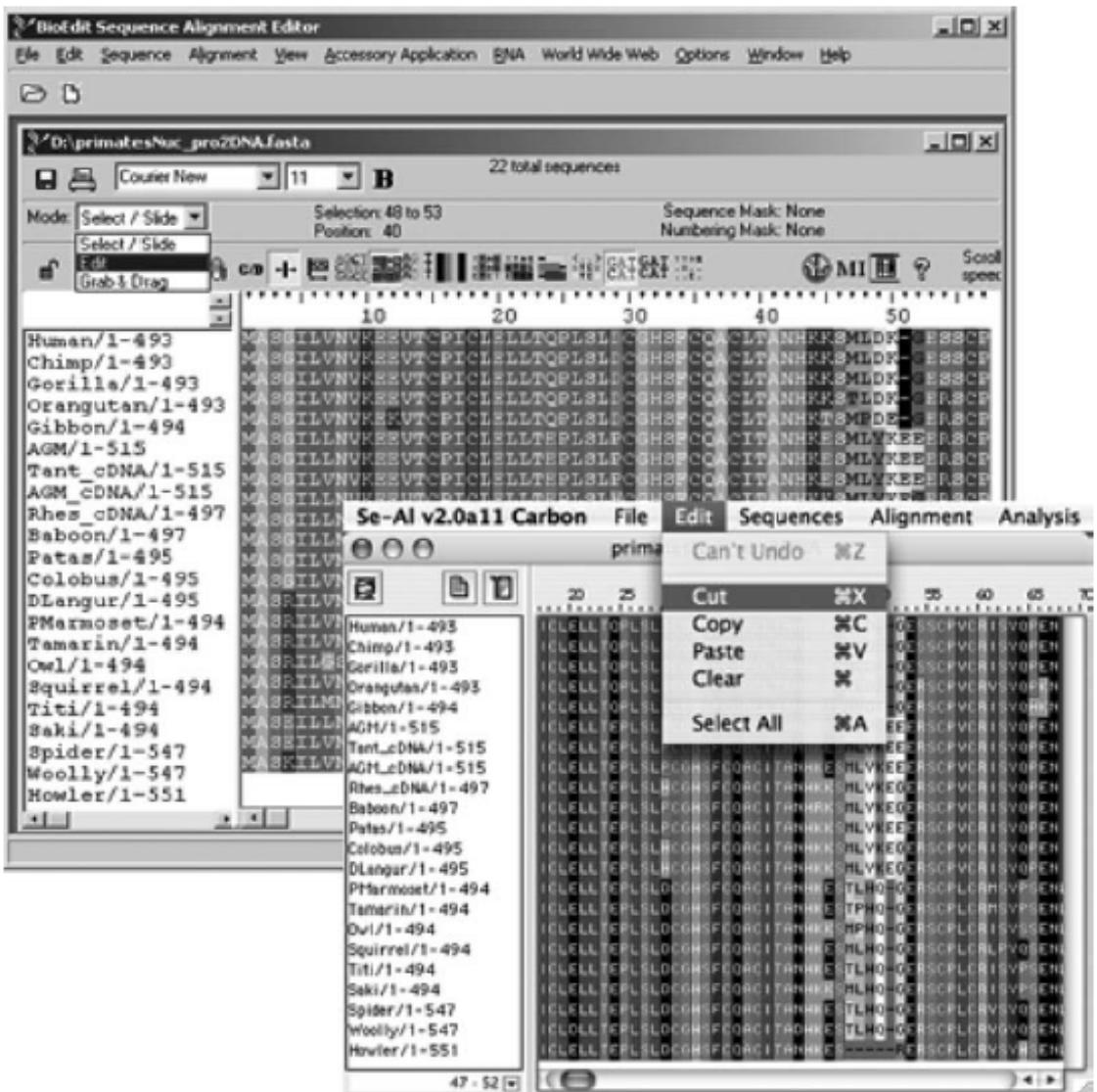


Sequence-group alignment

Group-group alignment

Final multiple alignment

Human	M..SMLDK-GE..PE-G..PKPQIIYGARGTRYQTFV-----N..QPDAMCNI
Chimp	M..SMLDK-GE..PE-G..PKPQIIYGARGTRYQTFM-----N..QPDAMCNI
Gorilla	M..SMLDK-GE..PE-G..PKPQIIYGAQGTRYQTFM-----N..QPDATCNI
Orangutan	M..STLDK-GE..PE-G..PEPQIIYGAQGTRYQTYV-----N..QPDAMYNI
Gibbon	M..SMPDE-GE..PEEG..PEPQIIFEAAQGTISQTFV-----N..QPDAMYNI
AGM	M..SMLYKEEE..PEEG..QNPQIMYQAPGSSPGSLTNFNYCTGVLGQSITSRKLTN..QPDATYNI
Tant_cDNA	M..SMLYKEEE..PEEG..QNPQIMYQAPGSSPGSLTNFNYCTGVLGQSITSRKLTN..QPDATYNI
AGM_cDNA	M..SMLYKEEE..PEEG..RNPQIMYQSPGSLFGSLTNFSYCTGVPGSQSITSGKLTN..QPDATYNI
Rhes_cDNA	M..SMLYKEGE..PEEG..RNPQIMYQAPGTLFTFPS-----LTN..QSDAMYNI
Baboon	M..SMLYKEGE..PEEG..RNPQITYQAPGTLFSPS-----LTN..QPDAMYNI
Patas	M..SMLYKEEE..PEEG..RNPQIMYWAQGKLFQSLK-----N..QPDAMYDV
Colobus	M..SMLYKEGE..PEEG..PNPQIMYRAQGTLFQSLK-----N..QPDAMYNI
DLangur	M..SMLYKEGE..PEEG..PNPQIMCRARGTLFQSLK-----N..QPDAMYNI
PMarmoset	M..STLHQ-GE..PEEG..Q-VPI-HQPLV-----K..KCNAKWNV
Tamarin	M..STPHQ-GE..PEEG..Q-FQI-HQPSV-----K..KCNAKWNV
Owl	M..SMPHQ-GE..PEEG..Q-KRI-YQPFL-----K..KRTASCV
Squirrel	M..SMLHQ-GE..PEER..Q-KPI-RHLLV-----K..KCTANQSV
Titi	M..STLHQ-GE..PEEG..Q-EWI-HQSSG-----R..KCAANRNG
Saki	M..SMLHQ-GE..PEEG..Q-ERI-HQSFG-----K..KCTANRNG
Spider	M..STLHQ-GE..PEEG..Q-EQI-HQPSV-----K..KCTAN--V
Woolly	M..STLHQ-GE..PEEG..Q-KQR-HRPSV-----K..KCTAN--V
Howler	M..S----RE..PEEG..Q-EQIHHHPSM-----E..KCIGN--F
	47 52 88 91 325 463 402 409

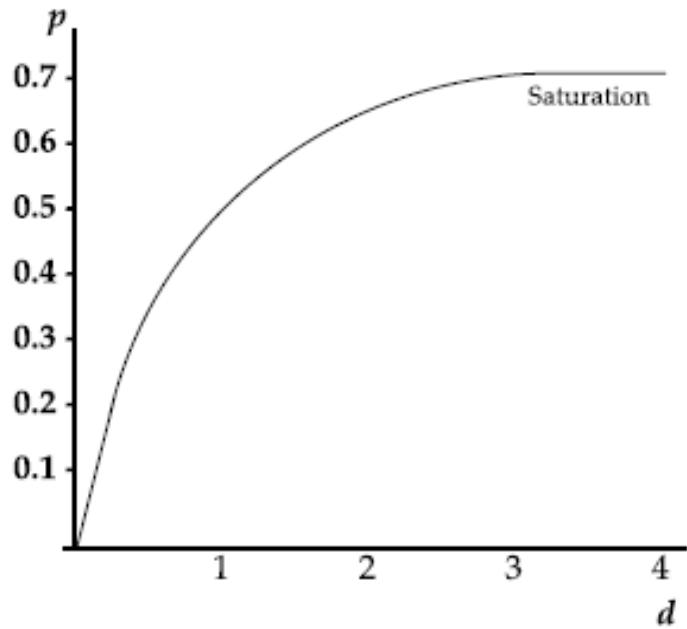


4. Genetik uzaklıklar ve nükleotid substitusyon modelleri

Ancestral sequence

AACCTGTGCA

Seq1 AATCTGTGTA * *	Seq2 ATCCTGGGTT * * *
Seq1 AATCTGTGTA seq2 ATCCTGGGTT ** * *	

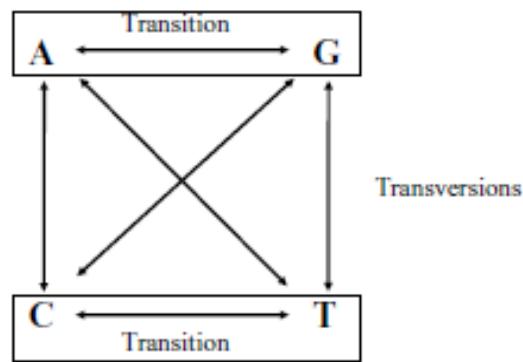


$$Q = \begin{pmatrix} & \mathbf{A} & \mathbf{C} & \mathbf{G} & \mathbf{T} \\ \mathbf{A} & -\mu(a\pi_C + b\pi_G + c\pi_T) & a\mu\pi_C & b\mu\pi_G & c\mu\pi_T \\ \mathbf{C} & g\mu\pi_A & -\mu(g\pi_A + d\pi_G + e\pi_T) & d\mu\pi_G & e\mu\pi_T \\ \mathbf{G} & h\mu\pi_A & i\mu\pi_C & -\mu(h\pi_A + j\pi_G + f\pi_T) & f\mu\pi_T \\ \mathbf{T} & j\mu\pi_A & k\mu\pi_C & l\mu\pi_G & -\mu(i\pi_A + k\pi_G + l\pi_C) \end{pmatrix}$$

$$Q = \begin{pmatrix} \mathbf{A} & \mathbf{C} & \mathbf{G} & \mathbf{T} \\ -\mu(a\pi_C + b\pi_G + c\pi_T) & a\mu\pi_C & b\mu\pi_G & c\mu\pi_T \\ a\mu\pi_A & -\mu(a\pi_A + d\pi_G + e\pi_T) & d\mu\pi_G & e\mu\pi_T \\ b\mu\pi_A & d\mu\pi_C & -\mu(b\pi_A + d\pi_C + f\pi_T) & f\mu\pi_T \\ c\mu\pi_A & e\mu\pi_C & f\mu\pi_G & -\mu(c\pi_A + e\pi_C + f\pi_G) \end{pmatrix}$$

$$R_{ij}^{HKY} = \kappa \quad \text{for Ts}$$

$$R_{ij}^{HKY} = 1 \quad \text{for Tv}$$



$$R_{ij}^{\text{TN}} = \kappa \left(\frac{2\gamma}{\gamma + 1} \right) \quad \text{for Ts}_Y$$

$$\rho = \frac{\pi_R \pi_Y [\pi_R \pi_Y \tau - (\pi_A \pi_G + \pi_C \pi_T)]}{(\pi_A \pi_G \pi_Y + \pi_C \pi_T \pi_R)}$$

$$R_{ij}^{\text{TN}} = \kappa \left(\frac{2}{\gamma + 1} \right) \quad \text{for Ts}_R$$

$$R_{ij}^{\text{TN}} = 1 \quad \text{for Tv}$$

$$\kappa = 1 + \frac{1}{2}\rho \left(\frac{1}{\pi_R} + \frac{1}{\pi_Y} \right)$$

$$\gamma = \frac{\pi_Y + \rho}{\pi_Y} \frac{\pi_R}{\pi_R + \rho}$$

Model

*Free parameters
in the Q-matrix*

