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

Simulation on the Ligand Leaving Process of Human Heat Shock Protein

Yi-Xiao Hu, Jun-wen Fei, Li-Hua Bie, Jun Gao**

Hubei Key Laboratory of Agricultural Bioinformatics, College of Informatics, Huazhong Agricultural University, Wuhan 430070, People's Republic of China

* gaojun@mail.hzau.edu.cn

*biebie@mail.hzau.edu.cn

Support information

Table S1 Convergence analysis of PMF calculations. All the PMFs are calculated by JE method using the cumulant expansion method. Standard deviations are provided for separate calculation of PMF by this method. But multiple times calculation by bootstrap method gives the standard deviation. For example, 60/70 means that 60 trajectories are randomly selected with replacement from 70 SMD trajectories and the PMF value is calculated. This process of random selection and calculation is repeated 110 times.

	50 trajs	60/70 trajs	70 trajs	70/80 trajs	80 trajs	80/100trajs	100trtajs
6FJ-HSP90	49.64	50.02 ± 0.52	50.92	50.36 ± 0.53	50.15	50.59±0.68	50.68
6G7-HSP90	34.44	35.70 ± 0.81	35.63	35.14 ± 0.66	34.88	34.37±0.79	34.36
ΔΔG	15.2	14.32 ± 1.33	15.29	15.22 ± 1.19	15.27	16.22±1.57	16.32

Table S2 Convergence analysis of PMF calculations. All the PMFs are calculated by JE method using the cumulant expansion method. Standard deviations are provided for separate calculation of PMF by this method. But multiple times calculation by bootstrap method gives the standard deviation. For example, 60/70 means that 60 trajectories are randomly selected with replacement from 70 SMD trajectories and the PMF value is calculated. This process of random selection and calculation is repeated 110 times.

	12of13trajs	13trajs	13of14trajs	14trajs	14of15trajs
6FJ-HSP90	5.34 ± 0.07	5.32	5.34 ± 0.07	5.40	5.53 ± 0.16
6G7-HSP90	3.32 ± 0.04	3.33	3.43 ± 0.06	3.37	3.34 ± 0.05
ΔΔG	2.02 ± 0.11	1.99	1.91 ± 0.13	2.03	2.19 ± 0.21

Table S3. The binding free energy of the two complex systems at 310K temperature. The data comes from the calculation by MM-GBSA method based on 10,000 snapshots extracted from the last 200ns trajectories. The entropy contribution was estimated using quasi-harmonic approximation. The units are kcal/mol.

System	ΔS(kcal/mol)	ΔH(kcal/mol)	ΔG(kcal/mol)	ΔG_{bind}^{e}
6FJ-HSP90	-23.44	-52.18± 4.14	-28.74 ± 4.14	-12.48 ± 0.00
6G7-HSP90	-18.52	-33.17± 2.96	-14.64± 2.96	-9.35 ± 0.07

The data of ΔG_{bind}^{e} comes from the experimental measurement of M.Amaral et.cl. (Amaral et al 2017)

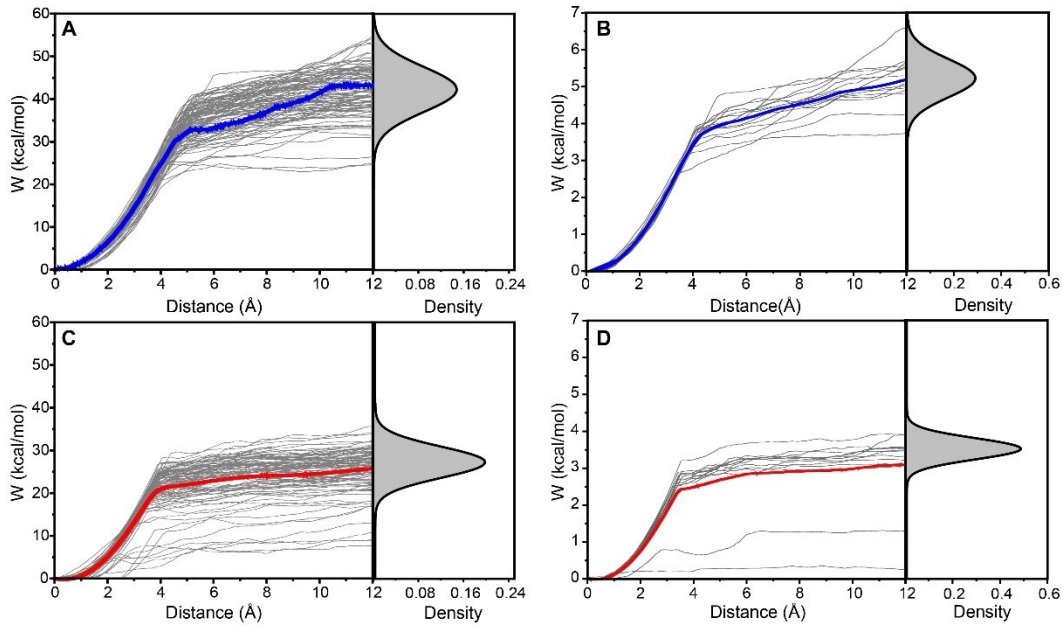

Figure S1. The distribution of W for 50 fast-pulling and 15 slow-pulling trajectories. **A)** The distribution of W of 6FJ-HSP90 with a pulling velocity of 0.1 nm/ns. **B)** The distribution of W of 6FJ-HSP90 with a pulling velocity of 0.01 nm/ns. **C)** The distribution of W of 6G7-NHSP90 with a pulling velocity of 0.1 nm/ns. **D)** The distribution of W of 6G7-NHSP90 with a pulling velocity of 0.01 nm/ns.

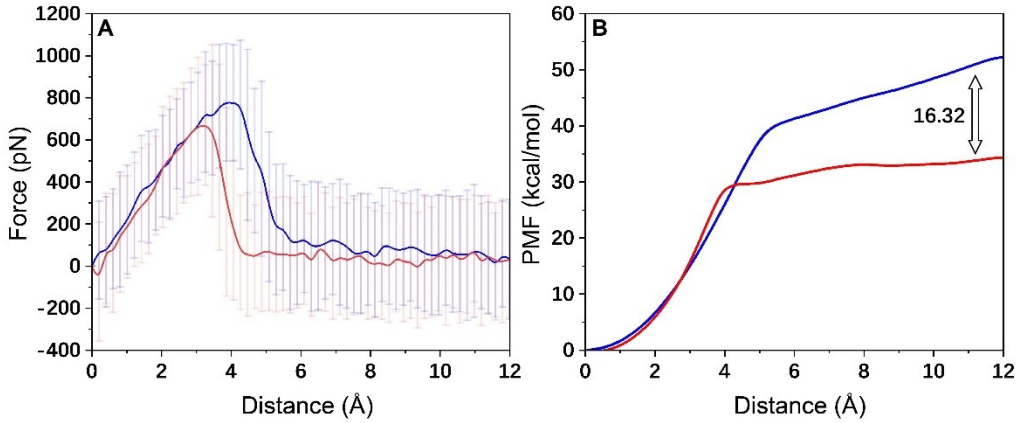

Figure S2. Profile of force and PMFs with the velocity of 0.01 nm/ns. **A)** Force profile of ligands pulled along the reaction coordinate. **B)** PMF was obtained through second-order cumulant expansion, and the bootstrap method was repeated 100 times to calculate the error value from 90 of the 100 trajectories.

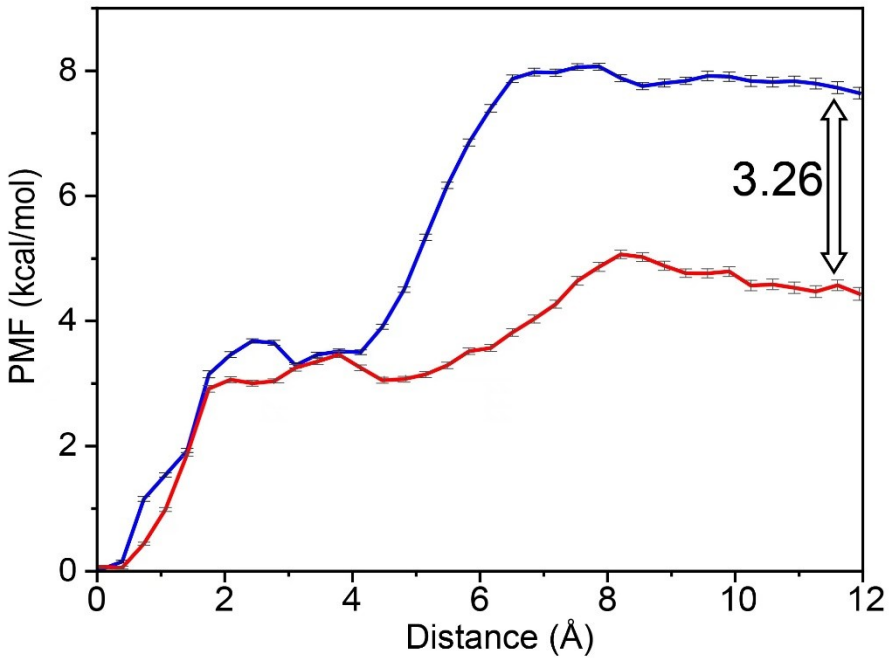

Figure S3. PMF results obtained from umbrella sampling. Based on the SMD trajectory to count the distance of ligand small molecules from the initial position, 12Å was divided into 24 windows, and an umbrella sampling was performed every 0.5Å, and the simulation duration of each window lasted for 10ns, in which the first 1ns trajectory was used as system equilibrium and the last 9ns trajectory was used for analysis. Limiting by the centroid distance of ligands, small molecules and proteins, the force constant added in the window is 2.5kcal/mol· The resonant potential of Å is calculated by combining the weighted histogram (WHAM) method for the average force potential, and the standard error is calculated using the bootstrap method.

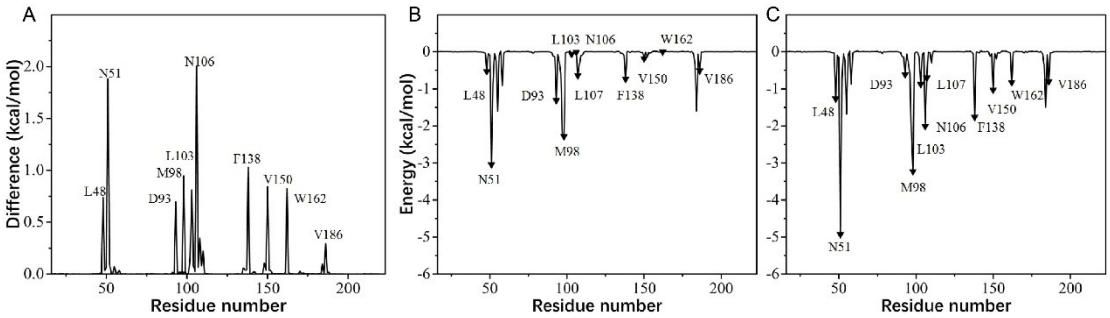

Figure S4. Residue energy decomposition. **A)** The difference between the energy decomposition of each residue between the 6G7-HSP90 system and the 6FJ-HSP90 system, expressed as an absolute value. **B)** Energy decomposition of residues in the 6G7-HSP90 system. **C)** Energy decomposition of residues in the 6FJ-HSP90 system