

Relative Rate Tests

part of “Fortgeschrittene Methoden der Bioinformatik”

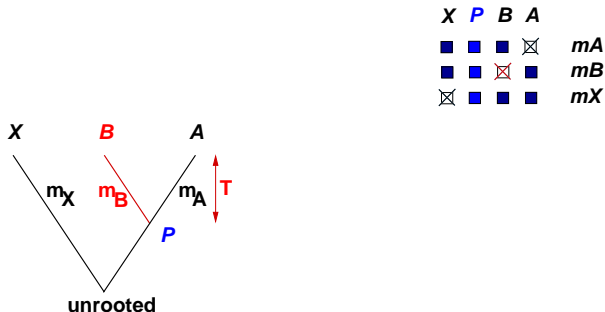
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Leipzig, SS 2011

Existing Tests for Equality of Evolutionary Rates

Tajima test

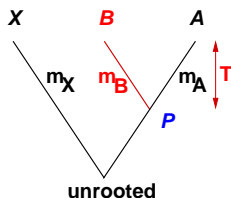


m_B = characters exclusively shared between X and A

m_A = characters exclusively shared between X and B

Existing Tests for Equality of Evolutionary Rates

Tajima test



$$E(m_A) = E(m_B)$$

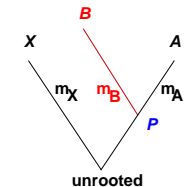
$$\chi^2 = \frac{(m_A - m_B)^2}{m_A + m_B}$$

χ^2 -test with one degree of freedom
significant difference at 5% level if
 $\chi^2 > 3.841$

m_B = characters exclusively shared between X and A

m_A = characters exclusively shared between X and B

Existing Tests for Equality of Evolutionary Rates

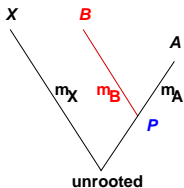


rate of B > *rate of A*

accelerated rate of B?

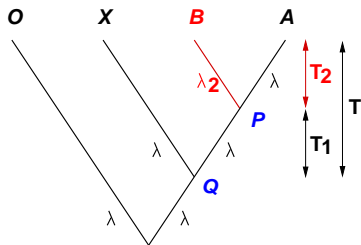
or

decelerated rate of A?



New Test for Relative Rates

Wagner's Test



- uses additional outgroup O to **estimate the conserved nucleotides at Q**
- assumes an **exponential decay law** for the retention of conserved nucleotides
- tests the hypothesis $\lambda = \lambda_2$

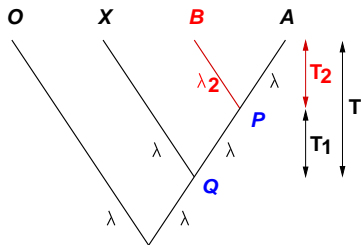
especially designed to compare evolution rates in non-coding sequences

accelerated evolution rates can be due to positive selection

New Test for Relative Rates

Wagner's Test

X	P	B	A	
■	■	■	⊗	<i>m</i> A
■	■	⊗	■	<i>m</i> B
⊗	■	■	■	<i>m</i> X

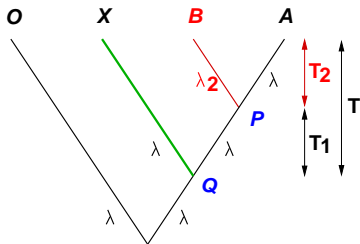


$m'_A = C_{XA} - C_{AB}$ = characters exclusively shared between X and A

$m'_B = C_{XB} - C_{AB}$ = characters exclusively shared between X and B

New Test for Relative Rates

Wagner's Test



$$r(QX) = e^{-\lambda T}$$

$$r(QP) = e^{-\lambda T_1}$$

$$r(PA) = e^{-\lambda T_2}$$

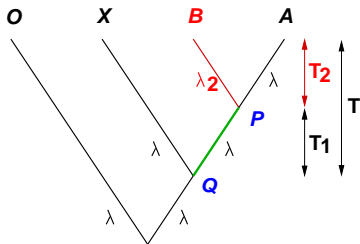
$$r(PB) = e^{-\lambda_2 T_2}$$

$$c_{AB}/q = e^{-\lambda T} e^{-\lambda T_1} e^{-\lambda T_2} e^{-\lambda_2 T_2}$$

calculate the retention (c_{AB}/q) of CNs in X, B and A,
given the set of CNs in Q

New Test for Relative Rates

Wagner's Test



$$r(QX) = e^{-\lambda T}$$

$$r(QP) = e^{-\lambda T_1}$$

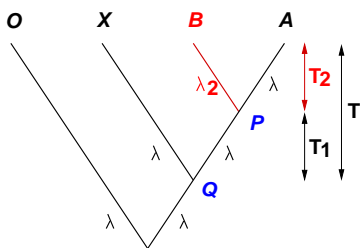
$$r(PA) = e^{-\lambda T_2}$$

$$r(PB) = e^{-\lambda_2 T_2}$$

$$c_{AB}/q = e^{-\lambda T} e^{-\lambda T_1} e^{-\lambda T_2} e^{-\lambda_2 T_2}$$

calculate the retention (c_{AB}/q) of CNs in X , B and A ,
given the set of CNs in Q

Wagner's Test



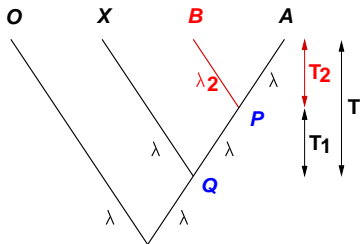
$$c_{AB}/q = e^{-\lambda T} e^{-\lambda T_1} e^{-\lambda T_2} e^{-\lambda_2 T_2}$$

$$c_{XA}/q = e^{-\lambda T} e^{-\lambda T}$$

$$c_{XB}/q = e^{-\lambda T} e^{-\lambda T_1} e^{-\lambda_2 T_2}$$

$$u/q = 1 - (1 - e^{-\lambda T}) \left[(1 - e^{-\lambda T_1}) + e^{-\lambda T_1} (1 - e^{-\lambda T_2}) (1 - e^{-\lambda_2 T_2}) \right]$$

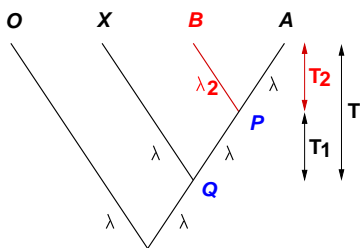
Wagner's Test



the amount of CNs
retained in Q is

$$q = c_{XA} \left(\frac{U + c_{A \vee B}}{c_{XA} + c_{A \vee B}} \right)^2$$

Wagner's Test



variance of an exponential process

$$s^2 = be^{-at}(1 - e^{-at})$$

$$\sigma^2 = 2qe^{-\lambda T_1}e^{-\lambda T_2}(1 - e^{-\lambda T_2})$$

$$2c_{XA} \left(\frac{U + C_{AVB}}{C_{XA} + C_{AVB}} \right) \left(1 - \frac{C_{AB}}{C_{XB}} \right)$$

Test Statistics for Conserved Non-Coding Nucleotide (CNCN) Sequence Elements

Wagner's Test - test statistic

$$z' = \frac{m'_A - m'_B}{\sqrt{\bar{\ell}\sigma^2}} \quad \text{normal distributed with variance 1}$$

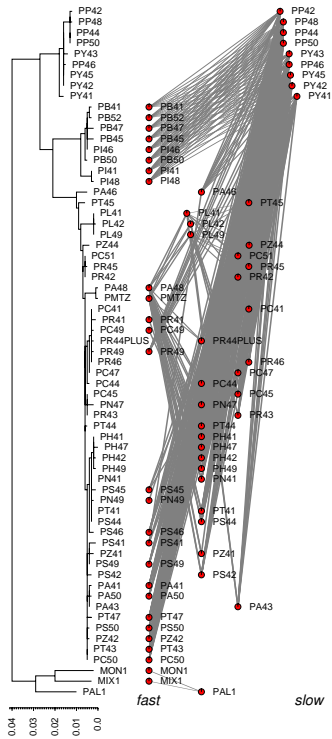
m'_A ...number of CNs exclusively lost along PA

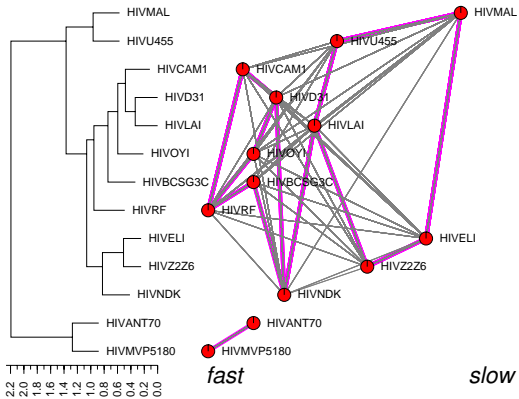
m'_B ...number of CNs exclusively lost along PB




σ^2 ...variance

$\bar{\ell}$...average length of a contiguous CN sequence element

To account for **stochastic dependency** among CNs we scale the sampling variance with $\bar{\ell}$.





-  [Tajima, 1993] F. Tajima. *Simple Methods for Testing the Molecular Evolutionary Clock Hypothesis*. *Genetics* 1993, 135(2):599-607.
-  [Wagner, 2004] Günter P. Wagner, Claudia Fried, Sonja J. Prohaska and Peter F. Stadler. *Divergence of Conserved Non-Coding Sequences: Rate Estimates and Relative Rate Tests*. *Mol.Biol.Evol.* 2004, 21:2116-2121.
-  [Prohaska, 2008] Sonja J. Prohaska, Guido Fritzsich and Peter F. Stadler. *Rate variations, phylogenetics, and partial orders*. In *Proceedings of the Fifth International Workshop on Computational Systems Biology, WCSB 2008*. 375-391.