Supplementary Information

RLDOCK: A new method for predicting RNA-ligand interaction

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Born radii of atoms

In the RLDOCK model, we use a pairwise algorithm to calculate the Born radius B_i[1–6] for an atom i in the RNA-ligand complex, RNA alone, or ligand alone,

$$\frac{1}{B_i} = \frac{1}{a_i} - \frac{1}{2}\sum_j A_j \tag{S1}$$

and

$$A_j = (\frac{1}{L_{ij}} - \frac{1}{U_{ij}}) + (\frac{S_j^2 a_j^2}{4r_{ij}} - \frac{r_{ij}}{4})(\frac{1}{L_{ij}^2} - \frac{1}{U_{ij}}^2) + \frac{1}{2r_{ij}}\ln\frac{L_{ij}}{U_{ij}}, \tag{S2}$$

where

$$L_{ij} = \begin{cases} 1 & \text{if } a_i \geq r_{ij} + S_j a_j \\ \max(a_i, r_{ij} - S_j a_j) & \text{if } a_i < r_{ij} + S_j a_j \end{cases} \tag{S3}$$

and

$$U_{ij} = \begin{cases} 1 & \text{if } a_i \geq r_{ij} + S_j a_j \\ r_{ij} + S_j a_j & \text{if } a_i < r_{ij} + S_j a_j \end{cases} \tag{S4}$$

Here a_i and a_j denote the VDW radii of atoms i and j, respectively. r_{ij} is the distance between the atoms i and j. S_j is the structural scaling factor, and it equals to unity if there is no overlap between the atoms. Basically, $S_j < 1$ in the RNA-ligand complex, RNA alone, or ligand alone. The value of VDW radii and structural scaling factor for various atom species are listed in table S3.

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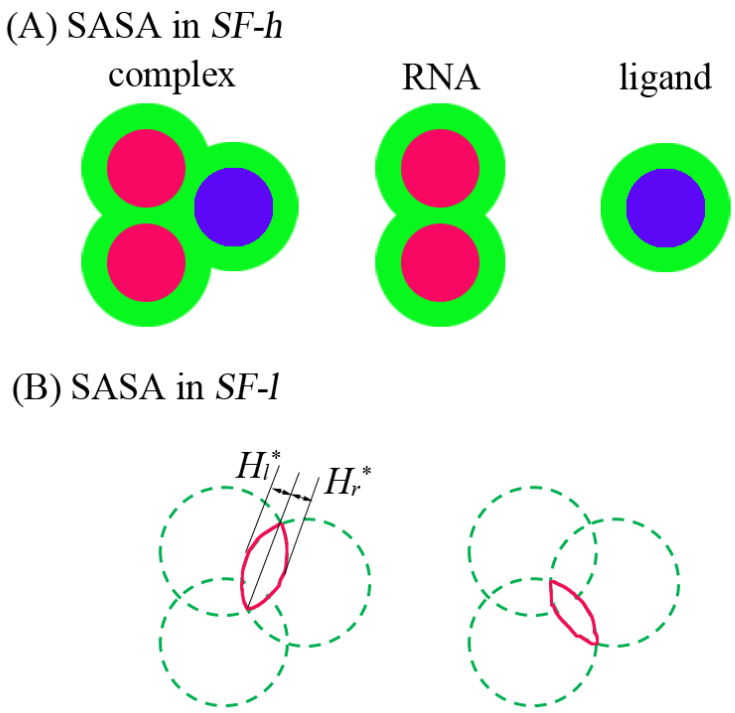

Figure S1: The 2D sketches of the solvent-accessible surface area (SASA) in the *SF-h* (A) and *SF-l* (B). (A) The red and blue spheres represent the atoms in RNA and ligand. The green areas are the water shell for the RNA-ligand complex, RNA, and ligand, respectively. The outlines of the green areas are the SASA in the 2D sketch. (B) In order to clearly show the calculations in *SF-l*, we use open spheres with dash line to represent the surface of the water shell and neglect the atoms at the same time. The red lines denote the 2D outlines of the penalty SASA for overlap of two water shells.

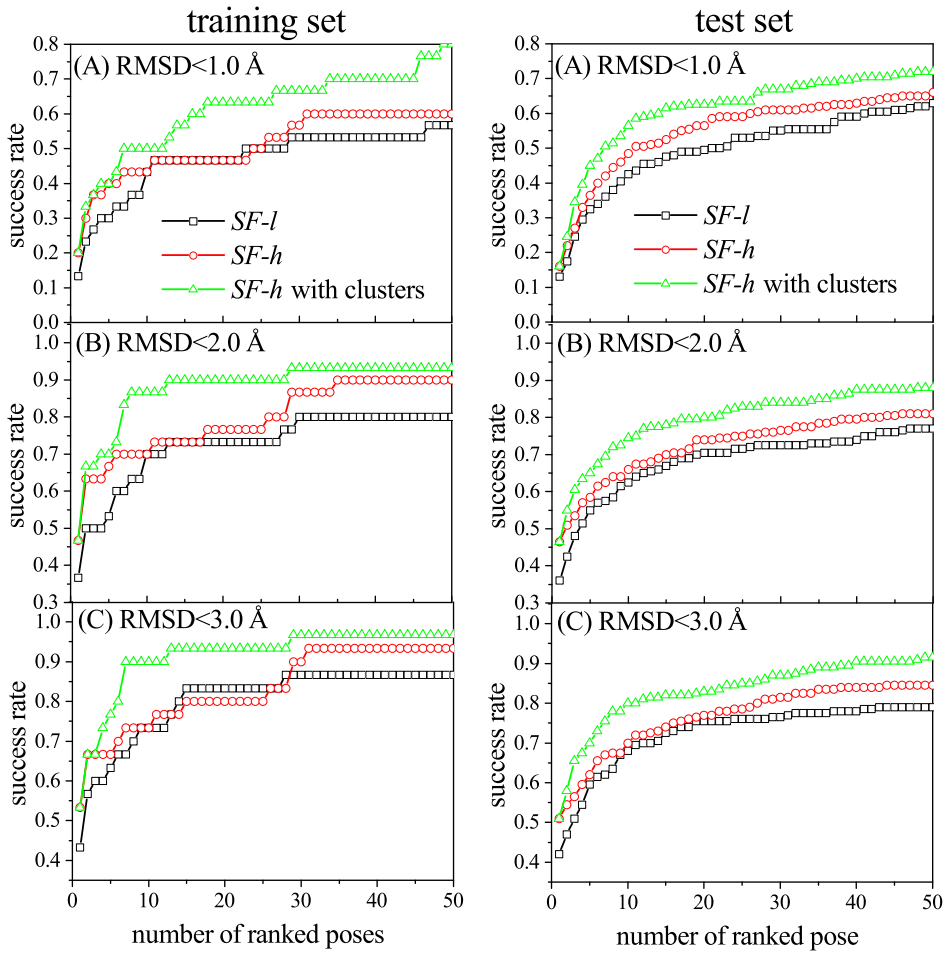

Figure S2: The success rate as a function of the number of the top-ranked poses with RMSD within 1 Å, 2 Å, and 3 Å for the training set and test set, respectively.

Table S1: List of PDB ID for RNA-ligand complexes in training and test sets

Training set					
1AKX	1ET4	1F27	1LVJ	1PBR	1J8G
1KOC	1QD3	1Y26	2ET4	2FD0	2BE0
2BEE	2F4T	2KTZ	2O3X	2XO1	3DIX
3FO4	3GES	3SUH	3SUX	3SKL	4LVW
4LW0	4FEJ	4FEO	4NYB	4KQY	5C45
Test set					
1AJU	1AM0	1ARJ	1BYJ	1DDY	1EHT
1EI2	1EVV	1F1T	1FMN	1FUF	1FYP
1I7J	1I9V	1J7T	1KOD	1LC4	1MWL
1NBK	1NEM	1NTA	1NTB	1O15	1O9M
1Q8N	1RAW	1TN1	1TN2	1TOB	1UTS
1UUD	1UUI	1XPF	1YKV	1YLS	1YRJ
1ZZ5	292D	2A04	2AU4	2B57	2EES
2EET	2EEU	2EEW	2ESI	2ESJ	2ET3
2ET5	2ET8	2F4S	2F4U	2FCX	2FCY
2FCZ	2G5K	2G5Q	2G9C	2GCV	2GDI
2GIS	2GQ5	2HOP	2JUK	2KD4	2KGP
2KU0	2KX8	2KXM	2L1V	2L8H	2MIY
2MXS	2N0J	2OE5	2OE8	2PWT	2QWY
2TOB	2W89	2XNW	2XNZ	2XO0	2YDH
2YIE	3B4B	3B4C	3C3Z	3C44	3C5D
3C7R	3D0U	3D2X	3DIG	3DIL	3DIM
3DIO	3DIY	3DIZ	3DJ0	3DJ2	3DS7
3DVV	3DVZ	3DW4	3DW6	3E5C	3E5E
3E5F	3F2Q	3F2T	3F4G	3F4H	3FO6
3FU2	3G4M	3GAO	3GCA	3GER	3GOG
3GOT	3GX2	3GX3	3GX5	3GX6	3GX7
3IQN	3IQR	3IRW	3K1V	3LA5	3NPN
3NPQ	3OWI	3OWZ	3Q3Z	3Q50	3RKF
3S4P	3SD3	3SKI	3SKR	3SKT	3SKW
3SKZ	3SLM	3SLQ	3TD1	3TZR	3WRU
4AOB	4B5R	4ERL	4F8U	4F8V	4FE5
4FEL	4FEN	4FEP	4FRG	4GPW	4GPX
4GPY	4JF2	4K32	4L81	4LVV	4LVX
4LVY	4LVZ	4LX5	4LX6	4NYA	4NYC
4NYD	4NYG	4OQU	4P20	4PDQ	4QK8
4QK9	4QKA	4QLM	4QLN	4RZD	4TS0
4TS2	4TZX	4TZY	4WCQ	4WCR	4XNR
4YAZ	4YB0	4YB1	4ZC7	5C7U	5C7W
5NDH	5NEF				

Table S2: List of results of RNA-ligand docking predictions for training and test sets[a]

PDB	exp.	charge	ligand[b]	top 1	top 3	top 200	success case[c]
Training set							
1AKX	nmr	GAS	ARG	15.73	4.97	2.12	—
1ET4	xray	AM1	CNC	0.98	0.98	0.98	0.98 (1)
1F27	xray	AM1	BTN	1.72	1.72	1.63	1.72 (1)
1J8G	xray	AM1	SPM	5.91	3.88	1.57	1.57 (7)
1KOC	nmr	GAS	ARG	3.46	3.46	1.07	1.07 (7)
1LVJ	nmr	GAS	PMZ	0.70	0.70	0.70	0.70 (1)
1PBR	nmr	GAS	PAR	1.21	1.21	1.21	1.21 (1)
1QD3	nmr	GAS	NEB	13.23	13.23	0.27	0.27 (29)
1Y26	xray	AM1	ADE	1.14	1.14	1.14	1.14 (1)
2BE0	xray	AM1	JS5	1.37	0.88	0.88	1.37 (1)
2BEE	xray	AM1	JS4	15.90	0.81	0.81	0.81 (2)
2ET4	xray	AM1	NMY	14.54	14.20	1.00	1.59 (4)
2F4T	xray	AM1	AB9	30.33	9.06	1.09	1.53 (58)
2FD0	xray	AM1	LIV	6.70	6.70	1.17	1.17 (8)
2KTZ	nmr	GAS	ISH	2.57	1.10	1.10	1.10 (2)
2O3X	xray	AM1	N30	15.17	1.35	1.10	1.35 (2)
2XO1	xray	AM1	N6M	3.06	0.99	0.99	0.99 (2)
3DIX	xray	AM1	LYS	59.16	10.80	1.23	1.23 (13)
3FO4	xray	AM1	6GU	0.81	0.81	0.81	0.81 (1)
3GES	xray	AM1	6GO	2.99	0.75	0.75	0.75 (2)
3SKL	xray	AM1	GNG	0.90	0.90	0.90	0.90 (1)
3SUH	xray	AM1	FFO	1.70	1.70	1.70	1.70 (1)
3SUX	xray	AM1	THF	34.63	34.54	1.04	1.04 (6)
4FEJ	xray	AM1	HPA	0.91	0.91	0.91	0.91 (1)
4FEO	xray	AM1	6AP	0.89	0.89	0.89	0.89 (1)
4KQY	xray	AM1	SAM	1.11	1.11	1.09	1.11 (1)
4LVW	xray	AM1	7DG	12.04	1.20	0.88	1.20 (2)
4LW0	xray	AM1	ADE	11.75	11.75	0.95	0.95 (7)
4NYB	xray	AM1	2QC	1.99	1.99	1.22	1.99 (1)
5C45	xray	AM1	51B	1.53	1.53	1.18	1.53 (1)
Test set							
1AJU	nmr	GAS	ARG	13.39	1.26	1.26	1.26 (2)
1AM0	nmr	GAS	AMP	0.88	0.88	0.88	0.88 (1)
1ARJ	nmr	GAS	ARG	10.89	10.56	1.54	1.87 (39)
1BYJ	nmr	GAS	C1A	1.56	1.56	1.21	1.56 (1)
1DDY	xray	AM1	B12	1.10	1.10	1.10	1.10 (1)
1EHT	nmr	GAS	TEP	3.13	1.10	0.81	1.10 (3)
1EI2	nmr	GAS	NMY	3.44	1.13	1.13	1.13 (2)
1EVV	xray	AM1	SPM	13.37	13.37	7.16	—
1F1T	xray	AM1	ROS	1.31	1.31	1.28	1.31 (1)
1FMN	nmr	GAS	FMN	1.21	1.21	1.21	1.21 (1)
1FUF	xray	AM1	SPM	4.87	1.40	1.25	1.40 (3)
1FYP	nmr	GAS	PAR	0.36	0.36	0.36	0.36 (1)

1I7J	xray	AM1	MPD	10.70	10.70	3.53	——
1I9V	xray	AM1	NMY	25.50	24.46	6.37	——
1J7T	xray	AM1	PAR	1.53	1.53	1.28	1.53 (1)
1KOD	nmr	GAS	CIR	5.26	5.26	0.70	0.70 (10)
1LC4	xray	AM1	TOY	16.57	16.42	0.66	0.66 (23)
1MWL	xray	AM1	GET	11.19	11.19	0.64	0.68 (5)
1NBK	nmr	GAS	GND	6.41	6.08	1.06	1.22 (11)
1NEM	nmr	GAS	NEB	0.41	0.41	0.41	0.41 (1)
1NTA	xray	AM1	SRY	15.84	2.63	1.35	1.99 (4)
1NTB	xray	AM1	SRY	1.55	0.99	0.99	1.55 (1)
1O15	nmr	GAS	TEP	3.73	3.25	1.54	1.80 (8)
1O9M	xray	AM1	AB6	21.32	13.11	1.28	1.28 (10)
1Q8N	nmr	GAS	MGR	0.20	0.20	0.20	0.20 (1)
1RAW	nmr	GAS	AMP	1.77	1.77	0.77	1.77 (1)
1TN1	xray	AM1	SPM	18.83	18.06	0.82	0.82 (40)
1TN2	xray	AM1	SPM	18.83	18.06	0.82	0.82 (40)
1TOB	nmr	GAS	TOB	8.51	8.51	0.24	1.55 (5)
1UTS	nmr	GAS	P13	10.12	9.22	1.34	1.34 (10)
1UUD	nmr	GAS	P14	6.21	2.44	1.16	1.16 (24)
1UUI	nmr	GAS	P12	13.46	12.44	4.27	——
1XPF	xray	AM1	SPM	5.43	5.43	1.96	1.96 (166)
1YKV	xray	AM1	DAI	1.53	1.19	1.19	1.53 (1)
1YLS	xray	AM1	DAI	1.54	1.42	1.42	1.54 (1)
1YRJ	xray	AM1	AM2	15.36	11.75	1.33	1.33 (66)
1ZZ5	xray	AM1	CNY	14.87	2.35	0.86	1.09 (28)
292D	xray	AM1	P24	10.19	9.01	3.94	——
2A04	xray	AM1	NMY	1.40	1.40	0.91	1.40 (1)
2AU4	nmr	GAS	GTP	19.72	18.65	0.57	0.57 (35)
2B57	xray	AM1	6AP	0.83	0.83	0.83	0.83 (1)
2EES	xray	AM1	HPA	26.39	3.95	1.14	1.14 (4)
2EET	xray	AM1	HPA	3.18	1.19	1.13	1.19 (2)
2EEU	xray	AM1	HPA	2.65	1.60	0.84	1.60 (2)
2EEW	xray	AM1	HPA	26.22	3.37	0.86	1.65 (6)
2ESI	xray	AM1	KAN	0.79	0.79	0.79	0.79 (1)
2ESJ	xray	AM1	LIV	11.11	11.11	1.17	1.88 (10)
2ET3	xray	AM1	LLL	15.97	1.33	1.19	1.33 (3)
2ET5	xray	AM1	RIO	0.99	0.99	0.99	0.99 (1)
2ET8	xray	AM1	XXX	22.20	1.46	1.20	1.46 (2)
2F4S	xray	AM1	XXX	18.76	8.90	1.03	1.75 (17)
2F4U	xray	AM1	AB6	25.32	19.51	1.22	1.22 (34)
2FCX	xray	AM1	XXX	1.09	1.08	1.08	1.09 (1)
2FCY	xray	AM1	NMY	9.70	0.98	0.98	0.98 (3)
2FCZ	xray	AM1	RIO	1.00	0.99	0.99	1.00 (1)
2G5K	xray	AM1	AM2	15.18	13.07	1.18	1.18 (70)
2G5Q	xray	AM1	AKN	16.01	1.02	1.02	1.02 (2)
2G9C	xray	AM1	3AY	25.97	25.42	0.70	1.60 (6)
2GCV	xray	AM1	MES	13.84	13.84	2.98	——

2GDI	xray	AM1	TPP	23.93	23.93	0.78	0.78 (148)
2GIS	xray	AM1	SAM	0.98	0.98	0.98	0.98 (1)
2GQ5	xray	AM1	GOL	21.03	20.38	2.90	—
2HOP	xray	AM1	218	6.81	3.10	1.34	1.34 (15)
2JUK	nmr	GAS	G0B	2.26	2.26	1.54	1.54 (6)
2KD4	nmr	GAS	PRL	1.69	1.69	1.47	1.69 (1)
2KGP	nmr	GAS	MIX	0.20	0.20	0.20	0.20 (1)
2KU0	nmr	GAS	ISI	1.68	1.68	0.97	1.68 (1)
2KX8	nmr	GAS	ARG	8.08	7.03	1.02	1.86 (23)
2KXM	nmr	GAS	RIO	0.98	0.98	0.98	0.98 (1)
2L1V	nmr	GAS	PRF	0.50	0.50	0.50	0.50 (1)
2L8H	nmr	GAS	VIB	0.69	0.69	0.69	0.69 (1)
2MIY	nmr	GAS	PRF	1.45	1.18	1.18	1.45 (1)
2MXS	nmr	GAS	PAR	3.84	2.98	1.25	1.25 (4)
2N0J	nmr	GAS	RIO	3.84	2.43	1.64	1.71 (12)
2OE5	xray	AM1	AM2	11.73	6.97	0.79	1.65 (55)
2OE8	xray	AM1	AM2	13.63	11.23	1.08	1.60 (12)
2PWT	xray	AM1	LHA	0.57	0.57	0.57	0.57 (1)
2QWY	xray	AM1	SAM	0.56	0.56	0.56	0.56 (1)
2TOB	nmr	GAS	TOB	1.02	1.02	0.80	1.02 (1)
2W89	xray	AM1	GOL	5.27	4.88	2.09	—
2XNW	xray	AM1	ZZR	2.37	2.37	0.49	0.49 (4)
2XNZ	xray	AM1	3AW	3.32	3.32	0.64	0.64 (6)
2XO0	xray	AM1	ZZS	4.05	3.42	1.00	1.40 (9)
2YDH	xray	AM1	SAM	1.15	1.15	1.15	1.15 (1)
2YIE	xray	AM1	FMN	13.15	12.52	0.93	0.93 (5)
3B4B	xray	AM1	GLP	35.47	27.87	1.29	1.29 (74)
3B4C	xray	AM1	GLP	31.33	30.40	0.90	0.90 (68)
3C3Z	xray	AM1	RIO	1.11	1.11	1.08	1.11 (1)
3C44	xray	AM1	PAR	1.42	0.83	0.83	1.42 (1)
3C5D	xray	AM1	LIV	1.91	1.91	0.92	1.91 (1)
3C7R	xray	AM1	NMY	1.33	1.33	1.02	1.33 (1)
3D0U	xray	AM1	LYS	1.63	1.63	1.40	1.63 (1)
3D2X	xray	AM1	D2X	30.70	30.70	1.08	1.43 (113)
3DIG	xray	AM1	SLZ	1.31	1.31	1.23	1.31 (1)
3DIL	xray	AM1	LYS	59.02	59.02	1.21	1.21 (8)
3DIM	xray	AM1	LYS	58.90	1.33	1.33	1.33 (2)
3DIO	xray	AM1	LYS	58.73	11.31	1.32	1.32 (6)
3DIY	xray	AM1	LYS	58.72	10.67	1.17	1.41 (4)
3DIZ	xray	AM1	LYS	58.72	11.03	1.39	1.80 (7)
3DJ0	xray	AM1	OLZ	1.55	1.41	1.11	1.55 (1)
3DJ2	xray	AM1	LYS	58.82	1.22	1.06	1.22 (3)
3DS7	xray	AM1	GNG	1.38	1.16	1.16	1.38 (1)
3DVV	xray	AM1	RIO	1.17	0.82	0.82	1.17 (1)
3DVZ	xray	AM1	GOL	23.71	4.14	2.84	—
3DW4	xray	AM1	GOL	3.97	3.97	2.62	—
3DW6	xray	AM1	GOL	3.98	3.98	2.62	—

3E5C	xray	AM1	SAM	1.13	1.13	1.13	1.13 (1)
3E5E	xray	AM1	SAH	1.40	1.27	1.27	1.40 (1)
3E5F	xray	AM1	EEM	1.21	1.21	1.21	1.21 (1)
3F2Q	xray	AM1	FMN	30.31	27.80	1.04	1.62 (20)
3F2T	xray	AM1	FMN	15.65	13.73	1.13	1.13 (7)
3F4G	xray	AM1	RBF	1.24	1.24	1.11	1.24 (1)
3F4H	xray	AM1	RS3	1.27	1.27	1.27	1.27 (1)
3FO6	xray	AM1	6GO	2.95	1.07	1.07	1.07 (2)
3FU2	xray	AM1	PRF	1.30	1.22	1.22	1.30 (1)
3G4M	xray	AM1	2BP	2.65	1.62	0.77	1.62 (2)
3GAO	xray	AM1	XAN	1.16	1.16	1.16	1.16 (1)
3GCA	xray	AM1	PQ0	4.84	2.60	0.59	0.59 (4)
3GER	xray	AM1	6GU	0.87	0.87	0.87	0.87 (1)
3GOG	xray	AM1	6GU	1.24	1.24	1.24	1.24 (1)
3GOT	xray	AM1	A2F	0.77	0.77	0.77	0.77 (1)
3GX2	xray	AM1	SFG	0.81	0.81	0.81	0.81 (1)
3GX3	xray	AM1	SAH	0.93	0.93	0.93	0.93 (1)
3GX5	xray	AM1	SAM	1.24	1.24	1.24	1.24 (1)
3GX6	xray	AM1	SAM	0.89	0.89	0.89	0.89 (1)
3GX7	xray	AM1	SAM	1.15	1.15	1.15	1.15 (1)
3IQN	xray	AM1	SAM	1.21	1.21	1.21	1.21 (1)
3IQR	xray	AM1	SAM	1.27	1.27	0.92	1.27 (1)
3IRW	xray	AM1	C2E	1.17	1.02	1.02	1.17 (1)
3K1V	xray	AM1	PRF	1.11	1.11	1.11	1.11 (1)
3LA5	xray	AM1	5AZ	3.28	3.17	0.55	0.55 (37)
3NPN	xray	AM1	SAH	0.69	0.69	0.69	0.69 (1)
3NPQ	xray	AM1	SAH	1.25	1.25	1.25	1.25 (1)
3OWI	xray	AM1	GLY	51.75	51.75	1.26	1.26 (114)
3OWZ	xray	AM1	GLY	46.87	46.87	1.13	1.13 (130)
3Q3Z	xray	AM1	C2E	1.18	1.18	1.18	1.18 (1)
3Q50	xray	AM1	PRF	1.26	1.26	1.14	1.26 (1)
3RKF	xray	AM1	DX4	1.38	1.38	1.01	1.38 (1)
3S4P	xray	AM1	JS6	0.97	0.97	0.97	0.97 (1)
3SD3	xray	AM1	FOZ	7.30	0.94	0.94	0.94 (3)
3SKI	xray	AM1	GNG	1.11	1.11	1.11	1.11 (1)
3SKR	xray	AM1	GNG	6.09	6.09	1.46	1.56 (8)
3SKT	xray	AM1	GNG	2.05	1.01	1.01	1.24 (2)
3SKW	xray	AM1	GNG	1.30	1.30	1.19	1.30 (1)
3SKZ	xray	AM1	GMP	29.33	27.41	1.19	1.19 (7)
3SLM	xray	AM1	DGP	29.01	27.17	0.80	1.37 (23)
3SLQ	xray	AM1	5GP	11.17	11.17	1.12	1.12 (13)
3TD1	xray	AM1	GET	0.70	0.70	0.70	0.70 (1)
3TZR	xray	AM1	SS0	5.70	1.26	1.26	1.26 (2)
3WRU	xray	AM1	SJP	17.20	11.35	1.16	1.42 (8)
4AOB	xray	AM1	SAM	0.77	0.77	0.77	0.77 (1)
4B5R	xray	AM1	SAM	1.05	1.05	1.05	1.05 (1)
4ERL	xray	AM1	LYS	1.23	0.91	0.91	1.23 (1)

4F8U	xray	AM1	SIS	13.53	0.68	0.68	0.68 (2)
4F8V	xray	AM1	SIS	14.44	14.44	0.88	1.18 (48)
4FE5	xray	AM1	HPA	2.66	1.19	1.19	1.19 (2)
4FEL	xray	AM1	HPA	0.91	0.91	0.91	0.91 (1)
4FEN	xray	AM1	HPA	1.22	1.22	1.21	1.22 (1)
4FEP	xray	AM1	6AP	0.92	0.92	0.92	0.92 (1)
4FRG	xray	AM1	I2A	27.25	27.01	1.17	1.17 (8)
4GPW	xray	AM1	6HS	16.16	0.86	0.82	0.86 (3)
4GPX	xray	AM1	6HS	11.64	11.64	0.66	0.66 (22)
4GPY	xray	AM1	6HS	0.63	0.63	0.63	0.63 (1)
4JF2	xray	AM1	PRF	0.57	0.57	0.57	0.57 (1)
4K32	xray	AM1	GET	1.04	1.04	1.04	1.04 (1)
4L81	xray	AM1	SAM	1.09	1.09	1.09	1.09 (1)
4LVV	xray	AM1	FFO	27.06	24.58	0.76	0.76 (7)
4LVX	xray	AM1	H4B	1.49	1.49	1.15	1.49 (1)
4LVY	xray	AM1	LYA	0.98	0.98	0.98	0.98 (1)
4LVZ	xray	AM1	6AP	12.17	11.76	1.23	1.23 (17)
4LX5	xray	AM1	29G	1.21	1.21	1.00	1.21 (1)
4LX6	xray	AM1	29H	0.65	0.65	0.65	0.65 (1)
4NYA	xray	AM1	2QB	2.77	2.77	1.16	1.16 (12)
4NYC	xray	AM1	SVN	4.35	2.20	0.77	0.77 (51)
4NYD	xray	AM1	HPA	3.37	1.62	1.54	1.62 (3)
4NYG	xray	AM1	VIB	3.75	3.75	2.14	—
4OQU	xray	AM1	SAM	1.09	1.09	1.09	1.09 (1)
4P20	xray	AM1	AKN	15.95	1.05	1.05	1.05 (3)
4PDQ	xray	AM1	NMZ	12.33	12.33	0.52	0.52 (12)
4QK8	xray	AM1	2BA	25.99	25.30	0.81	0.81 (28)
4QK9	xray	AM1	2BA	27.84	0.83	0.68	0.83 (3)
4QKA	xray	AM1	2BA	9.19	1.40	1.06	1.40 (3)
4QLM	xray	AM1	2BA	17.70	0.56	0.56	0.56 (2)
4QLN	xray	AM1	2BA	2.79	1.05	1.05	1.05 (2)
4RZD	xray	AM1	PRF	1.47	1.47	1.22	1.47 (1)
4TS0	xray	AM1	38E	1.07	1.07	1.07	1.07 (1)
4TS2	xray	AM1	38E	1.23	1.23	1.21	1.23 (1)
4TZX	xray	AM1	ADE	1.43	1.43	0.97	1.43 (1)
4TZY	xray	AM1	ADE	1.43	1.43	0.97	1.43 (1)
4WCQ	xray	AM1	GET	16.66	13.85	0.54	1.13 (37)
4WCR	xray	AM1	PAR	18.60	16.27	1.26	1.26 (25)
4XNR	xray	AM1	ADE	3.09	1.61	1.02	1.61 (2)
4YAZ	xray	AM1	4BW	1.16	1.16	1.16	1.16 (1)
4YB0	xray	AM1	C2E	1.00	1.00	1.00	1.00 (1)
4YB1	xray	AM1	4BW	0.83	0.83	0.83	0.83 (1)
4ZC7	xray	AM1	PAR	16.28	13.21	1.25	1.25 (63)
5C7U	xray	AM1	HPA	27.19	0.79	0.79	0.79 (2)
5C7W	xray	AM1	HPA	10.74	3.06	0.74	1.41 (16)
5NDH	xray	AM1	GAI	1.66	1.66	1.59	1.66 (1)
5NEF	xray	AM1	GAI	1.88	1.88	1.88	1.88 (1)

[a] In this table, the first column to the eighth column show the PDBID, experimental method, the method of partial charge assignment, the abbreviated ligand name, the RMSD of the top-ranked pose, the best RMSD in 3 top-ranked poses, the best RMSD in 200 top-ranked poses, and the RMSD of the first successful case (< 2Å), respectively.

[b] The abbreviation name of binding ligand. [c] The value with parenthesis is the ranked number of the success case.

Table S3: The value of the VDW radius[a] a and the structural scaling factor[b] S of various atom species

atom	O	P	H[c]	C	N	S	other atoms [d]
a	1.50	1.90	1.00	1.70	1.65	1.80	1.70
S	0.85	0.86	0.85	0.72	0.79	0.80	0.72

[a]The VDW radii (Å) are taken from http://www.rbvi.ucsf.edu/chimera/current/docs/UsersGuide/midas/vdwtables.html.

[b]The scaling factors for different types of atoms are taken from Ref. 5 in supplemental material.

[c]The hydrogen atoms are neglected in the RLDOCK model.

[d]For other atoms that have low possibility to appear in RNA-ligand complex, we use the value of atom C to replace them.

Table S4: The binding sites and the binding atoms for the training set[a]

PDB	RNA atoms	ligand atoms	number of sites	success rank	binding atom	distance (Å)	time (hours)
1AKX	638	11	157	143	C9	0.35	0.1
1ET4	747	90	244	5	N12	0.11	5.8
1F27	634	16	424	175	N12	0.18	0.6
1J8G	516	14	144	70	C4	0.18	0.2
1KOC	538	12	170	27	N11	0.31	0.1
1LVJ	662	23	435	10	C10	0.23	1.1
1PBR	572	42	411	128	C6	0.20	3.6
1QD3	615	42	432	4	C37	0.09	3.9
1Y26	1499	10	739	18	C4	0.16	0.7
2BE0	892	52	480	32	C9	0.08	4.7
2BEE	892	49	499	198	C11	0.16	4.0
2ET4	892	42	368	159	C11	0.29	2.5
2F4T	932	35	350	117	C22	0.23	3.4
2FD0	978	52	373	17	C1	0.32	4.8
2KTZ	800	23	336	167	C14	0.06	0.8
2O3X	892	31	343	118	C9	0.15	1.1
2XO1	1361	11	1227	67	C3	0.21	1.4
3DIX	3748	10	2929	207	C6	0.20	5.5
3FO4	1336	11	1299	80	C1	0.17	0.7
3GES	1422	12	1370	64	C11	0.11	1.1
3SKL	1413	19	1771	125	C5	0.09	4.2
3SUH	2173	34	932	2	N3	0.19	12.8
3SUX	2173	13	909	56	C2	0.11	1.3
4FEJ	1425	10	1177	78	O7	0.11	0.5
4FEO	1425	11	1206	6	C4	0.21	0.7
4KQY	2556	27	1785	20	O16	0.26	9.7
4LVW	1910	11	1030	113	C8	0.19	0.7
4LW0	1910	10	973	85	C2	0.31	0.5
4NYB	1673	13	1308	44	N10	0.22	1.2
5C45	2337	27	2287	146	N22	0.14	18.9

[a] The first column presents the PDB codes. The second and third columns show the number of heavy atoms in RNA and ligand. The forth to eighth columns show the number of candidate binding sites after the ball probe detects, the number of the ranked site for the successful global search, the name of the binding atom in the ligand which should be bound to the binding site, the distance between the success site and the closest atom in reference ligand, and the computational time of the global search on a PC with an Intel i7-4790 processor and 16 GB RAM.

Table S5: The prediction results of 51 cases containing multiple binding sites in crystal structures[a]

PDB	site 1	site 2	PDB	site 1	site 2
1I7J	—	—	1J7T	1.53(1)	1.79(8)
1LC4	0.66(23)	0.77(39)	1MWL	0.68(5)	0.64(7)
1NBK	1.22(11)	1.07(33)	1YRJ	1.33(66)	1.35(206)
2BE0	0.87(2)	1.37(1)	2BEE	0.80(2)	1.03(3)
2ESJ	1.59(25)	1.88(10)	2ET3	1.33(3)	1.26(36)
2ET4	1.59(4)	1.64(51)	2FCX	1.09(1)	1.08(2)
2FCY	1.35(5)	0.98(3)	2FCZ	1.00(1)	0.99(3)
2FD0	1.17(8)	1.43(93)	2G5K	1.18(70)	1.38(101)
2G5Q	1.02(2)	1.35(4)	2KD4	1.69(1)	1.47(4)
3C3Z	1.11(1)	1.53(2)	3C44	1.42(1)	1.59(3)
3C5D	1.91(1)	1.66(15)	3C7R	1.33(1)	1.90(35)
3D2X	—	1.43(113)	3DVV	1.17(1)	0.82(3)
3Q3Z	1.18(1)	—	3S4P	0.97(1)	1.93(6)
3TD1	0.70(1)	1.23(10)	3WRU	1.16(16)	1.42(8)
4F8U	0.68(2)	0.71(32)	4F8V	1.18(48)	1.85(67)
4GPW	0.82(5)	0.86(3)	4GPX	0.66(22)	0.77(74)
4GPY	0.63(1)	1.13(156)	4K32	1.04(1)	1.14(99)
4LVW	0.88(17)	1.20(2)	4LVX	1.49(1)	1.87(14)
4LVY	0.98(1)	1.81(9)	4P20	1.06(3)	1.36(4)
4QK8	0.82(28)	0.84(29)	4QK9	0.83(3)	0.67(15)
4QKA	1.40(3)	1.06(10)	4QLM	0.56(2)	1.21(74)
4QLN	1.05(2)	—	4WCQ	0.54(142)	1.13(37)
4YB0	—	1.00(1)	5NDH	1.75(2)	1.66(1)

PDB	site 1	site 2	site 3
2ESI	0.79(1)	1.76(7)	—
2PWT	0.57(1)	1.42(2)	—

PDB	site 1	site 2	site 3	site 4
1ZZ5	0.86(42)	—	1.09(28)	—
2A04	0.91(11)	—	1.40(1)	—
2ET5	0.99(1)	1.80(3)	1.73(72)	1.46(5)

[a] The value with parenthesis is the ranked number of the success case.

Table S6: RMSD of the top-ranked pose for various docking models[a]

PDB	LigandRNA	Drugscore^{RNA}	DOCK6	LigandRNA +DOCK6	rDOCK (2004)	original Drugscore^{RNA}	MORDOR	RLDOCK
1AJU	2.30	5.60	5.30	2.30	—	7.32	4.51	13.40
1AM0	4.60	5.70	**1.40**	**1.70**	**1.80**	2.86	**0.85**	**0.88**
1BYJ	6.80	**2.00**	7.40	6.80	**1.80**	**1.99**	5.37	**1.57**
1EHT	4.50	3.80	**0.30**	**1.40**	3.60	**1.95**	**1.25**	3.13
1EI2	6.90	6.90	5.90	6.60	—	**0.84**	3.23	3.44
1F1T	**1.10**	**1.20**	**1.20**	**1.20**	—	—	**0.31**	**1.31**
1F27	6.70	**1.50**	6.90	7.00	—	4.28	**0.96**	**1.72**
1FJG	6.30	**0.30**	**0.30**	**0.50**	—	—	—	—
1FMN	2.90	2.20	2.90	2.90	**0.80**	**1.55**	**1.42**	**1.21**
1FYP	5.10	5.10	3.20	**1.20**	—	**1.45**	2.54	**0.36**
1HNW	8.30	5.00	5.00	8.20	—	—	—	—
1J7T	8.60	2.60	**1.10**	8.60	—	3.80	**1.05**	**1.53**
1KOC	2.30	2.10	2.60	2.20	2.70	**1.61**	**1.62**	3.46
1KOD	**1.90**	5.10	5.30	**2.00**	3.20	**1.87**	**1.98**	5.26
1MWL	6.80	**0.70**	9.20	7.50	—	9.00	**1.00**	11.19
1NBK	3.00	**1.50**	2.60	2.10	—	8.20	3.57	6.41
1NEM	9.30	**1.10**	**0.70**	**1.20**	8.70	**0.66**	**0.95**	**0.41**
1PBR	6.20	8.30	8.50	8.90	**1.80**	**1.05**	**1.64**	**1.21**
1Q8N	**1.30**	**1.10**	7.70	**2.00**	—	3.65	**1.90**	**0.20**
1TOB	2.60	3.50	4.80	2.30	9.80	**1.52**	2.63	8.51
1UTS	4.40	9.50	4.20	9.70	—	11.04	4.90	10.12
1UUD	6.40	5.40	5.40	5.40	—	**1.59**	8.85	6.21
1UUI	5.60	**1.50**	**1.50**	**1.50**	—	5.56	8.35	13.46
1XBP	8.10	**1.80**	8.90	8.10	—	—	—	—
1XPF	3.40	6.60	6.60	3.30	—	—	5.26	5.43
1Y26	**0.50**	30.50	**0.50**	**0.50**	—	—	**0.54**	**1.14**
2BE0	10.70	9.50	3.50	10.70	—	—	**1.97**	**1.37**
2BEE	9.30	4.50	9.30	9.20	—	—	2.01	15.90
2ET8	**0.80**	4.60	**0.70**	**0.80**	—	—	**1.56**	22.20
2F4U	**1.00**	3.00	**1.90**	**1.00**	—	—	**2.00**	25.32
2FCZ	**0.60**	7.20	**0.90**	**0.60**	—	—	**1.74**	**1.00**
2FD0	4.60	3.50	3.50	4.60	—	—	**0.95**	6.70
2G5Q	**0.70**	**0.50**	**1.60**	**1.40**	—	—	—	16.01
2GDI	**1.80**	2.10	2.10	2.10	—	—	—	23.99
2O3X	**0.70**	2.40	2.10	**0.80**	—	—	—	15.17
2OE5	**0.70**	15.70	5.60	**0.70**	—	—	**1.82**	11.73
2OGN	8.60	2.10	8.50	8.60	—	—	—	—
2PWT	7.60	4.30	11.00	2.10	—	—	—	**0.57**
2TOB	**1.00**	**1.00**	**1.50**	**1.50**	**1.50**	**1.45**	**0.85**	**1.02**
3D2X	**1.60**	6.90	**1.90**	**1.90**	—	—	—	29.74
3GX2	**0.60**	5.30	4.70	**0.70**	—	—	—	**0.81**
3SUX	**0.40**	**0.40**	**0.50**	**0.40**	—	—	—	34.63
total	15/42	13/42	15/42	20/42	5/10	12/21	20/31	16/38

[a] The data of other models are taken from the Ref. (7)

Table S7: the best RMSD in the three top-ranked poses for various docking models[a]

PDB	LigandRNA	Drugscore^{RNA}	DOCK6	ligandRNA +DOCK6	RLDOCK
1AJU	2.30	5.10	4.90	2.30	**1.26**
1AM0	4.30	3.00	**1.20**	**1.40**	**0.88**
1BYJ	6.70	**1.80**	**1.10**	6.70	**1.57**
1EHT	**1.40**	3.80	**0.30**	**0.50**	**1.10**
1EI2	6.60	6.70	5.90	6.60	**1.13**
1F1T	**1.10**	**1.10**	**1.20**	**1.10**	**1.31**
1F27	6.70	**1.50**	6.90	6.70	**1.72**
1FJG	**0.50**	**0.30**	**0.30**	**0.50**	—
1FMN	2.90	**2.00**	2.20	2.90	**1.21**
1FYP	5.00	5.10	3.20	**0.70**	**0.36**
1HNW	8.20	5.00	5.00	5.00	—
1J7T	8.20	**1.10**	**1.10**	8.20	**1.46**
1KOC	**2.00**	2.10	2.60	**1.90**	3.46
1KOD	**1.90**	5.10	5.30	**2.00**	5.26
1MWL	6.80	**0.40**	**0.40**	6.80	**0.68**
1NBK	2.10	**1.50**	2.50	**1.50**	**1.22**
1NEM	5.40	**1.00**	**0.70**	**1.10**	**0.41**
1PBR	6.20	**0.50**	8.50	6.20	**1.21**
1Q8N	**1.30**	**1.10**	7.60	**2.00**	**0.20**
1TOB	2.20	3.50	4.80	2.30	8.51
1UTS	4.40	8.10	3.90	4.50	9.22
1UUD	3.40	5.40	5.40	5.40	2.44
1UUI	**1.40**	**1.50**	**1.40**	**1.40**	12.44
1XBP	6.90	**1.70**	8.80	8.10	—
1XPF	3.30	5.40	6.50	3.30	5.43
1Y26	**0.40**	14.40	**0.40**	**0.40**	**1.14**
2BE0	10.70	3.50	3.50	10.70	**0.88**
2BEE	9.30	3.00	9.30	9.20	**0.81**
2ET8	**0.80**	4.60	**0.70**	**0.70**	**1.46**
2F4U	**1.00**	2.90	**1.90**	**1.00**	19.51
2FCZ	**0.60**	4.80	**0.90**	**0.60**	**0.71**
2FD0	4.60	3.50	3.50	3.50	**1.17**
2G5Q	**0.60**	**0.50**	**1.60**	**0.60**	**0.89**
2GDI	**1.70**	2.10	2.10	**1.90**	23.93
2O3X	**0.70**	**0.90**	**1.70**	**0.70**	**1.35**
2OE5	**0.70**	13.60	5.60	**0.70**	6.97
2OGN	8.60	**2.00**	7.90	8.60	—
2PWT	7.60	3.40	11.20	2.10	**0.57**
2TOB	**1.00**	**1.00**	**1.50**	**1.50**	**1.02**
3D2X	**1.60**	2.30	**1.90**	**1.90**	29.20
3GX2	**0.60**	5.30	**0.70**	**0.60**	**0.81**
3SUX	**0.40**	**0.40**	**0.40**	**0.40**	34.54
total	19/42	18/42	18/42	23/42	23/38

[a] The data of other models are taken from the Ref. (7)