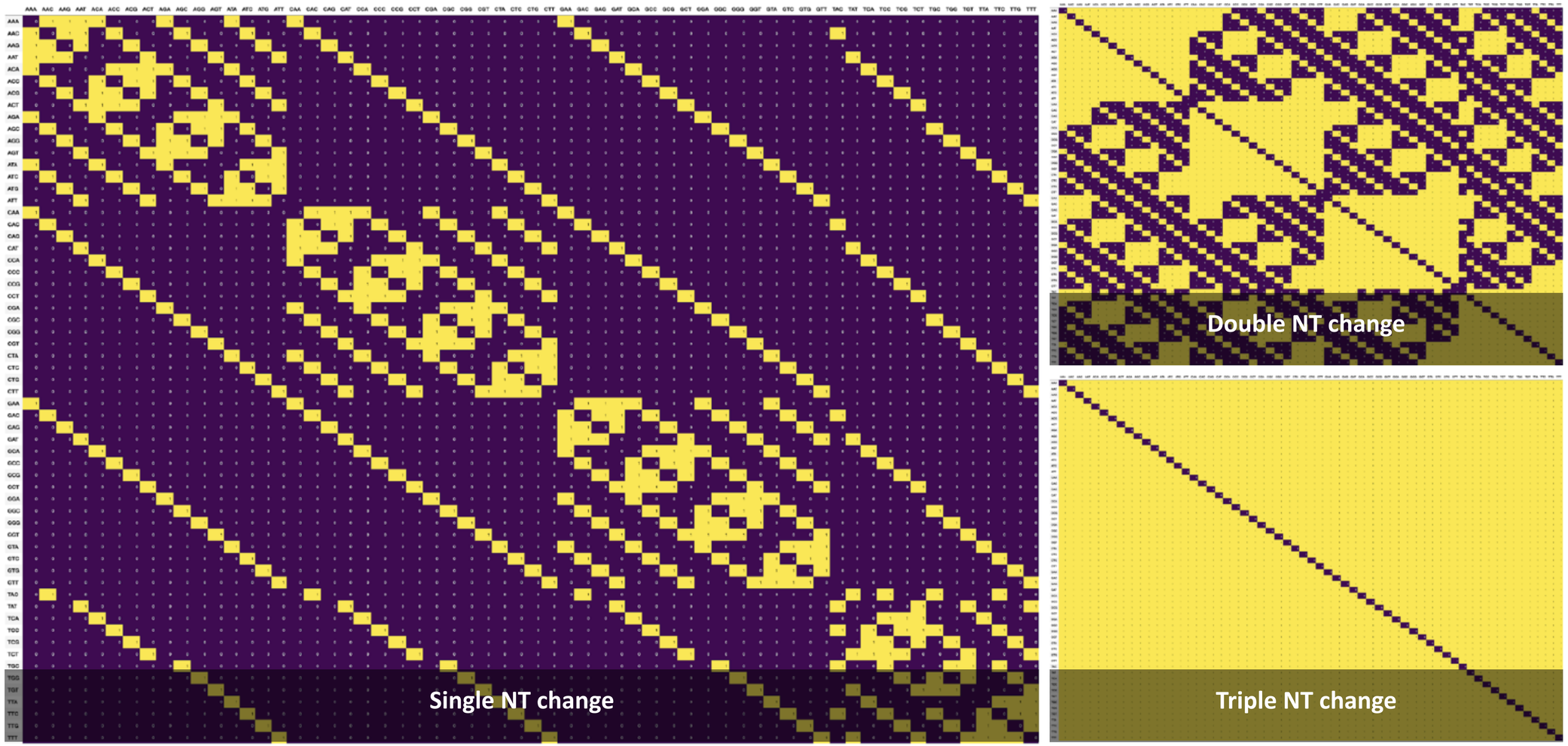
Illuminating the darkness in molecular evolution



Biological rationale for multiple nucleotide substitutions

Evidence for a High Frequency of Simultaneous Double-Nucleotide Substitutions

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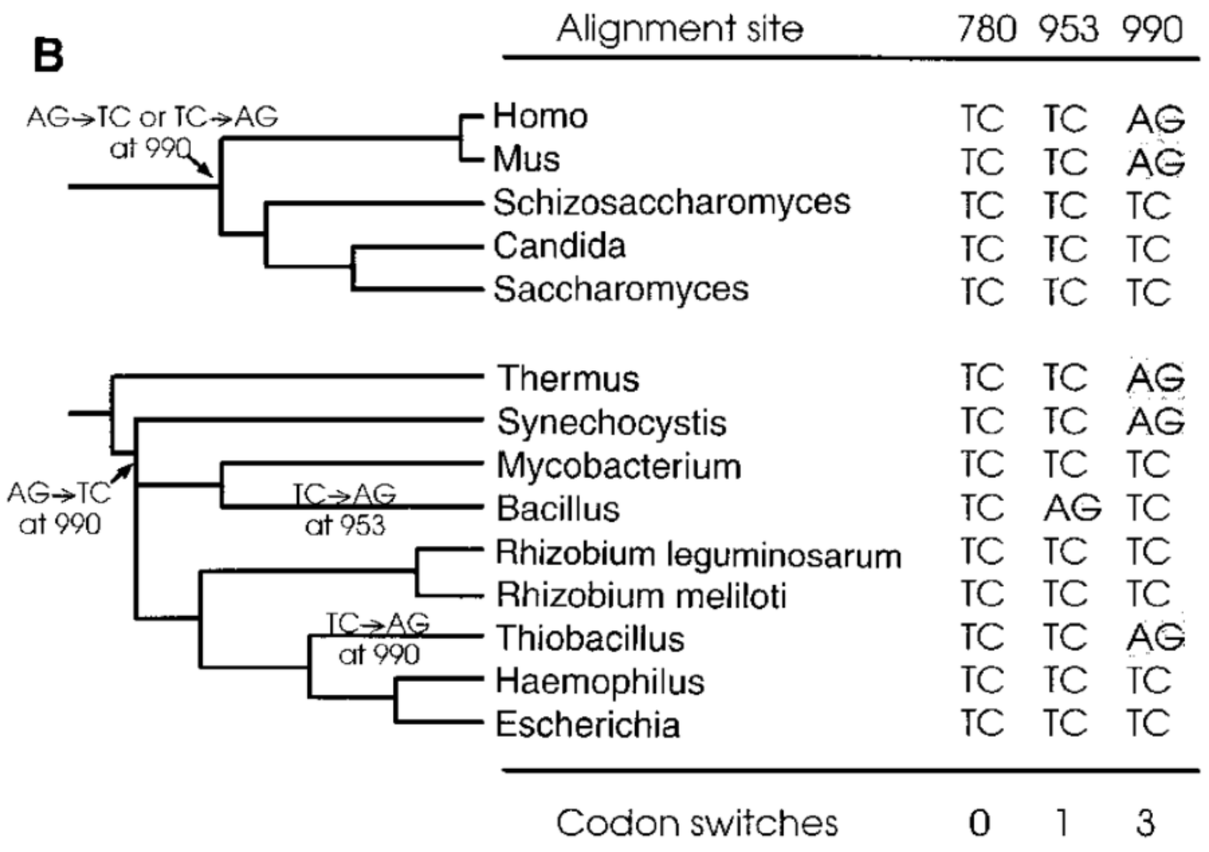
Point mutations are generally assumed to involve changes of single nucleotides. Nevertheless, the nature and known mechanisms of mutation do not exclude the possibility that several adjacent nucleotides may change simultaneously in a single mutational event. Two independent approaches are used here to estimate the frequency of simultaneous double-nucleotide substitutions. The first examines switches between TCN and AGY (where N is any nucleotide and Y is a pyrimidine) codons encoding absolutely conserved serine residues in a number of proteins from diverse organisms. The second reveals double-nucleotide substitutions in primate noncoding sequences. These two complementary approaches provide similar high estimates for the rate of doublet substitutions, on the order of 0.1 per site per billion years.



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