



**Figure S6. Models fitted to each of cpREV and mtREV.** Each element  $\log-O(\langle S \rangle(\hat{\tau}, \hat{\sigma}))_{ab}$  of the log-odds matrix of the model fitted to each empirical substitution matrix is plotted against the log-odds  $\log-O(S^{\text{obs}}(1 \text{ PAM}))_{ab}$  calculated from the corresponding empirical substitution matrix. Plus, circle, and cross marks show the log-odds values for one-, two-, and three-step amino acid pairs, respectively. The dotted line in each figure shows the line of equal values between the ordinate and the abscissa.