Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.
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Supporting material

The native contact energy function $U(r_{ij}, r_{ij}^0, \varepsilon, \varepsilon_{db}, \varepsilon_{ssm})$

As in references[1,2], the form of the native contact energy function, $U(r_{ij}, r_{ij}^0, \varepsilon, \varepsilon_{db}, \varepsilon_{ssm})$, is given by

$$U(r_{ij}, r_{ij}^0, \varepsilon, \varepsilon_{db}, \varepsilon_{ssm}) = \begin{cases} \varepsilon Z(r_{ij})\left[Z(r_{ij}) - 2\right] & \text{for } r_{ij} < r_{ij}^0 \\ CY(r_{ij})^s\left[Y(r_{ij})^s/2 - (r_{db} - r_{ij}^0)^{2s}\right]/2s + \varepsilon_{db} & \text{for } r_{ij}^0 \le r < r_{db} \\ -B\left[Y(r_{ij}) - h_1\right]/\left[Y(r_{ij})^m + h_2\right] & \text{for } r_{ij} \ge r_{db} \end{cases}$$

where

$$Z(r_{ij}) = \left(r_{ij}^0/r_{ij}\right)^k,$$

$$Y(r_{ij}) = \left(r_{ij} - r_{db}\right)^2,$$

$$C = 4s(\varepsilon + \varepsilon_{db})/(r_{db} - r_{ij}^0)^{4s},$$

$$B = m\varepsilon_{ssm}(r_{ssm} - r_{db})^{2(m-1)},$$

$$h_1 = (1 - 1/m)(r_{ssm} - r_{db})^2/(\varepsilon_{ssm}/\varepsilon_{db} + 1),$$

$$h_2 = (m - 1)(r_{ssm} - r_{db})^{2m}/(\varepsilon_{db}/\varepsilon_{ssm} + 1).$$

Here, $r_{ssm} = r_{ij}^0 + 3Å$, which followed from the consideration that 3Å is approximately equal to the diameter of a water molecule, and $r_{db} = \left(r_{ssm} + r_{ij}^0\right)/2$. The parameters k, m, and s are taken to be $k = 6$, $m = 3$, and $s = 2$.

The method for introducing the experimental zero-denaturant condition

As in previous studies[3,4], the zero-denaturant condition is introduced by matching the simulation folding stability with the experimental folding stability under zero-denaturant condition. At any ε/k_BT, the simulation folding stability $\Delta G/k_BT$ is given by

$$\Delta G/k_BT = -ln[P(Q > Q_F)/P(Q < Q_U)]$$

where the threshold Q values Q_F and Q_U are chosen to provide physically reasonable demarcations for the folded and unfolded states; $P(Q > Q_F)$ and $P(Q < Q_U)$ are, respectively, normalized conformation population for $Q > Q_F$ and $Q < Q_U$. The experimental folding stability under zero-denaturant condition can also be transformed into $\Delta G/k_BT$ (dimensionless). In the calculation of experimental folding stability $\Delta G/k_BT$, it should be noted that the ΔG is measured by experiment and the temperature T is the experimental absolute temperature. When the simulation folding stability $\Delta G/k_BT$ at certain ε/k_BT is comparable to the experimental folding stability under zero-denaturant condition, it is considered as zero-denaturant condition.

Supporting Figures

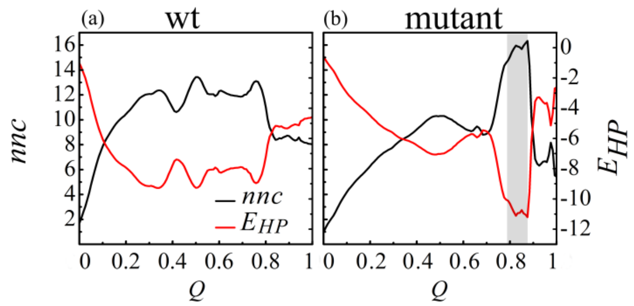

Fig.S1. Nonnative contact numbers (black lines, left scale) and nonnative interactions (red lines, right scale) as functions of fraction number of native contact Q by the $db + MJh\emptyset$ model under zero-denaturant conditions for the wildtype (a) and the mutant (b). The approximate range of Q values for the conformations constituting the transiently trapped intermediate in $db + MJh\emptyset$ model is highlighted by vertical gray shaded band.

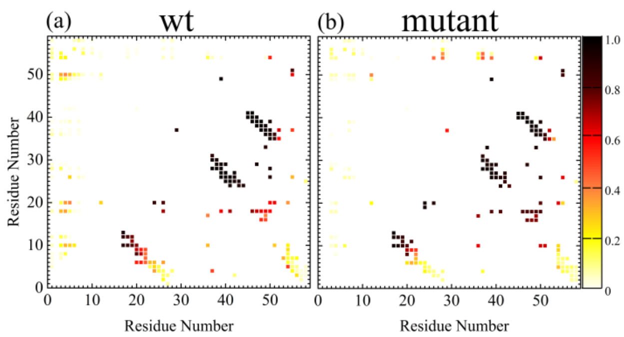

Fig. S2. Contact probability maps near transition state $0.58 < Q < 0.68$ under zero-denaturant conditions for Fyn SH3 domain (a) and A39V/N53P/V55L Fyn SH3 domain (b). In (a) and in (b), (upper left) nonnative contact probability map, (lower right) native contact probability map.

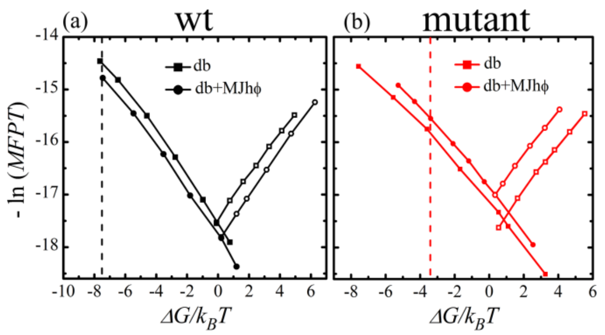

Fig. S3. Model chevron plots by the db model and the $db + MJh\emptyset$ model for the wildtype (a) and the mutant (b). The $\Delta G/k_BT$ values corresponding to the experimental stability under zero-denaturant conditions are marked by vertical dashed lines. Fitted curves are merely guides for eye.

References

1. Z. Liu and H. S. Chan, *Phys. Biol.*, 2005, **2**, S75-S85.
2. M. S. Cheung, A. E. García, and J. N. Onuchic, *Proc. Natl. Acad. Sci. U. S. A.*, 2002, **99**, 685-690.
3. T. Chen and H. S. Chan, *PLoS Comput. Biol.*, 2015, **11**, e1004260.
4. A. Badasyan, Z. Liu, and H. S. Chan, *J. Mol. Biol.*, 2008, **384**, 512-530.