



**Figure S1. Dependence of PPV on the number of characteristic variables used.** For each protein in  $\alpha$ ,  $\beta$ ,  $\alpha + \beta$ , and  $\alpha / \beta$  folds, PPVs are plotted against the number of characteristic variables used to score co-substitutions between sites. The characteristic variables except  $\alpha$  propensity listed in Table 4 are added in the listed order to define an overall coevolution score; that is, (1) occurrence of amino acid substitution, (2) side-chain volume, (3) charge, (4) hydrogen-bonding capability, (5) hydrophobicity, (6)  $\beta$  and (7) turn propensities, (8) aromatic interaction, (9) branched side-chain, (10) cross-link capability, and (11) ionic side-chain. The solid and dotted lines correspond to predictions in which the ratio of the predicted to the true contacts is equal to 1/3 or 1/4, respectively.