

Codon-substitution models

- In 1994, first tractable mechanistic evolutionary models for codon sequences were proposed by **Muse and Gaut** (MG94), and, independently, by **Goldman and Yang** (GY94) [in the same issue of MBE, back to back]
- Markov models of codon substitution provide a powerful framework for **estimating substitution rates** from coding sequence data, as they
 - *encode our mechanistic understanding of the evolutionary process,*
 - *enable one to compute the phylogenetic likelihood,*
 - *permit hypothesis testing or Bayesian inference,*
 - *systematically account for confounding processes (unequal base frequencies, nucleotide substitution biases, etc.),*
 - *afford many opportunities for extension and refinement (still happening today).*

A likelihood approach for comparing synonymous and nonsynonymous nucleotide substitution rates, with application to the chloroplast genome

S. V. Muse and B. S. Gaut
Mol Biol Evol 11 715-724 (1994)

~1000 citations

A codon-based model of nucleotide substitution for protein-coding DNA sequences.

N. Goldman and Z. Yang
Mol Biol Evol 11 725-736 (1994)

~2250 citations

Rate matrix for an MG-style codon model

$$(\text{Rate})_{X,Y}(dt) = \begin{cases} \alpha & \pi_t dt & , \text{ one-step, synonymous substitution,} \\ \beta & \pi_t dt & , \text{ one-step, non-synonymous substitution,} \\ 0 & & , \text{ multi-step.} \end{cases}$$

$X, Y = \text{AAA...TTT}$ (excluding stop codons),
 π_t - frequency of the target nucleotide.

Example substitutions:

AAC → AAT (one step, synonymous - Asparagine)

CAC → GAC (one step, non-synonymous - Histidine to Aspartic Acid)

AAC → GTC (multi-step).

αR_{CT}
 βR_{CG}

α (syn. rate) and β (non-syn. rate) are the key quantities for all selection analyses