

**Fig. S2.** Comparison of nucleotide substitution probabilities for 5% of top matrices that maximized the values of  $F_{\pi}$  (the normalized difference between the relative frequency of four-fold degenerated codons after the selection on amino acids and their expected frequency resulting only from a mutation process). The thick line indicates median, the grey box shows quartile range and the whiskers determine the range without outliers.

