NUCLEOTIDE SUBSTITUTION RATE

$r = K / (2T)$
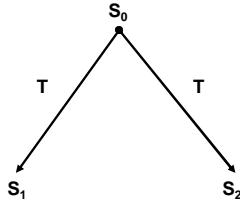
NON- & SYNONYMOUS SUBSTITUTION RATES

NON- & SYNONYMOUS SUBSTITUTIONS

TRANSITION TRANVERSION RATES

Type	L_0	L_2	L_4
α	0.40	1.86	2.24
β	0.38	0.38	1.47
Total	0.78	2.24	3.71

5' & 3' UNTRANSLATED REGIONS

TABLE 4.3 Rates of nucleotide substitution (± standard errors) in 5' and 3' untranslated regions and at fourfold degenerate sites of protein-coding genes, based on comparisons between human and mouse or rat genes.

Gene		5' untranslated		3' untranslated		Fourfold degenerate
	L	Rate	L	Rate	L	Rate
Corticotropin-β-lipoprotein precursor	99	1.87 ± 0.41	97	2.32 ± 0.49	275	2.78 ± 0.34
Aldolase A	124	1.08 ± 0.26	194	1.73 ± 0.32	195	3.16 ± 0.48
Apolipoprotein A-IV	83	3.06 ± 0.68	134	1.73 ± 0.33	160	3.38 ± 0.50
Apolipoprotein E	23	1.27 ± 0.69	94	1.70 ± 0.42	153	4.00 ± 0.60
Na,K-ATPase β	118	2.45 ± 0.45	1,117	0.57 ± 0.06	118	2.87 ± 0.54
Creatine kinase M	70	1.71 ± 0.46	168	1.79 ± 0.30	178	2.81 ± 0.41
α-fetoprotein	47	3.64 ± 1.13	144	2.79 ± 0.49	225	4.14 ± 0.74
α-globin	34	1.56 ± 0.65	90	2.21 ± 0.50	81	4.47 ± 0.98
β-globin	50	1.30 ± 0.46	126	2.85 ± 0.69	78	2.42 ± 0.56
Glyceraldehyde-3-phosphate dehydrogenase	70	1.34 ± 0.38	121	1.74 ± 0.36	170	2.43 ± 0.34
Growth hormone	21	1.79 ± 0.85	91	1.83 ± 0.41	83	3.82 ± 0.75
Insulin	56	2.92 ± 0.80	53	3.09 ± 0.81	62	4.19 ± 1.00
Interleukin I	59	1.09 ± 0.36	1,046	2.02 ± 0.14	105	2.97 ± 0.61
Lactate dehydrogenase A	95	2.79 ± 0.55	470	2.48 ± 0.23	152	3.64 ± 0.60
Metallothionein II	61	1.88 ± 0.52	111	2.57 ± 0.48	23	2.37 ± 1.00
Parathyroid hormone	84	1.79 ± 0.43	228	2.21 ± 0.30	38	3.85 ± 1.21
Average		1.96 (0.78)		2.10 (0.61)		3.33 (0.69)

[a] Rates are in units of substitutions per site per 10^9 years. As in Table 4.1, the time of divergence has been set at 80 million years ago.
[b] L = number of sites.
[c] Average is arithmetic mean, and values in parentheses are the standard deviations, computed over all genes.

PSEUDOGENES

TABLE 4.4 Numbers of nucleotide substitutions per site (K) between mouse and goat β- and η-globin genes and between mouse and goat β-globin pseudogenes.

Region	K[a]
5' flanking region	5.5 ± 1.2
5' untranslated region	4.0 ± 2.0
Fourfold degenerate sites	8.6 ± 2.5
Introns	8.1 ± 0.7
3' untranslated region	8.8 ± 2.2
3' untranslated region	8.0 ± 1.0
Pseudogenes	9.1 ± 0.9

[a] Mean and standard errors.

2

GENERALISATION
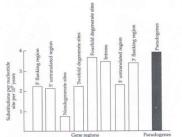
SIMILARITY PROFILES
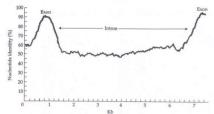
SUBSTITUTION RATE VARIATION

**Functional Constraints**
$$v_0 = v_T f_0$$
$$K = v_T f_0$$

Non- & Synonymous Rates
negative selection

Variation among Regions
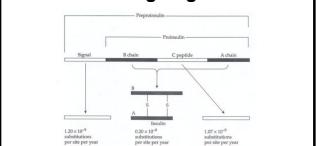
SUBSTITUTION RATE VARIATION (2)

Variation among Genes
    mutation rate
    selection intensity

Loss-Of-Function
    selection relaxation

Estimating Negative Selection
$$K_{\psi A} = v_{\psi A} \, f_{\psi A}$$
$$K_A = v_A \, f_A$$
$$fA = K_A / K_{\psi A}$$

SUBSTITUTION RATE VARIATION (3)

Gender-Driven Selection

$$\alpha = u_m / u_f$$

$$A = (u_m + u_f) / 2$$

$$X = (u_m + 2u_f) / 3, \quad Y = u_m$$

$$Y / A = 2\alpha / (1 + \alpha)$$

$$X / A = 2(2 + \alpha) / (3(1 + \alpha))$$

$$Y / X = 3\alpha / (2 + \alpha)$$