



**S2 Fig.** Distinguished residue pairs within an array of length  $L = 8,534$ , ordered by DC scores for Gna1 (pdb: 4ag9), as computed by CCMpred using the MSA for the corresponding analysis in Table 2. Distinguished pairs are represented by black and red blocks, the latter indicating pairs common to panels A and B; the remaining pairs are represented by dots. The region up to each cut point  $X$  is highlighted in yellow. **A.** Distinguished elements are those pairs in 4ag9 separated by  $\leq 5 \text{ \AA}$  within chain A or between chains A and B (whichever is shorter). ICA results:  $S = 91$ ;  $D = 260$ ;  $X = 663$ ;  $d = 144$ ; 55% of the distinguished pairs ( $d/D$ ) occur in the initial 7.8% of the array ( $X/L$ ). **B.** Distinguished elements are pairs of the 25 residues found by the BPPS program to be most distinctive of the Gna1 family. ICA results:  $S = 27.9$ ;  $D = 263$ ;  $X = 1,238$ ;  $d = 114$ ; 43% of the distinguished pairs occur in the initial 14.5% of the array. Note that because no ranking is available for the distinguished pairs in panel B we calculate  $S$  for both panels without the ball-in-urn component  $P_b$  and using only  $P_a$  [14].