Text S1. Energetics of the $Im_{H187}H^+$-Gu^+_{R136} ion pair in the native structure of mPrP

We estimated the strength of the electrostatic repulsion between $Im_{H187}H^+$ and Gu^+_{R136} in the native structure of mPrP. As shown in Fig. S6 and S7, once H187 is protonated, $Im_{H187}H^+$ and Gu^+_{R136} remain in their native pockets during at least 100 ns before one of the two moves out. This speaks for a subtle local perturbation which is then propagated to specific parts of the system. To quantify the strength of this repulsion, we used the Coulomb-type expression [1]:

$$\Delta G_{qq}(r) = 332 \frac{q(Im_{H187}H^+) q(Gu^+_{R136})}{\epsilon(r) r}$$

where the $q(i)$ are the charges of the corresponding groups (+1 here), r is the distance separating them in Å (8 Å here), and $\epsilon(r)$ is an effective distance-dependent dielectric function [2,3]. This expression can be simplified further by using the fact that the dielectric constant typically ranges between 20 and 40 in protein interiors [1,3,4]. This gives an estimates of $\sim$ 1–2 kcal/mol for the electrostatic repulsion between $Im_{H187}H^+$ and Gu^+_{R136} in the native structure of mPrP. This is significant compared to the typical value of the folding energy of a protein, and hence has some substantial consequences on the protein structure after a certain amount of time (Fig. S6 and S7).

References

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