Tests on the Reliability and Throughput Performance of hSMD

Computed Values of Binding Free Energy *vs* Experimental Data

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Binding complex (PDB code of complex/protein)	Model systems (# of atoms)	Computing time: hours on # of CPU-cores*	hSMD prediction in kcal/mol	Experimentally measured value in kcal/mol (method)	Other computed results in kcal/mol (method)
1. OCA-LGB (3NQ9)	96K	62 on 480	-5.76[1]	-5.57 (FS)[2]	-2.66 (GBSA)[3]
2. DKA-LGB (3NQ3)	96K	64 on 480	-4.44[4]	-5.22 (FS)[2]	-4.44 (GBSA)[3]
3. DAO-LGB (3UEU)	96K	66 on 480	-6.89[4]	-7.24 (ITC)[5]	-12.37 (GBSA)[3]
4. MYR-LGB (3UEV)	96K	68 on 480	-8.57[4]	-8.14 (ITC)[5]	-12.66 (GBSA)[3]
5. PLM-LGB (3UEW)	96K	70 on 480	-8.99[4]	-8.72 (ITC)[5]	-20.92 (GBSA)[3]
6. GSH-SjGST (1U87)	115K	88 on 512	-7.0[1]	-6.75 (ITC)[6]	-
7. 8ST-VEGFR1 (3HNG)	95K	63 on 256	-9.2[7]	-8.3 (IC50)[8]	-
8. Tuftsin-NRP-1 (2ORZ)	125K	53 on 512	-7.2	-7.2 (ITC)[9]	-32 (JE-SMD)
9. Ras-RalGDS (1LFD)	96K	72 on 400	-9.2[10]	-8.4 (ITC)[11]	-19.5 (GBSA)[12]
10. Barnase-Barstar (1BRS)	97K	72 on 320	-16.8[10]	-16.0 (ITC)[13]	-21.0 (wt, GRC)[14]
11. GOL-GLPF (1FX8)	78K	58 on 320	-3.5[15]	<-2.8 (XRD)[16] <-2.7 (IC50)[17]	-
12. GOL-PfAQP (3C02)	150K	58 on 640	-3.8[18]	<-2.8 (XRD)[19] <<-1.1 (IC50)[18, 20]	-
13. MRY-PfAQP (3C02)	150K	58 on 640	-8.4[18]	TBV[&]	-
14. AZM-AQP4 (3GD8)	73K	58 on 320	-3.7[21]	-3.4 (IC50)[22]	-6.5 (Virtual Screening)[23] -3.2 (GRC)[24]
15. EDO-AQP4 (3GD8)	73K	88 on 256	-1.5[21]	TBV	-
16. PDO-AQP4 (3GD8)	73K	88 on 256	-4.75[21]	TBV	-

17. AZM-caII (3HS4)	61K	71 on 200	-11.1[25]	-10.8 (multiple, *e.g.* IC50 [26])	-
18. J0Z-T4L (3HUK)	97K	120 on 480	-4.6[27]	-4.5 (ITC)[28]	-1.3 (apo) -3.9 (holo) (FEP)[28]
19. 265-T4L (2RBO)	97K	120 on 480	-4.9[27]	-4.9 (ITC)[28]	-5.7 (apo) -11.4 (holo) (FEP)[28]
20. BNZ-T4L (4I7J)	97K	120 on 480	-4.8[27]	-4.5 (ITC)[29]	-
21. RTL-CRBP1 (5HBS)	103K	132 on 480	-12.6[27]	10.9 (ITC)[30]	-

*Complexes 1-5 were computed on TACC supercomputers Lonestar, Complexes 6-8, 15, and 16 on Stampede, and Complexes 9-14 and 17 on Maverick all **without invoking GPU or MIC acceleration**. For comparison, Complex 17 was also computed on a single node of Maverick (20 CPU-cores) **with GPU** acceleration took 198 hours, a longer time but at a lower computing cost of about 4K SUs which is in contrast 14 K SUs on 200 CPU-cores without GPU.

[&]TBV: To be validated *in vitro/vivo*.

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