NG86 limitations: averaging across all sites in a gene

- Different sites in a gene will be subject to different selective forces.
- A gene-wide measure of selection is going to average these effects.
- Most sites in most genes will be maintained by purifying selection.
- Positively selected sites are of great biological interest, because they point to how a particular gene can respond to selective pressures.
- Negatively selected sites are also of interest, because they point to functional constraint, and could be used to guide drug or vaccine design.
- Must develop methods that are able to disentangle the contributions of individual sites.

Suzuki-Gojobori (SG99): the penultimate extension of NG86

Uses a tree to compute dN/dS at a given site

- 1. Reconstruct ancestral sequences by nucleotide-level parsimony
- 2. Compute EN and ES using labeled branches; define $p_e = ES/EN$
- 3. Compute s and ns for each site (minimum evolution)
- 4. Estimate the probability that the number of synonymous substitutions \mathbf{S} is unusually low (positive selection) or unusually high (negative selection), using the binomial distribution given \mathbf{p}_{e} from step 2.

A method for detecting positive selection at single amino acid sites

Y. Suzuki and T. Gojobori

>500 citations

Mol Biol Evol 16 1315-1328 (1999)