

# 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

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

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

Example substitutions:

$\text{AAC} \rightarrow \text{AAT}$  (one step, synonymous - Asparagine)

$\text{CAC} \rightarrow \text{GAC}$  (one step, non-synonymous - Histidine to Aspartic Acid)

$\text{AAC} \rightarrow \text{GTC}$  (multi-step).

$\alpha R_{\text{CT}}$   
 $\beta R_{\text{CG}}$

$\alpha$  (syn. rate) and  $\beta$  (non-syn. rate) are the key quantities for all selection analyses