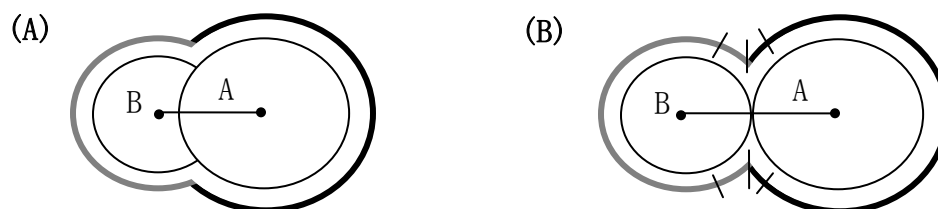
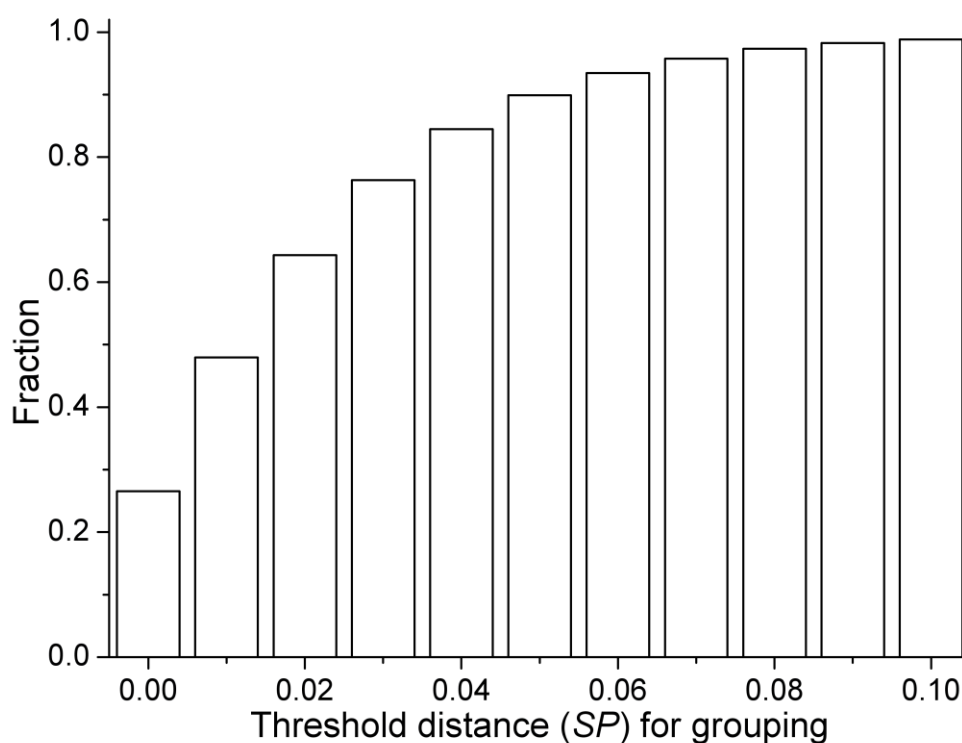


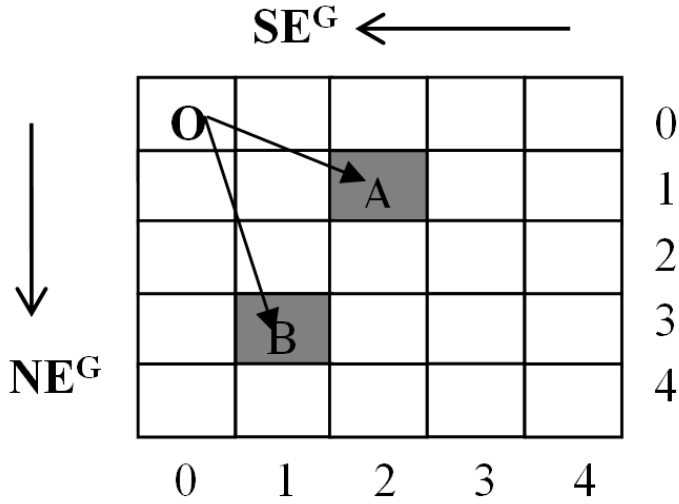
## Online Supplementary Material



**Figure S1. (A). ASA for atoms with steric clash. (B). ASA for atoms corrected for steric clash.** ASA in both of the figures is shown by thick circle. The additional ASA available to the atoms due to correction of the steric clash is shown by ticks on the bold line representing the ASA.

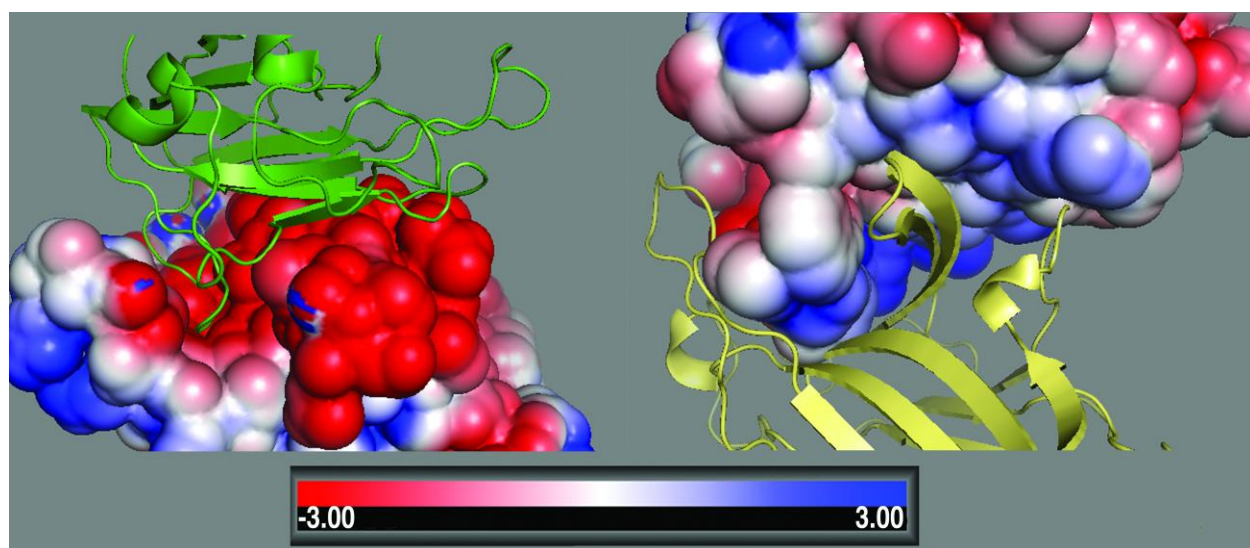


**Figure S2. Plot showing the cumulative distribution of occurrence of pairwise *SP* distances in groups of docking complexes calculated using 1Å RMSD threshold.** Note that about 85% of the cases are covered within a threshold *SP* value of 0.04.



**Figure S3. A 5×5 matrix depicting how  $NE^G$ ,  $SE^G$  are used for calculating score using Eq. 3.**

Origin O (0, 0) is located at the top-left corner of the matrix. If we move right,  $SE^G$  decreases, and  $NE^G$  increases if we move towards bottom. If the combination of  $NE^G$  and  $SE^G$  values are such that it occurs in cell A(1,2) The distance of cell A (1, 2) from O can be computed as  $\sqrt{(1-0) \times (1-0) + (2-0) \times (2-0)} = 2.24$ , and the score would be  $2.24 + 10 * SP^G$ , where  $SP^G$  is the lowest SP value for that group. Similarly if  $NE^G$  and  $SE^G$  values occur in cell B (3, 1) the score would be  $3.16 + 10 * SP^G$ . When calculating for unbound cases,  $NNE^G$  ( $NE^G$  per unit area) and  $NSE^G$  capacity ( $SE^G$  per unit area) is used for scoring in a 10 x 10 grid.



**Figure S4. Close view of the predicted interface from our docking method.** The structure of the complex is from PDB:2HLE, showing interaction of the EphB4 receptor with its preferred ligand, ephrinB2, in pathological forms of angiogenesis and in tumorigenesis. Note the groove binding mode of interaction and the compatible colors (blue↔red) suggesting a favorable interaction between positive and negatively charged surfaces.

**Table S1. Parameter and values used in solvation energy calculation<sup>1</sup>**

Atom Type	$\Delta\sigma$ (cal Å <sup>-2</sup> mol <sup>-1</sup> )
Carbon	16
Charged Nitrogen of Arg, Lys	-50
Charged Oxygen of Asp, Glu	-24
Rest Nitrogen and Oxygen	-6
Sulfur	21

**Table S2. Ranking of best near native quaternary structure output by various predictive docking methods**

PDB*  Target $IA$ ( $\text{\AA}^2$ )  Unbound:Unbound	Our method			ZDOCK  $L_{\text{RMSD}}$  $R_{\text{Rank}}^{++}$ $I_{\text{RMSD}}$ ( $\text{\AA}$ ) $F_{\text{NAT}}$	GRAMMX  $L_{\text{RMSD}}$  $R_{\text{Rank}}^{++}$ $I_{\text{RMSD}}$ ( $\text{\AA}$ ) $F_{\text{NAT}}$	PATCHDOCK  $L_{\text{RMSD}}$  $R_{\text{Rank}}^{++}$ $I_{\text{RMSD}}$ ( $\text{\AA}$ ) $F_{\text{NAT}}$	FIREDOCK  $L_{\text{RMSD}}$  $R_{\text{Rank}}^{++}$ $I_{\text{RMSD}}$ ( $\text{\AA}$ ) $F_{\text{NAT}}$											
	With interface size	Without interface																
	filter	size filter																
	$L_{\text{RMSD}}$  $R_{\text{Rank}}^{++}$ $I_{\text{RMSD}}$ ( $\text{\AA}$ ) $F_{\text{NAT}}$	$L_{\text{RMSD}}$  $R_{\text{Rank}}^{++}$ $I_{\text{RMSD}}$ ( $\text{\AA}$ ) $F_{\text{NAT}}$																
Unbound-Unbound cases (24)																		
1AVX <u>AB</u> (792)	>100	-	-	17	9.8	0.4	1	9.9	0.4	>100	-	-	>100	8.7	-	1	9.2	-
1QQU <u>A</u> :1BA7 <u>B</u>					8.1			8.4						4.7			2.9	
1BRCE <u>I</u> (657)	60	7.3		3	6.3		>100	-	-	>100	-	-	>100	15.9		1	6.7	
1BRA <u>A</u> :1AAP <u>B</u>		5.2	0.5		4.4	0.8								3.9	-		1.6	-
1BUH <u>AB</u> (662)	>100	-	-	>100	-	-	7	8.8	0.3	>100	-	-	>100	-	-	>100	5.9	0.6
1HCL:1DKS <u>A</u>								9.0									4.1	
1BVN <u>PT</u> (1111)	3	9.6					1	4.1	0.5	22	8.9	0.5		8.9			7.7	
1PIG:1HOE		10.0	0.1	>100	-	-		4.0			7.8		74	3.3	-	6	3.5	-

PDB*	Our method						ZDOCK			GRAMMX			PATCHDOCK			FIREDOCK		
Target <i>IA</i> (Å <sup>2</sup> )	With interface size			Without interface														
Unbound:Unbound	filter			size filter														
1CGIEI (1026)	3	9.5	0.3	43	7.6	0.4	33	7.1	0.4	15	5.0	0.4	>100	-	-	10	4.1	-
2CGAB:1HPT		7.1			5.8			5.4			4.5						2.0	
1CSEEI (744)	1	9.0	0.1	>100	-	-	>100	-	-	7	1.4	0.8	>100	-	-	2	5.8	-
1SCDA:1ACBI		7.7									0.8						1.7	
1DFJEI (1291)	3	7.7	0.5	>100	-	-	1	4.8	0.7	>100	-	-	>100	-	-	>100	-	-
9RSAB:2BNH		6.0						3.8										
1J2JAB (605)	20	7.0	0.5	1	7.7	0.2	1	9.8	0.2	56	7.4	0.4	>100	-	-	26	7.0	0.3
1O3YA:1OXZA		6.5			7.5			9.6			7.0						6.9	
1JLTAB (1426)	3	8.2	0.4	>100	-	-	2	7.3	0.3	1	3.8	0.4	18	6.7	0.4	5	5.8	0.4
1VPIA:2IOUE		8.8						6.9			3.5		18	6.8		5	4.6	
1K9OIE (914)	>100	-	-	43	8.8	0.2	>100	-	-	>100	-	-	>100	-	-	>100	-	-
1SEKA:3TGJE					6.6													
1KXPAD (1670)	9	7.7	0.5	>100	-	-	1	6.5	0.6	7	5.4	0.6	15	4.9	0.4	1	4.4	0.6
1IJJB:1KW2B		5.3						4.0			3.2		15	3.4			3.1	

PDB*	Our method						ZDOCK			GRAMMX			PATCHDOCK			FIREDOCK		
Target <i>IA</i> (Å <sup>2</sup> )	With interface size			Without interface														
Unbound:Unbound	filter			size filter														
1LW6 <u>E</u> I (853)	1	3.4	0.8	3.5	10	0.8	1	2.0	0.9	1.9	1	0.9	-	-	-	-	-	-
2SICE:1TM1 <u>I</u>		2.2		2.6				1.5		1.7								
1MA9 <u>A</u> B (1786)	14	6.6	0.4	>100	-	-	4	3.1	0.4	>100	-	-	>100	-	-	>100	-	-
1J78 <u>A</u> :1IJ <u>B</u>		5.4		2.7														
1PPE <u>E</u> I (844)	1	1.6	0.9	9.9	27	0.2	1	3.2	0.6	3.3	1	0.7	3	10.0	-	1	3.6	-
1BTP:1LU0 <u>A</u>		1.7		9.6				3.3		3.2		4.4		1.2				
1R0R <u>E</u> I (704)	51	9.7	0.4	>100	-	-	>100	-	-	9.0	5	0.5	>100	-	-	9	3.3	0.7
1SCNE:2GKR <u>I</u>		7.3			6.5	2.7												
1UDIE <u>I</u> (1011)	1	3.3	0.7	>100	-	-	69	3.6	0.8	6.4	19	0.4	8	4.2	-	5	3.6	-
1UDH:2UGI <u>B</u>		3.3			3.5	6.0		2.1		1.6								
1UGHE <u>I</u> (1096)	10	5.2	0.6	>100	-	-	14	6.8	0.4	7.0	6	0.2	42	5.5	-	1	4.7	-
2SSPE:1UDI <u>I</u>		4.6			6.2	7.1		2.5		2.4								
1XD3 <u>A</u> B (1140)	3	9.6	0.2	>100	-	-	7	7.9	0.4	7.1	43	0.2	>100	-	-	>100	-	-
1UCH:1YJ1 <u>A</u>		9.1			5.3	7.8												

PDB*	Our method						ZDOCK			GRAMMX			PATCHDOCK			FIREDOCK		
Target <i>IA</i> (Å <sup>2</sup> )	With interface size			Without interface														
Unbound:Unbound	filter			size filter														
1YVBA <u>I</u> (871)	70	7.4	0.7	>100	-	-	5	9.1	0.6	4	8.8	0.6	>100	-	-	2	7.2	0.7
2GHUA:1CEW <u>I</u>		3.5						4.3			3.7						3.8	
1Z0K <u>A</u> B (893)	>100	-	-	12	9.3	0.1	3	4.9	0.7	58	9.4	0.3	>100	-	-	1	8.7	0.5
2BME <u>A</u> :1YZM <u>A</u>					9.0			4.6			8.9						8.3	
2BTF <u>A</u> P (1031)	46	7.1	0.2	>100	-	-	>100	-	-	>100	-	-	>100	-	-	>100	-	-
1IJ <u>J</u> B:1PNE		7.6																
2HLE <u>A</u> B (1058)	2	5.5	0.5	>100	-	-	39	8.6	0.4	81	6.4	0.5	>100	-	-	31	4.2	0.4
2BB <u>A</u> A:1IKO <u>P</u>		5.0						6.9			5.4						3.9	
2SNIE <u>I</u> (814)	49	9.3	0.1	64	3.7	0.7	7	5.9	0.7	3	6.2	0.6	>100	-	-	13	11.2	-
1UBN <u>A</u> :2CI2 <u>I</u>		9.0			2.7			4.5			4.6						3.1	
2UUY <u>A</u> B (640)	>100	-	-	>100	-	-	>100	-	-	>100	-	-	>100	-	-	>100	-	-
1HJ9 <u>A</u> :2UUX <u>A</u>																		
Unbound-Bound cases (6)																		



PDB*	Our method						ZDOCK			GRAMMX			PATCHDOCK			FIREDOCK		
Target <i>IA</i> (Å <sup>2</sup> )	With interface size			Without interface														
Unbound:Unbound	filter			size filter														
1CT0 <u>E</u> I (523)	67	9.6	0.1	>100	-	-	>100	-	-	>100	-	-	39	9.6	0.2	>100	-	-
3SGB <u>E</u> :1CT0 <u>I</u>		9.5												8.6				
1E44 <u>B</u> A (1268)	1	1.2	1	71	1.3	0.9	1	1.3	1.0	1	0.5	0.9	1	0.8	0.9	1	1.2	1
2B5U <u>C</u> :1E44 <u>A</u>		1.2			1.2			1.2			0.5			0.8			1.1	
1JT <u>D</u> B (1090)	3	1.4	0.9	74	10.0	0.5	>100	-	-	>100	-	-	6	5.2	0.7	21	3.4	0.8
1JT <u>D</u> :1ZG4 <u>A</u>		1.2			7.6									3.4			2.3	
1JT <u>G</u> <u>C</u> B (1302)	1	1.7	0.8	>100	-	-	1	5.0	0.6	1	2.2	0.7	20	3.0	0.7	3	3.1	0.7
1ZG4 <u>A</u> :1JT <u>G</u> <u>B</u>		1.6						3.9			2.0			2.5			2.7	
1STF <u>E</u> I (895)	1	1.8	1.0	6	1.4	1.0	5	1.4	1.0	1	1.8	1.0	5	1.3	-	1	1.6	-
1PPN <u>A</u> :1STF <u>I</u>		1.5			1.4			1.1			1.3			0.4			0.4	
2TEC <u>E</u> I (780)	6	1.8	0.9	>100	-	-	>100	-	-	1	2.8	0.9	26	1.3	-	1	0.6	-
1THM <u>A</u> :2TEC <u>I</u>		1.5									1.9			0.4			0.3	

\*The four letter PDB code followed by the chain identifier (underlined) wherever present. ++ Acceptable accuracy according to Mendez

definition <sup>2</sup> is used. Cases italicized are directly taken from literature <sup>3</sup>.

— in some cases  $F_{\text{NAT}}$  values were not available.

**Table S3.** RPScore and Pair Score evaluation on the unbound data set according to acceptable accuracy Mendez definition<sup>2</sup>

PDB	With interface size filter								Without interface size filter							
	RPScore <sup>4</sup>				Pair Score <sup>5</sup>				RPScore <sup>4</sup>				Pair Score <sup>5</sup>			
	Rank	L <sub>RMSD</sub>	I <sub>RMSD</sub>	F <sub>NAT</sub>	Rank	L <sub>RMSD</sub>	I <sub>RMSD</sub>	F <sub>NAT</sub>	Rank	L <sub>RMSD</sub>	I <sub>RMSD</sub>	F <sub>NAT</sub>	Rank	L <sub>RMSD</sub>	I <sub>RMSD</sub>	F <sub>NAT</sub>
1AVX	-	-	-	-	-	-	-	-	1	5.1	2.7	0.7	1	9.4	7.9	0.4
1BRC	8	7.3	5.1	0.5	9	9.8	9.2	0.4	1	9.9	5.6	0.8	520	9.4	6.1	0.4
1BUH	-	-	-	-	-	-	-	-	3	9.9	9.8	0.3	24	8.8	8.8	0.3
1BVN	14	3.2	3.2	0.6	9	6.7	6.1	0.4	26	6.1	5.2	0.7	1	4.1	4.1	0.5
1CGI	24	9.5	7.2	0.3	79	9.7	7.3	0.2	5	4.8	4.0	0.4	119	7.5	7.9	0.1
1CSE	158	9.4	7.5	0.1	86	9.4	7.5	0.1	9344	2.8	1.8	0.7	6914	4.8	3.2	0.7
1CT0	78	9.6	9.5	0.1	61	9.6	9.5	0.1	7427	8.8	9.8	0.1	213	8.8	9.8	0.1
1DFJ	1	6.8	5.3	0.6	18	7.2	5.6	0.5	3	7.4	5.7	0.5	1	4.8	3.8	0.7
1E44	1	1	1.1	0.9	32	5	4.7	0.3	402	1.3	1.2	0.9	3076	9.5	9.0	0.2
1J2J	-	-	-	-	-	-	-	-	6	7.1	6.7	0.5	1	9.6	9.5	0.3
1JLT	4	5.8	5.6	0.3	15	8.2	7.9	0.2	46	5.6	5.4	0.3	472	8.5	8.9	0.1
1JTD	5	1.4	1.2	0.9	6	7.7	6.2	0.1	137	4.3	2.8	0.7	971	8.7	8.4	0.1
1JTG	9	1.7	1.5	0.8	29	9.7	7.7	0.4	148	2.8	2.4	0.7	650	9.9	8.9	0.1
1K9O	-	-	-	-	-	-	-	-	5	9.0	4.9	0.6	530	8.0	6.9	0.1
1KXP	107	7.7	5.3	0.5	149	7.7	5.3	0.5	265	7.7	5.3	0.5	104	8.5	6.5	0.3
1LW6	34	8.1	5.7	0.6	106	5.9	4.1	0.8	3	4.9	5.4	0.2	162	9.6	10.1	0.1
1MA9	1	3.5	2.9	0.5	114	5.8	2.9	0.5	1	9.4	5.5	0.3	301	9.7	6.3	0.1
1PPE	1	4	4	0.6	11	3.9	3.9	0.3	1	6.4	6.5	0.1	102	9.6	9.9	0.1
1R0R	27	3.1	2.6	0.7	20	6.5	4.7	0.5	3698	5.7	4.5	0.5	4535	9.0	7.3	0.3
1STF	39	3.4	2.2	0.8	7	3.4	2.2	0.8	3614	4.7	3.0	0.7	933	9.6	7.0	0.2
1UDI	35	4.9	4.6	0.6	12	9.8	8.9	0.3	110	9.6	9.4	0.2	146	3.6	3.5	0.8
1UGH	16	5.3	5.4	0.4	6	3.4	3.5	0.4	408	9.9	10.0	0.1	147	9.1	8.7	0.2
1XD3	2	8.2	7.5	0.3	9	8.2	7.5	0.3	1	4.8	5.1	0.3	177	7.0	6.5	0.2
1YVB	116	7.4	3.6	0.7	182	7.4	3.6	0.7	2508	9.5	4.5	0.6	26	7.7	3.4	0.7
1Z0K	-	-	-	-	-	-	-	-	129	6.5	6.3	0.6	113	7.6	7.0	0.1
2BTF	4	7.1	7.6	0.2	119	7.1	7.6	0.2	22	4.9	6.0	0.4	219	8.9	8.9	0.1
2HLE	17	5.8	4.7	0.5	22	5.5	4.5	0.5	3071	9.4	7.6	0.3	2121	9.9	7.8	0.3
2SNI	29	9.5	8.6	0.1	90	9.2	8.7	0.1	15	9.5	7.1	0.3	25	5.9	4.5	0.7
2TEC	276	1.8	1.5	0.9	197	1.8	1.5	0.9	9386	3.5	2.5	0.7	339	9.1	9.5	0.1
2UUY	-	-	-	-	-	-	-	-	1049	10.0	5.5	0.3	1182	9.8	11.4	0.1

**Table S4. RPScore and Pair Score re-ranking results for the top 50 ranked decoys from our method**

PDB ID	IA of target	Our method (with interface size filter)				RPScore <sup>4</sup>				Pair Score <sup>5</sup>			
		Rank <sup>++</sup>	L <sub>RMSD</sub>	I <sub>RMSD</sub>	F <sub>NAT</sub>	Rank <sup>++</sup>	L <sub>RMSD</sub>	I <sub>RMSD</sub>	F <sub>NAT</sub>	Rank <sup>++</sup>	L <sub>RMSD</sub>	I <sub>RMSD</sub>	F <sub>NAT</sub>
<b>1BVN</b>	<b>1111</b>	<b>3</b>	<b>9.6</b>	<b>10.0</b>	<b>0.1</b>	<b>2</b>	<b>3.2</b>	<b>3.2</b>	<b>0.6</b>	5	7.8	7.2	0.1
1CGI	1026	3	9.5	7.1	0.3	6	9.5	7.2	0.3	25	9.5	7.2	0.3
1CSE	744	1	9.0	7.7	0.1	38	9.4	7.5	0.1	31	9.4	7.5	0.1
<b>1DFJ</b>	<b>1291</b>	<b>3</b>	<b>7.7</b>	<b>6.0</b>	<b>0.5</b>	<b>1</b>	<b>6.8</b>	<b>5.3</b>	<b>0.6</b>	8	8.6	6.5	0.6
1E44	1268	1	1.2	1.2	1.0	1	1.0	1.1	0.9	21	5.0	4.7	0.3
1J2J	605	20	7.0	6.5	0.5	20	7.0	6.5	0.5	20	7.0	6.5	0.5
<b>1JLT</b>	<b>1426</b>	<b>3</b>	<b>8.2</b>	<b>8.8</b>	<b>0.4</b>	<b>3</b>	<b>5.2</b>	<b>5.4</b>	<b>0.4</b>	<b>2</b>	<b>8.2</b>	<b>7.9</b>	<b>0.2</b>
1JTD	1090	3	1.4	1.2	0.9	5	1.4	1.2	0.9	5	7.3	4.2	0.6
1JTG	1302	1	1.7	1.6	0.8	4	1.7	1.5	0.8	9	6.5	5.6	0.4
<b>1KXP</b>	<b>1670</b>	<b>9</b>	<b>7.7</b>	<b>5.3</b>	<b>0.5</b>	<b>2</b>	<b>4.8</b>	<b>5.1</b>	<b>0.3</b>	9	7.7	5.3	0.5
1LW6	853	1	3.4	2.2	0.8	12	8.1	5.7	0.6	25	5.9	4.1	0.8
<b>1MA9</b>	<b>1786</b>	<b>14</b>	<b>6.6</b>	<b>5.4</b>	<b>0.4</b>	<b>3</b>	<b>5.5</b>	<b>4.7</b>	<b>0.5</b>	47	6.5	3.9	0.4
1PPE	844	1	1.6	1.7	0.9	1	4.0	4.0	0.6	1	4.9	4.6	0.5
1STF	895	1	1.8	1.5	1.0	13	3.4	2.2	0.8	2	3.4	2.2	0.8
1UDI	1011	1	3.3	3.3	0.7	8	5.1	5.0	0.3	3	7.1	7.1	0.2
1UGH	1096	10	5.2	4.6	0.6	12	4.0	3.6	0.6	15	4.2	3.9	0.4
<b>1XD3</b>	<b>1140</b>	<b>3</b>	<b>9.6</b>	<b>9.1</b>	<b>0.2</b>	<b>1</b>	<b>8.2</b>	<b>7.5</b>	<b>0.3</b>	<b>2</b>	<b>8.2</b>	<b>7.5</b>	<b>0.3</b>
<b>2BTF</b>	<b>1031</b>	<b>46</b>	<b>7.1</b>	<b>7.6</b>	<b>0.2</b>	<b>4</b>	<b>7.1</b>	<b>7.6</b>	<b>0.2</b>	48	7.1	7.6	0.2
2HLE	1058	2	5.5	5.0	0.5	17	4.2	3.5	0.6	15	4.2	3.5	0.6
<b>2SNI</b>	<b>814</b>	<b>49</b>	<b>9.3</b>	<b>9.0</b>	<b>0.1</b>	<b>28</b>	<b>9.3</b>	<b>9.0</b>	<b>0.1</b>	<b>18</b>	<b>9.3</b>	<b>9.0</b>	<b>0.1</b>
2TEC	780	6	1.8	1.5	0.9	45	1.8	1.5	0.9	36	1.8	1.5	0.9

**Bold** case indicates improvement in rank by RPScore and **background shaded** indicates improvement by Pair Score.

<sup>++</sup>Acceptable accuracy according to Mendez definition <sup>2</sup> is used.

## ***References***

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