Perturb	Exp	$\Delta\Delta F_{bind}$	$\Delta\Delta F_{solv}$	$\Delta F_{protein}$	ΔF_{water}	ΔF_{vac}
1t2	-1.63	1.61 ± 0.21	-0.68 ± 0.20	-0.03 ± 0.13	-1.64 ± 0.17	-0.96 ± 0.11
1t3	-2.67	-4.64 ± 0.19	-1.32 ± 0.15	22.60 ± 0.11	27.24 ± 0.15	28.57 ± 0.01
2t3	-1.04	-2.67 ± 0.32	-3.54 ± 0.17	23.25 ± 0.27	25.92 ± 0.17	29.46 ± 0.01
3t4	-4.09	-4.48 ± 0.23	-0.10 ± 0.12	-11.11 ± 0.20	-6.63 ± 0.11	-6.53 ± 0.03
5t6	-3.45	-4.53 ± 0.15	-2.72 ± 0.13	20.56 ± 0.08	25.09 ± 0.12	27.81 ± 0.01
5t7	-5.15	-5.28 ± 0.26	-3.17 ± 0.20	13.69 ± 0.17	18.98 ± 0.19	22.15 ± 0.06
2t4	-5.13	-7.38 ± 0.34	-4.83 ± 0.31	10.97 ± 0.14	18.35 ± 0.31	23.18 ± 0.01
2t9	0.08	-5.99 ± 0.56	0.58 ± 0.52	-1.17 ± 0.22	4.82 ± 0.51	4.24 ± 0.03
6t7	-1.70	-2.83 ± 0.21	1.64 ± 0.18	-6.00 ± 0.17	-3.17 ± 0.13	-4.81 ± 0.12
7t8	0.65	-5.17 ± 0.53	1.53 ± 0.45	2.24 ± 0.29	7.41 ± 0.65	5.88 ± 0.04
4t10	0.25	-4.41 ± 0.28	-1.23 ± 0.21	4.68 ± 0.21	9.09 ± 0.19	10.32 ± 0.09
9t10	-4.80	-9.83 ± 0.38	-3.93 ± 0.33	13.23 ± 0.19	23.06 ± 0.33	26.98 ± 0.04

TABLE 1: Experimental and calculated relative binding free energies for 12 neuraminidase purturbations, with the protein-ligand and solvent-ligand free energies used in their calculation. Also, relative solvation free energies calculated with the vacuum-ligand free energies used in their calculation. Experimental free energies are calculated with the formula $\Delta\Delta F = \Delta F_2 - \Delta F_1 = RTln(K_1/K_2)$ assuming that the ratio of the IC_{50}s is equal to the dissociation constants [1]. All calculated free energies in this table were found using NE-BY10 and the BAR estimator.

Perturb	Exp	$\Delta\Delta F_{bind}$	$\Delta F_{protein}$	ΔF_{water}
1t2	-1.63	1.81 ± 0.21	0.67 ± 0.18	-1.14 ± 0.12
1t3	-2.67	-5.53 ± 0.19	22.28 ± 0.07	27.81 ± 0.18
2t3	-1.04	-4.32 ± 0.3	22.21 ± 0.22	26.53 ± 0.19
3t4	-4.09	-3.84 ± 0.43	-9.61 ± 0.36	-5.77 ± 0.23
5t6	-3.45	-5.25 ± 0.22	21.04 ± 0.06	26.29 ± 0.22
5t7	-5.15	-7.52 ± 0.46	12.62 ± 0.36	20.15 ± 0.28
2t4	-5.13	-8.95 ± 0.28	10.13 ± 0.1	19.08 ± 0.26
2t9	0.08	-3.93 ± 0.4	-1.54 ± 0.16	2.39 ± 0.37
4t10	-1.70	-6.2 ± 0.64	4.08 ± 0.37	10.28 ± 0.52
6t7	0.65	-2.53 ± 0.24	-6.78 ± 0.14	-4.25 ± 0.19
7t8	0.25	-6.16 ± 0.4	-0.5 ± 0.25	5.66 ± 0.3
9t10	-4.80	-11.84 ± 0.78	12.86 ± 0.71	24.70 ± 0.33

TABLE 2: Experimental and calculated relative binding free energies for 12 neuraminidase purturbations, with the protein-ligand and solvent-ligand free energies used in their calculation. All free energies in this table are in kcal.mol^{-1} and were found with the RENE-BY10 protocol and the BAR estimator.

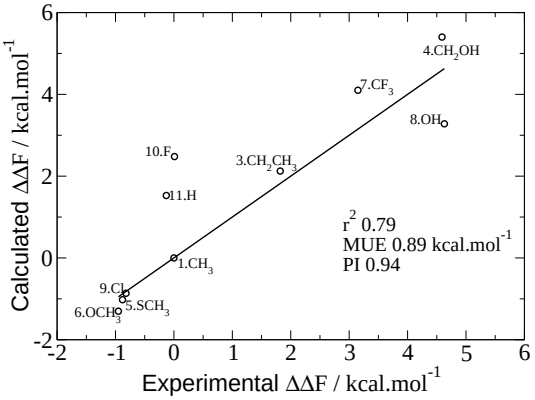

Figure 1. Comparison of RENE-BY10x3 calculated and experimental $\Delta\Delta F$s relative to ligand 1 for 10 COX2 ligands. The solid line represents perfect agreement with experimental values.

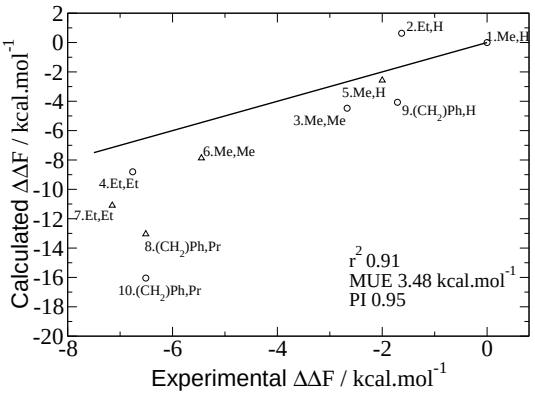

Figure 2. Comparison of calculated and experimental $\Delta\Delta F$s for 10 neuraminidase ligands using RENE-BY10x3. The solid line represents perfect agreement with experimental values.

References and Notes

(1) Cheng, Y. and Prusoff, W. H., *Biochem. Pharmacol.*, 1973, **22**(23), 3099–3108.