

Table I. Optimized Protein-Protein Binding Affinity Benchmark 1.0 of protein-protein complexes. Cross-validated 46 cases out of the 81 published in the Benchmark.

PDB ID (Complex)	Protein 1 (Receptor)	Protein 2 (Ligand)	K_d (M^{-1})	pK_d	Method ^a	pH	T (°C)	Primary Reference	Type
7CEI_A:B	Colicin E7 nuclease	Im7 immunity protein	5.0×10^{-15}	14.30	F	7.0	25	Keeble et al. (2006) Biochemistry 3243.	E
1DFJ_E:I	Ribonuclease A	Rnase inhibitor	5.9×10^{-14}	13.23	B	6.0	25	Vincentini et al. (1990) Biochemistry 8827.	E
1BVN_P:T	α -amylase	Tendamistat	9×10^{-12}	11.05	D	7.0	25	Piervincenzi and Chilkoti (2004) Biomol Eng 21:33.	E
1IQD_AB:C	Fab	Factor VIII domain C2	1.4×10^{-11}	10.85	D	5.0	25	Jacquemin et al. (1998) Blood 92:496.	AB
1MAH_A:F	Acetylcholinesterase	Fasciculin 2	2.5×10^{-11}	10.6	C	7.5	25	Marchot et al. (1993) J Biol Chem 12458.	E
1EZU_C:AB	D102N Trypsin	Y69F D70P Ecotin	8.0×10^{-11}	10.10	E	8.0	25	Yang and Craik (1998) J Mol Biol 1001.	E
1JPS_HL:T	Fab D3H44	Tissue factor	1.0×10^{-10}	10.00	D	7.4	25	Presta et al. (2001) Thromb Haem 3:379.	A
1IBR_A:B	Ran GTPase	Importin β	3.0×10^{-10}	9.52	C	7.4	25	Görlich et al. (1996) EMBO 5584.	O
1R0R_A:C	Subtilisin Carlsberg	OMTKY	3.4×10^{-10}	9.47	F	8.3	21	Horn et al. (2003) J Mol Biol 331:497.	E
1T6B_X:Y	Anthrax protective antigen	Anthrax toxin receptor	4.0×10^{-10}	9.40	D	7.4	25	Wigdelsworth et al. (2004) J Biol Chem 23349.	O
1KXP_A:D	Actin	Vitamin D binding protein	1.0×10^{-9}	9.00	C	7.5	25	McLeod et al. (1989) J Biol Chem 1260.	O
2FD6_HL:U	Urokinase plasminogen receptor antibody	Urokinase plasminogen activator receptor	1.0×10^{-9}	9.00	C	7.4	23	Appella et al (1987) J Biol Chem 4437.	A
2I25_N:L	Shark single domain antigen receptor	Lysozyme	1.0×10^{-9}	9.00	D	7.4	25	Dooley et al. (2006) PNAS 1846.	A
2B42_A:B	Xylanase	Xylanase inhibitor	1.07×10^{-9}	8.97	D	5.0	22	Fierens et al (2005) Febs J 5872.	E
2JEL_HL:P	Fab Jel42	HPr	2.8×10^{-9}	8.55	A	7.2	23	Smallshaw et al. (1998) J Mol Biol 280:765.	AB
1ML0_ABC:H	Hpr Kinase C-ter domain	HPr	3.1×10^{-9}	8.51	D	8.0	25	Lavergne (2002) Biochemistry 41(20):6218.	E

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1BJ1_HL:VW	Fab	vEGF	3.4×10^{-9}	8.47	D	7.4	25	Muller et al. (1998) Structure 6(9):1153.	AB
1KXQ_H:A	Camel VHH	Pancreatic α -amylase	3.5×10^{-9}	8.46	D	7.4	25	Lauwereys et al. (1998) EMBO 13:3512.	AB
1OPH_A:B	α -1-antitrypsin	Trypsinogen	5×10^{-9}	8.30	A	7.4	25	Stratikos and Gettins (1997) PNAS 94:453.	E
1M10_A:B	Von Willebrand Factor Domain A1	Glycoprotein IB- α	5.8×10^{-9}	8.24	D	7.4	25	Huizinga et al. (2002) Science 297:1176.	E
2AJF_A:E	ACE2	SARS spike protein receptor binding domain	1.62×10^{-8}	7.79	D	7.4	25	Li et al. (2005) EMBO 24:1634.	O
1IJK_A:BC	Von Willebrand Factor Domain A1	Botrocetin	2.3×10^{-8}	7.64	C	7.4	25	Miura et al. (2000) J Biol Chem 7539.	E
1H1V_A:G	Actin	Gelsonin	2.3×10^{-8}	7.64	B	7.0	20	Kinosian et al. (1996) Biochemistry 16550.	O
1E6J_HL:P	Fab	HIV-1 capsid protein 24	2.9×10^{-8}	7.53	D	7.4	25	Monaco-Malbet et al. (2000) Structure 8:1069.	A
2HLE_A:B	Ephrin B4 receptor	Ephrin B2 ectodomain	4.0×10^{-8}	7.40	F	7.8	25	Chrencik et al. (2006) J Biol Chem 28185.	O
1A2K_C:AB	Ran GTPase	Nuclear Transport Factor 2	1×10^{-7}	7.00	F	7.5	25	Chaillan-Huntington et al. (2000) J Biol Chem 5874.	O
2C0L_A:B	PTS1 and TRP region of PEX5	SCP2	1.09×10^{-7}	6.96	F	7.4	35	Stanley et al. (2006) Mol Cell 24:653.	O
1RLB_ABCD:E	Transthyretin	Retinol binding protein	1.34×10^{-7}	6.87	A	7.4	25	Noy et al. (1992) Biochemistry 31:11118.	O
1GRN_A:B	CDC42 GTPase	CDC42 GAP	3.88×10^{-7}	6.41	A	8.0	25	Hoffman et al. (1998) J Biol Chem 4392.	O
1E6E_A:B	Adrenoxin reductase	Adrenoxin	0.86×10^{-6}	6.07	D	7.4	25	Schiffler et al. (2004) J Biol Chem 34269.	E
1J2J_A:B	Arf1 GTPase	GAT domain of GGA1	1.1×10^{-6}	5.96	D	8.0	25	Shiba et al. (2003) Nat Struct Biol 10:386.	O
2BTF_A:P	Actin	Profilin	2.3×10^{-6}	5.70	A	7.0	25	Schlüter et al. (1998) J Cell Sci 111:3261.	O
1HE8_B:A	Ras GTPase	PIP3 kinase	2.5×10^{-6}	5.60	A	7.5	20	Pacold et al. (2000) Cell 103:931.	O
1B6C_A:B	FKBP Binding Protein	TGF β receptor	2.8×10^{-6}	5.55	D	7.4	25	Huse et al. (2001) Mol Cell 8:671.	O
1I4D_D:AB	Rac GTPase	Arfaptin	3×10^{-6}	5.52	F	8.7	22	Tarricone et al. (2001) Nature 411:215.	O

PDB ID (Complex)	Protein 1 (Receptor)	Protein 2 (Ligand)	K_d (M^{-1})	p K_d	Method ^a	pH	T (°C)	Primary Reference	Type
1GHQ_A:B	Complement C3	Epstein-Barr virus receptor CR2	4.3×10^{-6}	5.37	D	7.4	25	Sarrias et al. (2001) J Immun 167:1490.	O
2MTA_HL:A	Methylamine Dehydrogenase	Amicyanin	4.5×10^{-6}	5.35	G	7.5	25	Davidson et al. (1993) BBA 1144:39.	E
1E96_A:B	Rac GTPase	p67 Phox	6×10^{-6}	5.22	F	7.0	18	Lapouge et al. (2000) Mol Cell 6:899.	O
1Z0K_A:B	Rab4A GTPase	RAB4 binding domain of Rabenosyn	7.2×10^{-6}	5.14	D	7.5	25	Eathiraj et al. (2005) Nature 436:415.	O
1QA9_A:B	CD2	CD58	9×10^{-6}	5.05	D	7.4	37	van der Merwe et al. (1994) Biochemistry 10149.	O
1AK4_A:D	Cyclophilin	HIV capsid	1.60×10^{-5}	4.80	F	6.5	20	Yoo et al. (1997) J Mol Biol 269:780.	O
1GCG_B:C	GRB2 C-ter SH3 domain	GRB2 N-ter SH3 domain	1.68×10^{-5}	4.77	D	7.4	25	Nishida et al. (2001) EMBO 20:2995.	O
1WQ1_R:G	Ras GTPase	Ras GAP	1.7×10^{-5}	4.77	B	7.5	25	Eccleston et al. (1993) J Biol Chem 270:12.	O
2OOB_A:B	Ubiquitin ligase	Ubiquitin	6.0×10^{-5}	4.22	F	7.0	25	Kozlov et al (2007) J Biol Chem 357:87.	O
1AKJ_AB:DE	MHC Class I HLA-A2	T-cell CD8 coreceptor	1.26×10^{-4}	3.90	D	7.4	25	Wyer et al (1999) Immunity 10:219.	O
1S1Q_A:B	UEV domain	Ubiquitin	6.35×10^{-4}	3.19	D	7.2	20	Pornillos et al (2002) EMBO J 21:2397.	O

The protein-protein complexes used in this study are included in the Weng's protein-protein docking benchmark 3.0

(<http://zlab.bu.edu/benchmark/>).

^aMethods: (A) fluorescence spectroscopy; (B) Stopped-flow fluorimetry; (C) Radioligand binding (Competitive binding experiments); (D) Surface plasmon resonance; (E) Spectrophotometric assays; (F) Isothermal titration calorimetry (G) HPLC/UV absorption analysis