

Supplementary material

Towards prediction of functional protein pockets using blind docking and pocket search algorithms

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Contents

Supplementary Table I.

Performance of blind docking and pocket search using ligand-bound (holo) target conformations

Supplementary Table II.

Performance of blind docking and pocket search using primary-ligand-free (apo) target conformations

Supplementary Table III.

Influence of multiple ligands on blind docking

Supplementary Table IV.

Influence of hydrating water molecules on blind docking

Supplementary Table I. Performance of blind docking and pocket search using ligand-bound (holo) target conformations

Complex Codes		AutoDock4		EADock _{FF}		EADock _{SF}		SITEHOUND _C		SITEHOUND _{OP}		Q-SiteFinder		Pocket-Finder		PASS	
Protein	Ligand	Rank#	RMSD	Rank#	RMSD	Rank#	RMSD	Rank#	Distance	Rank#	Distance	Rank#	Distance (Å)	Rank#	Distance (Å)	Rank#	Distance
	(j)	/Total	(Å)	/Total	(Å)	/Total	(Å)	/Total	(Å)	/Total	(Å)	/Total	(Precision)	/Total	(Precision)	/Total	(Å)
1b70	1	1/26	1.0	1/14	0.6	1/13	0.6	9/218	0.8	2/263	2.6	3/10	0.7(87)	5/10	17.9(0)	15/31	0.9
1cea	1	1/2	1.2	1/4	1.1	1/4	1.0	1/23	0.6	2/27	3.6	1/10	0.7(92)	7/7	3.1(62)	1/1	0.4
1dy4	1	1/22	1.1	5/10	5.6	3/10	5.4	4/80	1.7	4/107	2.2	1/10	1.7(26)	7/10	10.2(0)	7/11	3.5
	2a	5/26	15.8	3/8	15.2	8/9	15.2	31/80	5.2	10/107	2.6	7/10	4.8(54)	9/10	10.8(0)	10/11	12.1
	2b	22/26	16.2	4/8	17.2	9/9	17.2	53/80	7.1	73/107	2.2	6/10	16.6(0)	7/10	23.0(0)	4/11	14.5
1e7a	1a	1/12	1.4	1/14	2.6	1/14	2.6	4/137	0.5	24/204	2.4	2/10	1.3(69)	5/10	1.0(38)	7/23	0.6
	1b	3/12	3.3	12/14	5.2	14/14	5.2	12/137	2.2	17/204	1.7	3/10	0.8(57)	9/10	20.8(0)	1/23	3.2
1eqg	1	1/10	1.0	2/9	11.9	2/10	11.7	5/112	1.9	3/141	1.0	3/10	1.6(87)	3/10	14.1(0)	1/16	3.2
	2a	2/26	14.4	6/8	31.6	5/8	31.6	111/112	4.4	93/141	3.8	7/10	11.8(0)	7/10	13.0(0)	16/16	12.8
	2b	6/26	12.6	8/8	18.0	7/8	17.9	55/112	3.0	18/141	0.8	5/10	11.7(0)	4/10	11.8(0)	13/16	11.8
	2c	2/26	16.1	6/8	35.5	5/8	35.5	53/112	6.0	93/141	5.0	7/10	10.6(0)	7/10	12.2(0)	15/16	11.8
	2d	15/26	15.8	2/8	24.1	1/8	23.9	88/112	2.9	27/141	1.8	6/10	20.4(0)	3/10	19.5(0)	16/16	19.9
	2e	21/26	14.1	2/8	31.3	1/8	31.2	44/112	11.5	29/141	8.7	6/10	23.8(0)	9/10	21.3(0)	16/16	29.8
	3a	30/40	3.2	9/10	18.6	9/12	18.6	7/112	2.1	80/141	5.1	3/10	11.2(0)	6/10	14.3(0)	8/16	2.1
	3b	3/40	15.6	2/10	19.8	2/12	19.8	98/112	5.1	13/141	5.6	7/10	18.5(0)	7/10	18.6(0)	6/16	13.7
	4	2/30	1.4	9/17	8.5	6/17	8.5	2/112	3.6	1/141	3.7	2/10	3.0(86)	2/10	13.0(36)	3/16	5.2
1h61	1	3/10	1.0	4/14	0.6	5/14	0.6	1/68	2.3	9/87	3.8	5/10	5.5(0)	1/10	5.6(17)	2/8	4.6
	2	1/53	1.5	3/10	5.3	1/8	4.4	3/68	6.3	9/87	3.6	1/10	2.3(36)	1/10	4.0(30)	1/8	2.9
1hvy	1	2/44	5.3	1/6	3.5	1/6	3.5	2/63	2.9	1/73	4.7	1/10	3.8(53)	1/10	4.6(25)	1/5	3.1
	2	8/25	3.4	1/13	4.0	2/12	4.0	5/63	3.7	1/73	4.8	1/10	5.4(39)	1/10	4.8(14)	1/5	6.6
1hz4	1	1/2	28.0	7/12	20.0	7/12	20.0	24/80	4.1	30/90	2.2	10/10	0.9(88)	3/10	3.0(39)	4/7	10.1
	2	19/34	5.1	7/10	8.8	5/10	8.8	5/80	1.2	1/90	2.1	1/10	0.7(44)	6/10	8.6(0)	3/7	1.7
1ivb	1	9/16	5.2	3/12	2.4	1/12	2.4	2/72	0.5	3/90	2.9	2/10	2.4(79)	2/10	1.4(53)	2/8	2.3
	2	3/32	8.7	2/11	13.0	1/11	13.1	8/72	8.7	58/90	2.6	9/10	8.0(0)	1/10	13.8(0)	3/8	9.4
1ju4	1	3/7	3.0	3/10	20.7	7/11	18.9	21/104	1.6	2/181	1.6	2/10	1.6(67)	9/10	13.6(0)	1/7	5.7
1lna	1	10/17	2.8	3/8	1.3	2/10	3.1	1/59	2.4	48/79	4.4	1/10	5.4(39)	1/10	3.5(39)	2/5	3.4
1m2z	1	1/4	0.4	1/14	0.3	1/13	0.3	1/62	0.3	3/70	3.3	1/10	0.2(85)	1/10	0.5(56)	1/6	1.1
	2a	11/14	15.1	6/6	16.1	6/6	16.1	20/62	4.4	38/70	3.6	4/10	14.1(0)	3/10	14.6(0)	4/6	14.6
	2b	13/14	15.4	6/6	14.8	6/6	14.8	20/62	7.5	38/70	7.2	4/10	14.3(0)	8/10	15.6(0)	4/6	14.8
	2c	13/14	2.2	6/6	4.5	6/6	4.5	8/62	2.2	47/70	2.8	4/10	2.9(54)	6/10	4.0(50)	4/6	2.6
1ngp	1	1/11	1.0	8/20	4.8	1/21	4.2	8/89	3.2	1/162	0.4	2/10	1.4(95)	5/10	1.8(52)	6/6	1.5
1pth	1	5/9	17.0	4/12	16.0	9/12	15.9	20/111	2.1	5/145	1.9	2/10	5.0(22)	10/10	11.9(0)	11/17	3.1
	2a	3/30	8.9	3/10	13.6	2/9	13.6	72/111	7.8	13/145	4.1	5/10	12.0(0)	5/10	12.9(0)	2/17	12.8
	2b	21/30	16.3	7/10	15.2	4/9	15.2	89/111	5.9	34/145	2.8	7/10	20.9(0)	3/10	18.5(0)	10/17	17.7
	2c	24/30	20.1	7/10	15.0	4/9	15.0	96/111	6.4	34/145	7.0	7/10	25.5(0)	3/10	19.5(0)	10/17	18.2
	2d	4/30	11.3	2/10	18.4	8/9	18.4	70/111	4.8	14/145	2.2	4/10	11.3(0)	4/10	11.0(0)	12/17	10.6
	3	20/38	3.8	16/18	12.7	13/19	12.7	2/111	2.0	98/145	4.5	10/10	4.0(45)	6/10	14.2(0)	2/17	1.9
	4	1/44	7.0	11/21	8.5	9/21	8.8	17/111	4.4	82/145	5.2	3/10	8.0(83)	2/10	6.1(39)	6/17	6.0
3pcn	1	3/11	4.6	5/17	5.1	3/16	1.8	26/65	7.5	80/109	4.1	1/10	1.8(68)	2/10	2.3(33)	1/9	1.5
3tpi	1	1/21	0.9	1/10	2.6	1/10	2.6	1/53	1.2	58/70	4.0	1/10	0.8(70)	1/10	1.9(34)	1/4	2.5

Notes to Supplementary Table I.

Rank #: serial number of the rank. Total: total number of ranks found. RMSD/Distance: the Root Mean Squared Deviation/distance between the docked and the crystallographic (measured) ligand structures/centers of ligand structures. Lists of all ranks can be found in a compressed file attached as Supplementary material.

Supplementary Table II. Performance of blind docking and pocket search using primary ligand-free (apo) target conformations

Complex Codes		AutoDock4		EADock _{FF}		EADock _{SF}		SITEHOUND _C		SITEHOUND _{OP}		Q-SiteFinder		Pocket-Finder		PASS	
Protein	Ligand (j)	Rank# /Total	RMSD (Å)	Rank# /Total	RMSD (Å)	Rank# /Total	RMSD (Å)	Rank# /Total	Distance (Å)	Rank# /Total	Distance (Å)	Rank# /Total	Distance (Å) (Precision)	Rank# /Total	Distance (Å) (Precision)	Rank# /Total	Distance (Å)
1b70	1	3/24	0.7	3/20	4.3	1/21	1.6	1/214	3.1	5/260	1.0	2/10	1.0(87)	8/10	17.3(0)	6/24	1.2
1cea	1	1/3	2.1	1/13	2.8	1/13	2.2	1/21	1.6	18/26	3.8	1/10	0.7(83)	5/10	2.7(58)	1/1	0.7
1dy4	1	4/29	3.5	5/12	5.6	5/12	5.6	3/83	0.8	11/101	3.6	1/10	1.0(49)	6/10	10.5(0)	1/10	6.8
1e7a	1a	1/15	12.8	12/12	12.4	9/12	12.4	26/134	2.2	24/143	1.0	6/10	1.6(68)	3/10	1.2(49)	14/21	2.8
	1b	3/15	5.9	3/12	11.6	7/12	12.2	5/134	7.2	103/143	1.7	10/10	5.0(11)	8/10	4.0(18)	7/21	4.7
1eqg	1	4/9	2.4	2/13	12.0	3/14	11.9	6/110	1.6	1/145	1.6	3/10	1.6(81)	3/10	15.0(0)	2/13	2.3
1h61	1	3/9	7.7	1/18	4.7	2/18	4.5	1/64	7.0	2/84	3.8	8/10	7.3(0)	1/10	6.2(16)	4/5	2.8
1hvy	1	4/37	4.6	16/24	4.2	9/24	4.2	26/59	4.7	30/72	6.1	2/10	7.4(19)	1/10	8.4(3)	1/5	6.0
1ju4	1	5/9	3.3	2/19	20.7	2/19	20.6	50/104	2.0	19/122	2.6	3/10	2.7(51)	1/10	2.6(18)	2/11	5.7
1lna	1	11/11	7.5	3/13	1.9	9/14	4.0	1/63	2.1	10/72	3.5	1/10	3.4(62)	1/10	3.8(32)	1/5	45.2
1ngp	1	1/12	4.6	1/14	0.9	3/15	5.0	7/85	1.9	1/115	1.5	2/10	1.0(91)	4/10	2.3(46)	6/7	1.8
1pth	1	5/11	16.7	6/20	12.0	11/21	9.1	6/110	2.7	1/141	2.6	3/10	2.8(42)	3/10	15.7(0)	2/11	3.4
3pcn	1	1/7	2.7	11/18	4.6	10/18	4.6	10/88	5.2	1/101	4.1	4/10	4.6(36)	2/10	3.4(27)	1/14	7.3

Notes to Supplementary Table II.

Rank #: serial number of the rank. Total: total number of ranks found. RMSD/Distance: the Root Mean Squared Deviation/distance between the docked and the crystallographic (measured) ligand structures/centers of ligand structures. Lists of all ranks can be found in a compressed file attached as Supplementary material.

Supplementary Table III. Influence of multiple ligands on blind docking

Protein	Reference ligand (j)	Interfering pocket (n≠j)	Rank # of docked reference ligand L _j (Distance between L _j and L _n , Å)
AutoDock4			
1dy4	1	2	17(3.2)
	2	1	1(4.8) 2(2.4) 13(3.7) 15(4.1)
1e7a	1	2	3(2.3) 9(1.6)
1eqg	1	4	8(4.8)
	2	1	20(3.4)
	2	4	4(4.4)
	3	2b	33(3.4)
	3	4	8(4.1) 9(4.2) 13(4.0) 20(4.0)
1h61	1	2	11(4.7) 12(4.6)
	2	1	1(0.7) 2(1.9) 4(4.9)
1hvy	1	2	6(2.6) 11(1.0) 15(3.0) 30(3.3)
1hz4	1	2	4(4.6) 5(2.3) 17(4.7)
1m2z	1	2c	1(2.5)
	2	1	2(1.2)
1pth	2	1	1(2.8) 2(1.9) 4(2.0) 6(0.5)
	3	4	15(4.0) 18(3.1)
	4	3	10(3.9) 12(3.9)
			9(4.7) 15(5.0) 29(4.8)
EADock			
1dy4	2	1	8(2.2)
1eqg	1	3a	2(4.2) 5(4.7)
	1	4	1(2.1)
	2	3a	6(2.2)
	2	4	2(3.8) 3(3.5) 7(2.2)
	3	4	1(2.0) 3(3.4) 4(3.1) 5(3.4) 6(2.2) 7(1.7)
1h61	1	2	1(3.2) 2(3.2)
	2	1	1(0.7) 2(2.5) 5(1.7) 6(3.2) 7(4.3) 8(2.8) 10(4.3)
1hvy	2	1	11(2.2) 13(3.3)
1ivb	2	1	11(2.9)
1m2z	2	1	1(0.5) 2(0.3)
1pth	2	4	2(4.6)
	3	4	1(2.2) 7(3.0) 10(2.8) 15(2.8)

Notes to Supplementary Table III.

Lists of all ranks can be found in a compressed file attached as Supplementary material.

Supplementary Table IV. Influence of hydrating water molecules on blind docking

Protein	Reference ligand (j)	Interfering water molecules				Total Count
		inside the pocket (Type 1)		at the bottom of the pocket (Type 2)		
		Count	Rank # of Pocket (Count)	Count	Rank # of Pocket (Count)	
AutoDock4						
1b70	1	16	2(2) 3(1) 4(1) 5(1) 8(1) 9(1)	5	2(1) 6(1) 7(1) 9(1)	21
1cea	1	2	2(2)	0		2
1dy4	1	51	2(7) 5(2) 6(2) 8(3) 9(2) 10(1)	6	2(1) 8(2)	57
	2	60	3(3) 4(4) 5(1) 6(2) 7(1) 8(6) 9(2) 10(3)	15	5(1) 7(2) 8(2) 9(2)	75
1e7a	1	4	2(1) 6(2) 7(1)	3	5(2) 10(1)	7
1eqg	1	12	2(3) 3(1) 4(1) 5(1) 6(1) 7(2) 9(2) 10(1)	0		12
	2	22	1(1) 2(2) 5(1) 6(1) 8(1) 9(1) 10(1)	7	1(1) 7(1)	29
	3	36	1(1) 3(1) 6(1) 7(2) 10(2)	4	10(1)	40
	4	24	5(1) 9(3) 10(1)	7	1(1) 9(1)	31
1h61	1	52	2(3) 3(1) 5(4) 6(4) 7(14) 8(10) 9(6) 10(10)	10	2(1) 3(1) 5(2) 7(1) 9(1) 10(4)	62
	2	170	1(1) 2(1) 3(1) 4(4) 6(1) 7(1) 8(3) 9(4) 10(1)	24	1(1) 2(1) 9(1)	194
1hvy	1	65	1(4) 2(1) 3(2) 4(2) 6(2) 7(2) 10(2)	14	4(1) 5(1) 9(1)	79
	2	49	1(1) 2(2) 3(2) 4(5) 6(3) 7(6) 8(1) 9(2) 10(1)	10	1(1) 2(1) 3(1) 8(1) 10(1)	59
1hz4	1	3	2(3)	6	1(3) 2(3)	9
	2	95	1(3) 2(2) 3(4) 4(3) 5(1) 6(3) 7(2) 8(4) 9(4) 10(5)	20	2(1) 3(1) 4(2) 5(1) 6(2) 8(1) 10(1)	115
1ju4	1	17	1(5) 2(5) 4(1) 5(3) 7(3)	5	2(2) 4(1) 5(1) 7(1)	22
1lna	1	33	1(2) 2(1) 3(3) 4(4) 5(3) 6(2) 7(1) 8(2) 9(2)	1	1(1)	34
1m2z	1	6	2(2) 3(2) 4(2)	2	4(2)	8
	2	16	3(2) 5(4) 7(2) 10(2)	0		16
1ngp	1	13	1(1) 2(1) 3(3) 4(1) 6(3) 7(1) 8(1) 9(1)	3	3(2) 6(1)	16
3pcn	1	12	1(1) 3(2) 5(2) 6(2) 7(2) 10(3)	11	3(3) 5(2) 6(1) 7(1) 8(2) 9(1) 10(1)	23
3tpi	1	32	3(2) 4(5) 5(4) 6(2) 8(3) 9(3) 10(3)	11	1(1) 2(2) 8(2) 10(2)	43
EADock_{FF}						
1b70	1	12	2(1) 3(1) 4(3) 5(1) 7(2) 8(1) 9(1) 10(1)	2	4(1) 9(1)	14
1dy4	1	21	1(2) 2(2) 3(3) 4(2) 6(3) 8(2) 9(5) 10(2)	6	3(2) 6(2) 9(2)	27
	2	12	1(2) 2(2) 3(2) 4(2) 5(1) 6(2) 7(1)	7	2(1) 5(4) 7(2)	19
1eqg	1	3	9(3)	2	7(2)	5
	3	2	2(2)	4	2(3) 6(1)	6
	4	4	1(1) 3(1) 5(1)	1	4(1)	5
1h61	1	39	1(1) 2(2) 5(2) 6(2) 7(6) 8(2) 9(2) 10(5)	10	7(2) 9(1) 10(3)	48
	2	26	2(1) 4(7) 5(2) 6(4) 7(1) 8(2) 9(8) 10(1)	15	3(1) 4(6) 5(1) 6(2) 8(2) 9(2) 10(1)	41
1hvy	1	10	1(2) 2(3) 4(1) 5(1) 6(3)	3	2(1) 3(1) 5(1)	13
	2	24	2(5) 3(2) 4(3) 5(5) 8(2) 9(1) 10(2)	7	5(1) 8(2) 10(2)	31
1hz4	1	29	1(2) 2(3) 3(2) 4(3) 5(5) 6(1) 8(2) 10(3)	11	2(2) 3(2) 4(4) 8(1) 9(1) 10(1)	40
	2	26	1(3) 2(4) 3(4) 4(2) 5(3) 6(4) 7(3) 8(2) 10(1)	8	2(3) 3(3) 4(1) 8(1)	34
1ju4	1	18	1(2) 2(3) 3(2) 4(1) 5(2) 6(3) 7(2) 8(1) 9(2)	5	5(1) 6(1) 7(2) 10(1)	23
1lna	1	8	1(1) 2(1) 4(1) 5(3) 6(1) 7(1)	3	1(2) 5(1)	11
1m2z	1	4	9(1) 10(2)	0		4
	2	1	6(1)	1	6(1)	2
3pcn	1	8	2(1) 3(3) 8(1)	8	2(3) 7(2)	16
3tpi	1	21	1(1) 2(1) 3(1) 4(4) 5(4) 6(4) 7(3) 9(1) 10(2)	7	1(1) 2(2) 3(2) 8(2)	28

Notes to Supplementary Table IV.

The first 10 ranks are tabulated in detail. Lists of all ranks can be found in a compressed file attached as Supplementary material.