Transition Redundant Exchange as a Clock to Correlate the Genomic, Paleontological, and Geological Records

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Estimates of the rate constants for nucleotide substitutions at silent sites of encoding DNA is important to understanding the dynamics of molecular sequence evolution. We have analyzed transitions at synonymous sites within two-fold redundant coding systems, where the encoded amino acid is conserved, as a subset of these. This analysis exploits a simple two-state approach-to-equilibrium formalism well known in chemical kinetics, but only infrequently applied in molecular evolution. This formalism captures multiple substitutions at individual sites within a single equation, directly connected to specific rate constants, and avoiding any need to correct for multiple substitutions. The analysis yields a transition redundant exchange (TREx) distance for gene pairs. TREx sites are shown not to have fully equilibrated in the time separating mammals and birds. Pyrimidine-pyrimidine transitions are found to occur only modestly faster than purine-purine transitions in the rat:mouse lineages. Transition rate constants were also found to differ in different genes only slightly, therefore only modestly increasing the dispersion of the resulting molecular clock. The TREx clock is therefore useful to interpret and reconstruct the history of transition rate constants, at least within mammals over the past 100 million years, and helps us use genomics to understand major changes in the history of recent life on Earth.