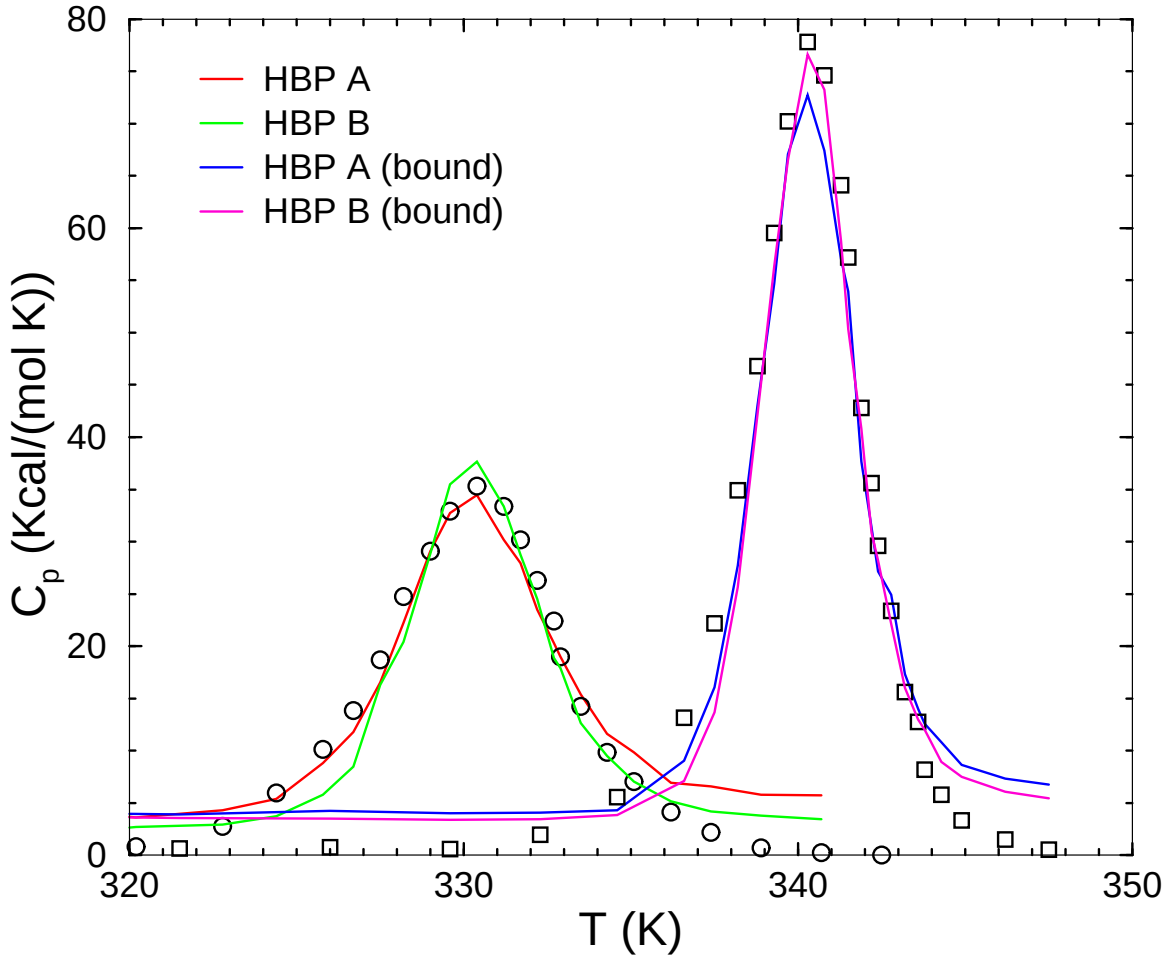

FIGURE S1: The best-fits to measured heat capacity for histidine binding protein. circle symbols - measured in apo form, square symbols - measured with histidine bound form. Chain (A) and (B) structures where used as template frameworks, where the apo structures are generated by computationally plucking out the His-substrate as explained in the main text.

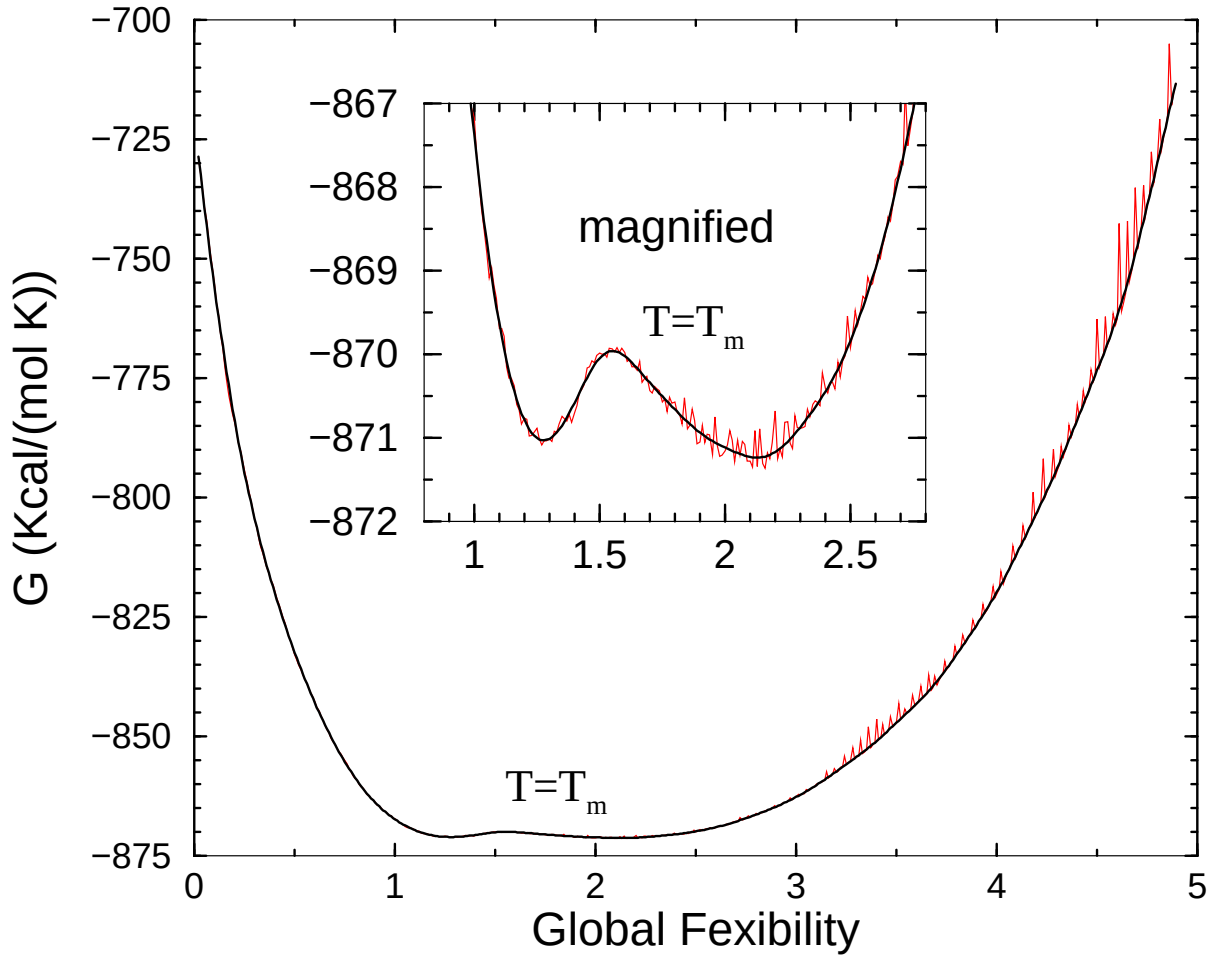

FIGURE S2: Shown here is the Landau free energy at T_m for UBQ at pH 3.0 and is typical of all calculations. $G(\theta, T)$ appears to be a continuous function of the flexiblity order parameter on large free energy scales. However, noise enters the data due to finite Monte Carlo sampling and small bin-size selection in $\Delta\theta$. Local smoothing of the data is reproduciable in the sense that the same smoothed functions can be obtained with arbitrary seeds for the random number generator. However, the noise is different. Also note that less sampling is done at higher free energies, which is why there is more noise seen at large flexibility order parameters. At low values of flexibility order parameter the much smaller enesemble of low energy frameworks are most probable, resulting in inherently less noise.

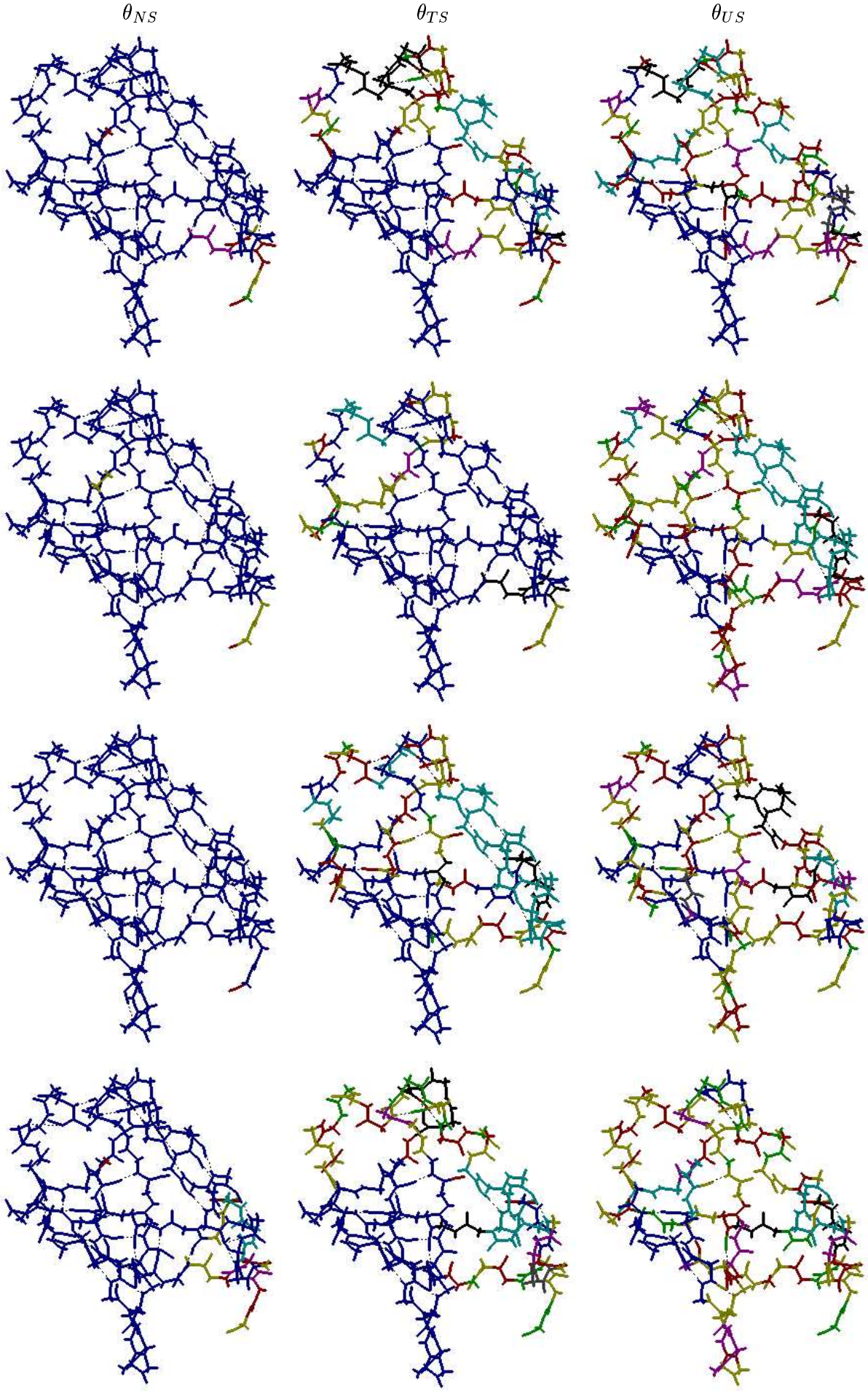

FIGURE S3: Sample of rigid cluster decompositions for UBQ pH 3.0

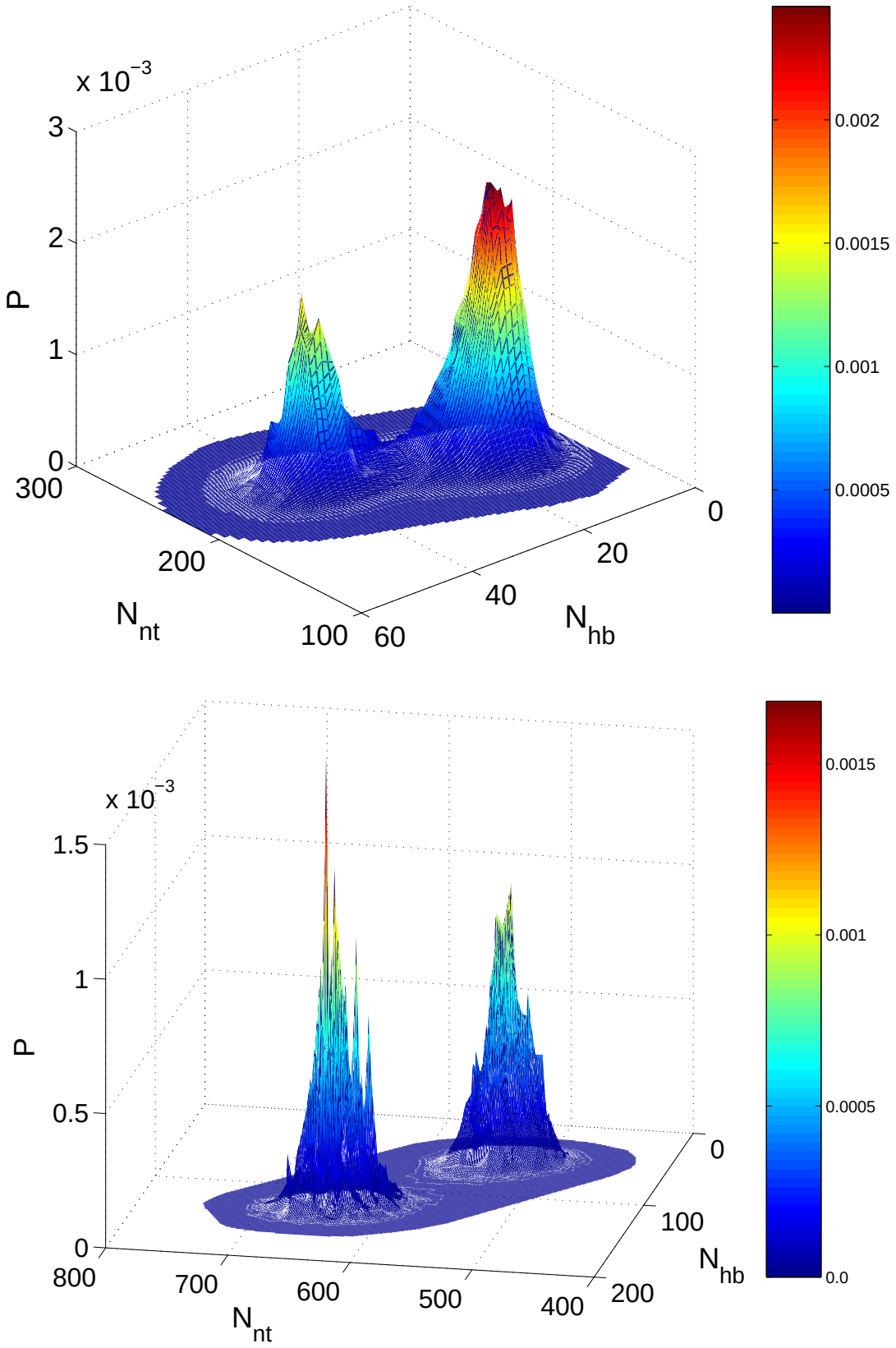

FIGURE S4: In (top, bottom) panels the probability for the protein to consist of N_{hb} H-bonds and N_{nt} native-torsion constraints is shown for (UBQ, HBP) for (pH 3.0, chain-B apo-form). A direct path can be seen between the two peak heights only in UBQ, where the barrier height is comparatively much lower.

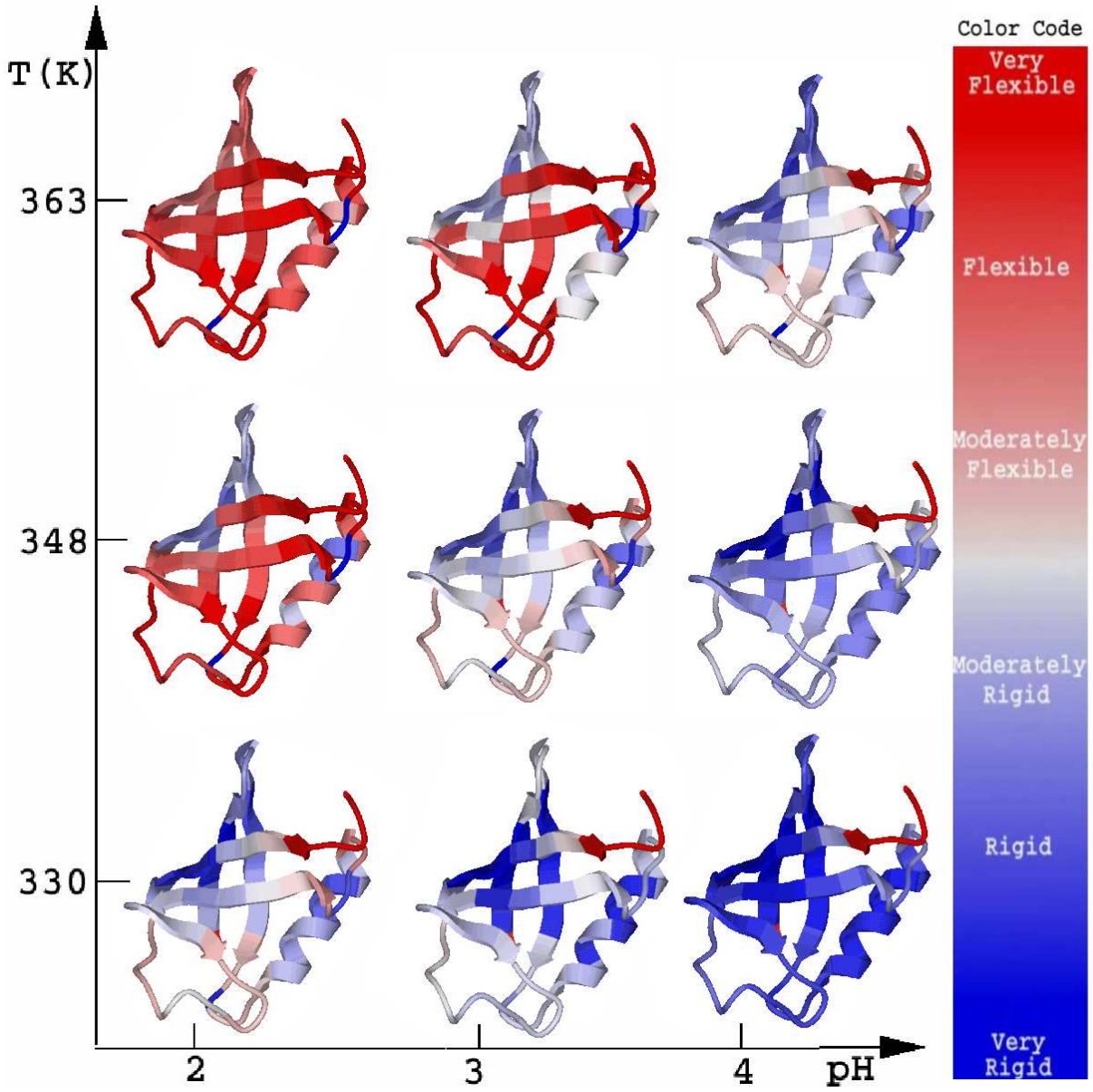

FIGURE S5: DCM predictions for backbone flexibility using the color code to the right for UBQ at various pH and T_m conditions. Here the flexibility measure is the probability that a covalent bond will rotate.

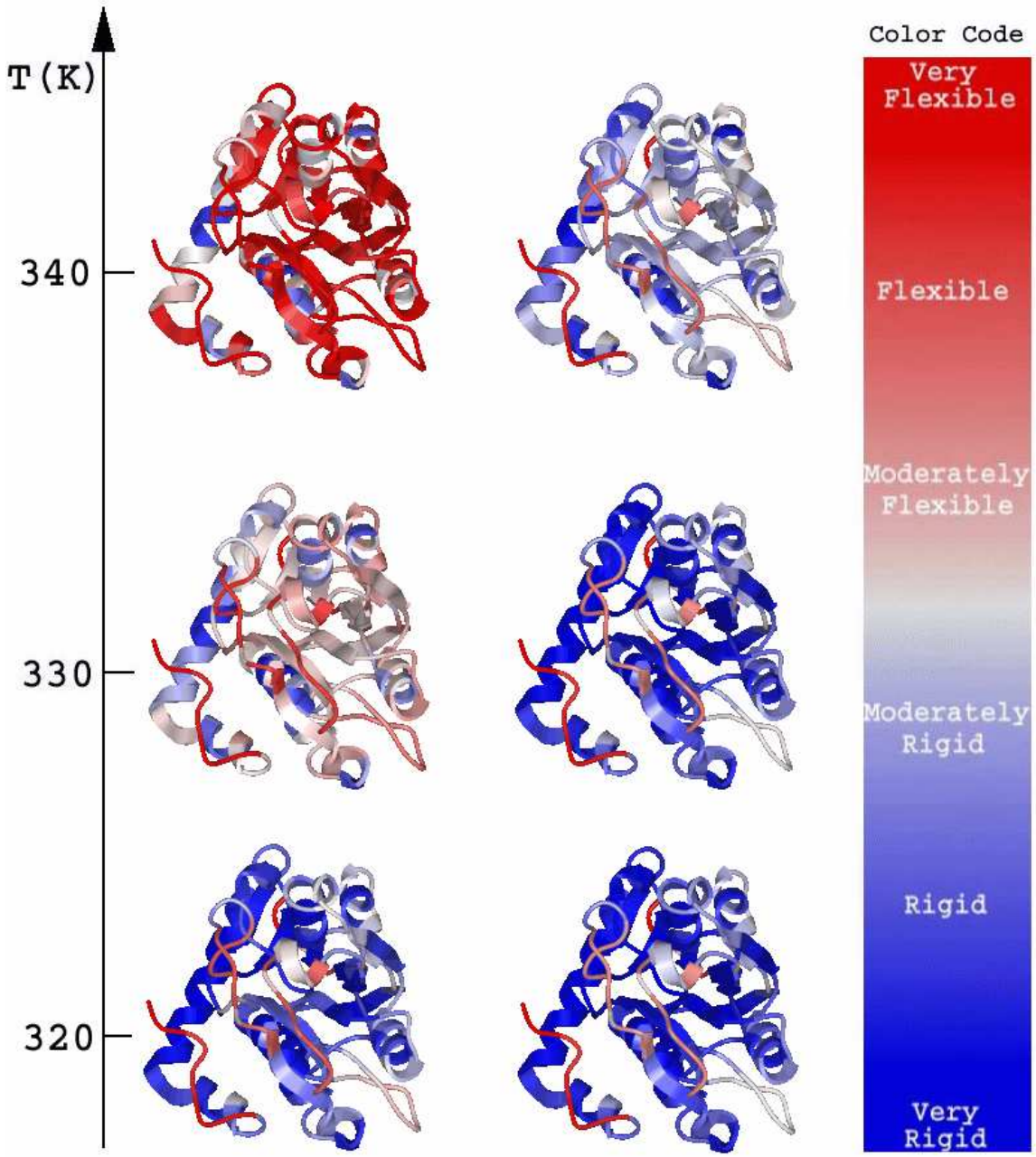

FIGURE S6: DCM predictions for backbone flexibility using the color code to the right for HBP in apo and HIS-bound forms. Here the flexibility measure is the probability that a covalent bond will rotate.