Supporting Information for

Connecting Protein Conformational Dynamics with Catalytic Function as Illustrated in Dihydrofolate Reductase

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Table S1. Computed free energies of activation, $\Delta G^{\neq}$, (kcal/mol) from potentials of mean force obtained from classical mechanical (CM) and centroid paith integral free energy perturbation and umbrella sampling (PI-FEP/UM) simulations at 5, 25 and 45 ^{o}C for the hydride transfer from NADPH to H3F catalyzed by wild-type and M42W/G121V DHFR. Nuclear quantum effects are included in the PI-FEP/UM calculations.

Temperature	Wild-type DHFR		M42W-G121V double mutant	
	CM	PI-FEP/UM	CM	PI-FEP/UM
5°C	15.8	12.9	16.4	13.7
25°C	16.4	13.6	17.6	14.8
45°C	16.6	13.9	17.9	15.5