

Nei-Gojobori dN/dS estimate (NG86)

- For each codon C we define $ES(C)$ and $EN(C)$ - the numbers of synonymous and non-synonymous *sites* of a codon
 - e.g., $ES(GAA) = 1/3$, $EN(GAA) = 8/3$.
- May also define them as fractions of substitutions that do not lead to stop codons,
 - e.g., $ES(GAA) = 1/3$, $EN(GAA) = 7/3$.
- The sum of ES and EN over all codons in a sequence gives an estimate of expected synonymous and non-synonymous **sites** in a sequence.
- For two sequences (the target of the original method), we average $ES(C)$ and $EN(C)$ at each site.
- EN/ES is thus the ***expected ratio of non-synonymous to synonymous substitutions counts under neutral evolution***

Simple methods for estimating the numbers of synonymous and nonsynonymous nucleotide substitutions

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>5,300 citations

NG86 limitations: underestimation of substitution counts for higher divergence levels

Simulated divergence vs that estimated by p-distance

- Simulated 100 replicates of 1000 nucleotide long sequences for various divergence levels (substitutions/site)
- Even for divergence of 0.25 (1/4 sites have mutation on average), p-distance already underestimates the true level: 0.2125 (0.19–0.241 95% range)
- Underestimation becomes progressively worse for larger divergence levels

