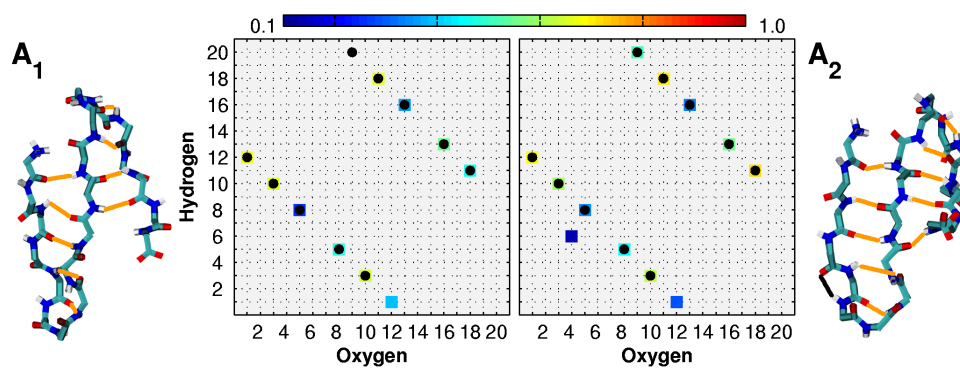
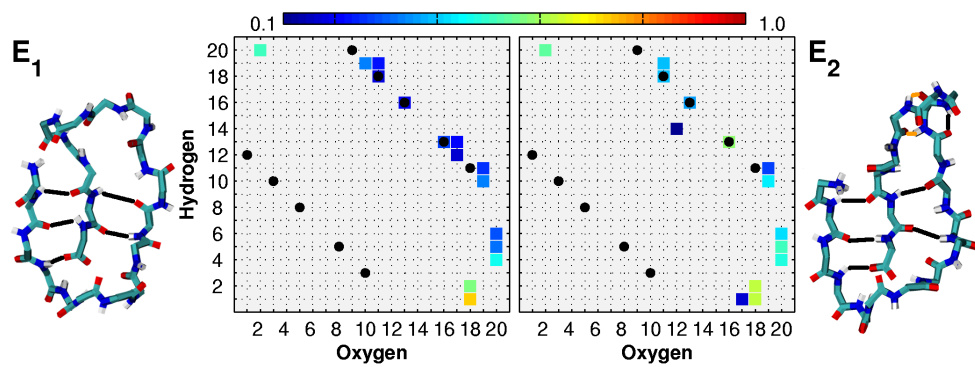


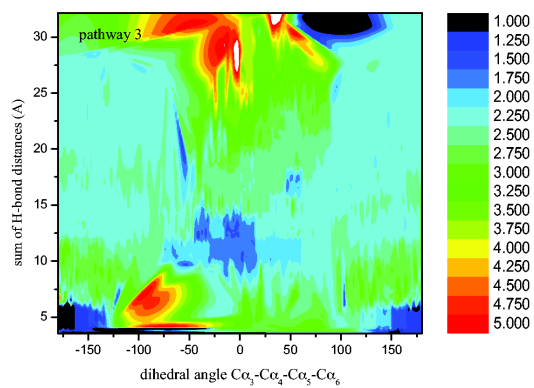
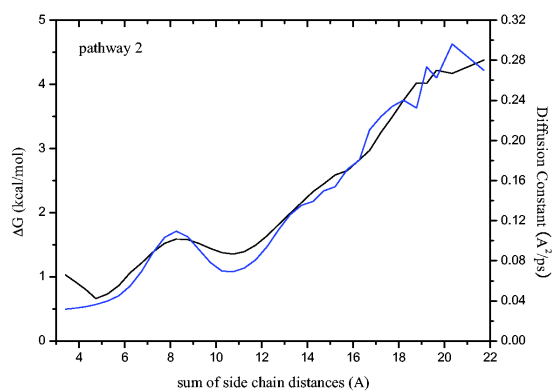
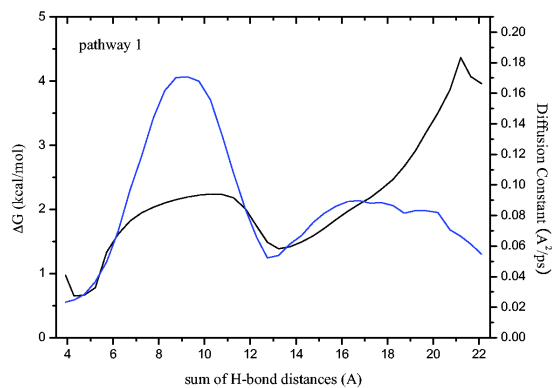
Supplementary Material



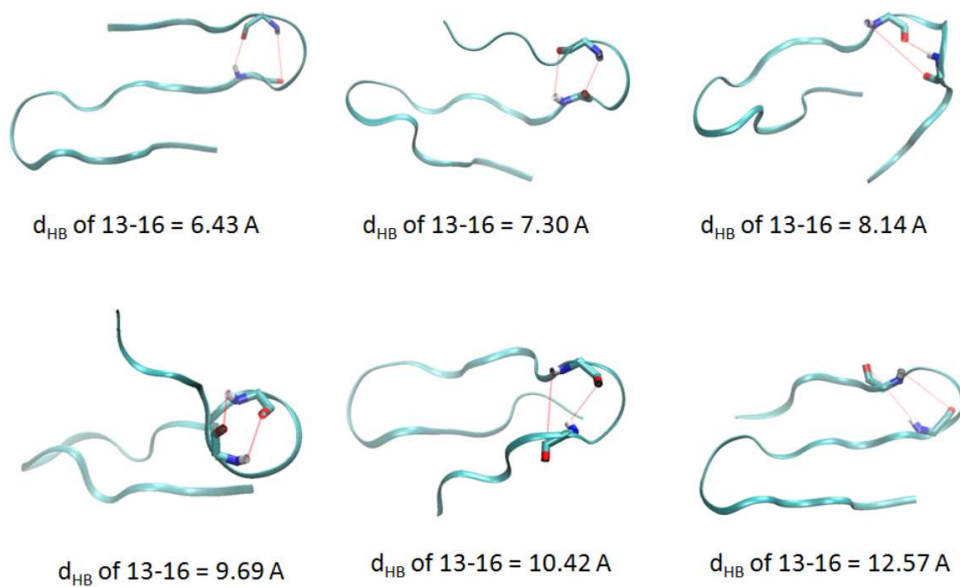
S 1: Representative structure and probability to form hydrogen bonds in state A_1 and A_2 .



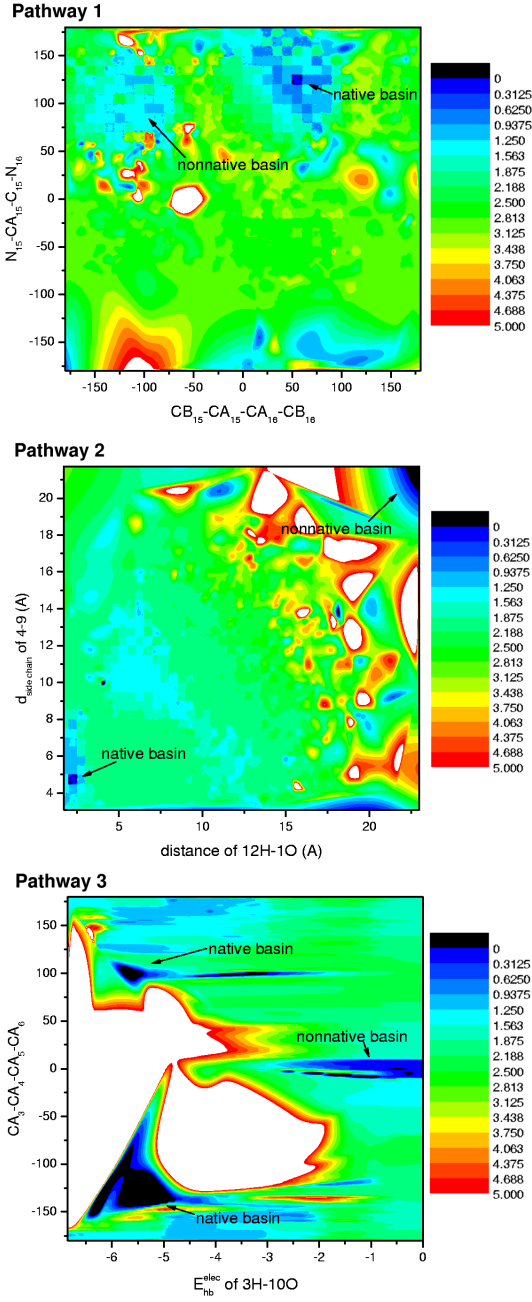
S 2: Representative structure and probability to form hydrogen bonds in state E_1 and E_2 .



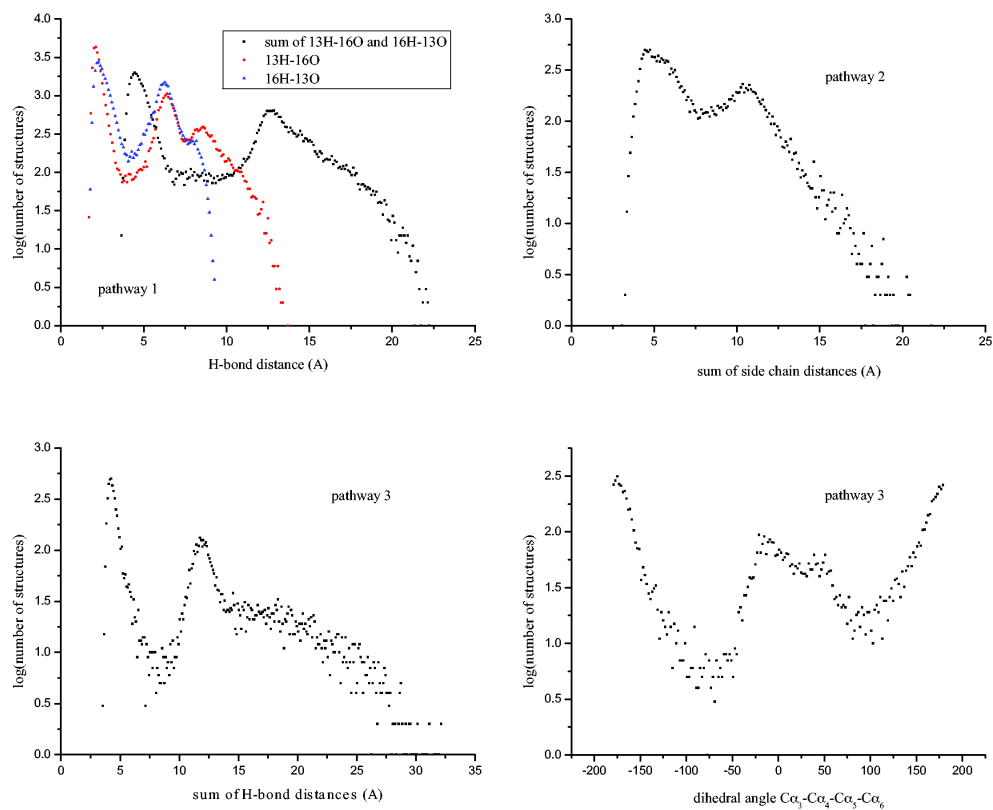
S 3: Top and middle panel: Cut-based free energy profile (black) and diffusion coefficient (blue) as a function of the top physical variable identified by the one-descriptor NN models for pathway 1 and 2. **Bottom panel:** Cut-based free energy profile as a function of the top two physical variables identified by the one-descriptor NN models for pathway 3.



S 4: Representative structures in pathway 1 showing the change of the distances between H and O atoms in the hydrogen bonds between residue 13 and 16.



S 5: Cut-based free energy profile as a function of the top two physical variables identified by the two-descriptor NN models. Pathways are as marked.



S 6: Distributions of the top physical variables identified by the one-descriptor NN models. Pathways are as marked.