

Any questions on the previous material?



- **We have covered:**
 - Brief background and examples of natural selection
 - **dN/dS** as a tool to measure the action of natural selection, explained using the first counting method for estimating dN/dS (Nei-Gojobori, 1986) and its extensions
 - **Next section:** Codon substitution models — the basis of modern (1998-) dN/dS estimation approaches

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