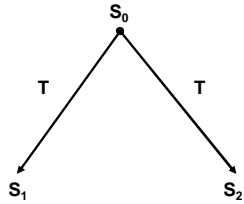
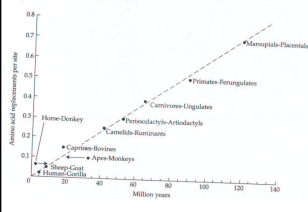


MOLECULAR CLOCK

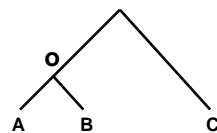
$$t = K / (2r)$$



“For each protein, the rate of evolution in terms of amino acid substitutions is approximately constant per year per site for various lines, as long as the function and tertiary structure of the molecule remain essentially unaltered.”



RELATIVE RATE TEST



$$K_{AB} = K_{OA} + K_{OB}$$

$$K_{AC} = K_{OA} + K_{OC}$$

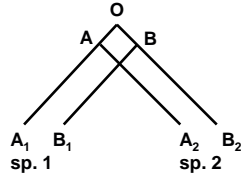
$$K_{BC} = K_{OB} + K_{OC}$$

$$K_{OA} = (K_{AC} + K_{AB} - K_{BC}) / 2$$

$$K_{OB} = (K_{AB} + K_{BC} - K_{AC}) / 2$$

$$K_{OC} = (K_{AC} + K_{BC} - K_{AB}) / 2$$

RELATIVE RATE TEST



$$K_{A_1B_1} = K_{AA_1} + K_{OA} + K_{OB} + K_{BB_1}$$

$$K_{A_2B_2} = K_{AA_2} + K_{OA} + K_{OB} + K_{BB_2}$$

$$K_{A_1B_1} - K_{A_2B_2} = K_{AA_1} + K_{BB_1} - (K_{AA_2} + K_{BB_2})$$

Species 2	Species 3	m_1	m_2	χ^2
<i>Pan paniscus</i>	<i>Homo sapiens</i>	21	14	1.40
<i>Pan paniscus</i>	<i>Gorilla gorilla</i>	33	55	5.50*
<i>Pan troglodytes</i>	<i>Gorilla gorilla</i>	34	61	7.67**
<i>Gorilla gorilla</i>	<i>Pongo pygmaeus</i>	56	58	5.15*
<i>Gorilla gorilla</i>	<i>Pongo pygmaeus</i>	63	56	0.41
<i>Gorilla gorilla</i>	<i>Pongo pygmaeus</i>	56	58	0.04
<i>Pongo pygmaeus</i>	<i>Hylobates lar</i>	91	105	1.00
<i>Pongo pygmaeus</i>	<i>Hylobates lar</i>	120	104	1.14
<i>Pongo pygmaeus</i>	<i>Hylobates lar</i>	109	104	0.12
<i>Pongo pygmaeus</i>	<i>Hylobates lar</i>	106	112	0.17

TABLE 4.12 Differences in the number of nucleotide substitutions per 100 sites in noncoding regions and the relative rates of substitution between (a) (species monkey (species 1)) and the human (species 2) lineage, with a New-World monkey (species 3) as reference.

Type of sequence	Sequence length	K_A^*	K_S^*	K_D	$K_A - K_S$	Ratio ^b
Intergenes	878	6.7	11.8	10.7	1.1 ± 0.3**	1.4
Introns	8,478	7.1	14.7	13.9	0.8 ± 0.2**	1.3
Flanking and untranscribed regions	936	7.9	14.9	11.7	3.1 ± 1.1**	2.3

Data from Bailey et al. (1991), Porter et al. (1995), and Elsworth et al. (1995).

*Significant at the 1% level.

^b K_A = number of substitutions per 100 sites between species 1 and 2.

^cThe ratio of the rate in the African monkey region to that in the human lineage.

TABLE 4.10 Differences in the number of substitutions per 100 sites between mice (species 1) and rats (species 2), with humans (species 3) as a reference.

Type of substitution	Number of sites compared	Number of substitutions ^a			
		K_{12}^b	K_{13}	K_{23}	$K_{12} - K_{13}$
Synonymous	4,857	19.9 ± 0.7	31.1 ± 0.9	32.4 ± 1.0	-1.3 ± 7.9
Nonsynonymous	17,440	1.9 ± 0.1	2.9 ± 0.1	2.7 ± 0.1	0.3 ± 1.3

Modified from Ohlgin and Li (1992).

^aMean ± standard error. K_{ij} = number of substitutions per 100 sites between species i and j .

TABLE 4.13 Numbers of nucleotide substitutions per synonymous site (K_S) and per nonsynonymous site (K_A) between duplicated genes in humans and rodents

Gene pair	K_S	K_A
β-like globin genes*		
Human adult-Human fetal	0.73	0.18
Mouse adult-Mouse fetal	0.90	0.21
Human adult-Human embryonic	0.62	0.16
Mouse adult-Mouse embryonic	0.97	0.18
Human fetal-Human embryonic	0.56	0.10
Mouse fetal-Mouse embryonic	0.96	0.15
Aldolase A and B genes		
Human A-Human B	1.55	0.21
Rat A-Rat B	1.92	0.21

From Li et al. (1987a)

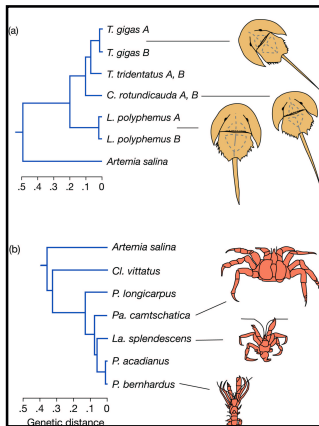
*The adult globin genes are β in human and β_{H2} in mouse; the fetal genes are γ in human and β_{F1} in mouse; and the embryonic genes are ϵ in human and $\beta 2$ in mouse.

SUBSTITUTION RATE VARIATION

Replication-Dependent
Generation Time Effect
DNA repair efficiency

Replication-Independent
metabolic scaling

Phyletic Gradualism vs.
Punctuated Equilibrium
mutation rate
negative selection
relaxed selection
positive selection



SUBSTITUTION RATES IN ORGANELLES

TABLE 4.1 Genetic content of plant mitochondrial and chloroplast genomes.

Species	Size (bp)	Open reading frames*	rRNAs	tRNAs	Introns
Mitochondria					
<i>Chenopodium</i>	25,836	36	3	23	1
<i>Phaseolus vulgaris</i>	55,328	36	3	26	5
<i>Morone saxatilis</i>	156,699	74	3	29	32
<i>Arabidopsis thaliana</i>	366,923	117	3	21	22
Chloroplasts					
<i>Erythraea variegata</i>	70,028	34	8	28	12
<i>Chenopodium</i>	119,294	140	4	29	8
<i>Ficus thuyoides</i>	119,707	156	4	36	15
<i>Morone saxatilis</i>	121,024	89	8	34	21
<i>Oryza sativa</i>	134,525	108	8	44	14
<i>Zea mays</i>	140,387	111	8	39	23
<i>Eugenia grandis</i>	143,172	65	8	43	146
<i>Nicotiana glauca</i>	153,939	102	7	28	25

*Relative protein-coding genes larger than 100 codons. Some of the differences in protein-coding gene numbers among chloroplast genomes may be attributed to the presence of variable numbers of *dnaA* and *dnaB* genes.

TABLE 4.14 Comparison of the number of nucleotide substitutions per site (in standard units) in plant chloroplast, mitochondrial, and nuclear genomes.

Genome	K _s	L _s	K _n	L _n
Comparison between monocot and dicot species				
Chloroplast	0.96 ± 0.02	4.177	0.05 ± 0.00	14.421
Mitochondrial	0.21 ± 0.01	1.219	0.04 ± 0.00	4.380
Comparison between maize and wheat or barley				
Nuclear	0.71 ± 0.04	1.473	0.06 ± 0.00	5.098
Chloroplast	0.17 ± 0.01	2.068	0.01 ± 0.00	7.001
Mitochondrial	0.03 ± 0.01	413	0.01 ± 0.00	1,526

From Nei et al. (1987, 1988).
 K_s, number of synonymous substitutions per synonymous site; K_n, number of nonsynonymous substitutions per nonsynonymous site; L_s and L_n are the number of synonymous and nonsynonymous sites, respectively.

SUBSTITUTION RATES IN VIRUSES

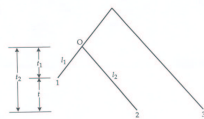


FIGURE 4.20 Model tree for estimating the rate of nucleotide substitution in RNA viruses. l_1 and l_2 denote the expected number of substitutions on the branches leading to isolates 1 and 2, respectively. Sequence 1, which was isolated at t_1 , was collected t years earlier than sequence 2, which was isolated at t_2 . Modified from Li et al. (1988).

$$l_2 - l_1 = rt_2 - rt_1 = rt$$

$$l_2 - l_1 = d_{23} - d_{13}$$

$$r = (d_{23} - d_{13}) / t$$