Supplementary Materials

Table S1. Aptamer-proteins complexes. A list of nucleotides forming polar contacts (N), amino acids forming polar contacts (PC), amino acids within 4 Å vicinity of atoms in polar contacts (4 Å) and amino acids in 4Å vicinity to nucleotides forming ≥3 polar contacts (HS). If more than one conformation of complex was reported, the alternative variants of interfaces are divided with dashes.

4pdb				4wb2				5hrt				4r8i				3agv			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
A4	S53	P51	A112	Oa4	R684	R684	K695	Omg7	R244	R244	K316	Og5	R18	N17	S21	G4	K340	A339	K340
G6	K54	A52	K113	Ou5	E688	E688	H696	G8	R246	G245	K467	Ou6	K19	R18	Q23	Uft6	G341	K340	G341
C7	Q80	S53	A114	Og6	S697	H696	S697	Omg9	E247	R246	F469	Oc7	I20	K19	R24	G7	Q342	G341	R344
C16	A114	K54	S132	3ka7	K701	S697	K701	A10	K316	E247		Oc9	S21	I20		-----	R344	Q342	Y373
C17	S130	I55	K133	Ou21	D705	V698	D705	Omg15	R455	K248		Ou10	V22	S21		G4	Y373	R344	L398
A24	S132	E58	T146	Og25	R708	K701	R708	Omc20	L458	K316		Oc11	Q23	V22		G7	G402	Y373	G402
A26	K133	Q80	G147	Og26	N710	Y704	R721	T21	S465	Y317		Og22	R24	Q23			-----	L398	
U27	T146	K113	G148	3ka28	R718	D705	V722	T22	K467	L384		Oa26	S63	R24			K340	D401	
	G147	A114		3ka30	R721	R708	T723	T23		A454		Og27	H66	L25			Q342	G402	
	E149	D115		Oc31	T723	V709	I724	C28		R455				W59			R344	S403	
		S130		Og32	-----	N710		T29		K456				S63			Y373	F404	
		T131		Og39	K695	F711				P457				H66			G402	-----	
		S132		-----	S697	E713				L458				Q70				A339	
		K133		Oa4	K701	R718				D459								K340	
		V135		Ou5	D705	R721				S465								G341	
		T146		Og6	R708	V722				G466								Q342	
		G147		Ou21	R721	T723				K467								R344	
		G148		3ka28	T723	I724				F469								Y373	
		E149		Og29		G725												L398	
				Oc31		-----												D401	
				Og32		Y694												G402	
				Og39		K695												S403	
						H696													
						S697													
						V698													
						K701													
						D705													
						R708													
						R721													

						V722 T723 I724													
4ni7				4ni9				5uc6				3zh2				5hto			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
G5 Omg6 Duz7 2JU12 A13 Duz14 G29 Duz30	R16 R24 K27 Q28 R30 S118 K128 K171 Q175	R16 L19 R24 D26 K27 Q28 R30 Y31 A114 S118 V121 K128 K171 Q175	K27 Q28 R30 Y31 D34 M117 S118 V121	2JU12 A13 Duz14 G29 ----- G5 Omg6 Duz7 2JU12 A13 Duz14	R16 K27 Q28 R30 S118 ----- R24 K27 Q28 R30 Y31 S118 Q124 K128	R16 L19 R24 D26 K27 Q28 R30 Y31 A114 S118 V121 F125 K128 ----- R24 D26 K27 Q28 R30 Y31 A114 M117 S118 V121 Q124 F125 K128	K27 Q28 R30 Y31 D34 M117 S118 V121	85y7 G11 85y14	R16 S61 D64 D65 K67 I68 W113	R16 K60 S61 S62 K63 D64 D65 A66 K67 I68 T69 W113 E114 T115	K60 S61 K63 D64 D65 A66 K67 I68 W113 T115	C6 G7 G8 T9 A10 G11 G19 A22 ----- C6 G7 G8 T9 A10 G11 G19 A22 ----- G4 C6 G7 G8 T9 A10 G11 A18 A22	D35 I36 K84 A85 G87 K88 S89 D90 H232 ----- D35 I36 K84 A85 G87 K88 S89 D90 H232 ----- D35 I36 K84 A85 G87 K88 S89 D90 K91 H232	F34 D35 I36 V37 A80 F82 K84 A85 P86 G87 K88 S89 D90 H232 ----- F34 D35 I36 V37 A80 F82 K84 A85 P86 G87 K88 S89 D90 H232 ----- F34 D35 I36 V37 A80	K84 A85 P86 G87 K88 S89 D90	G10 T12 G23 ----- T8 G10 T12 G23	K44 T83 ----- K44 G81 T83	S12 G13 M14 K44 F82 T83 K84 L98 ----- S12 G13 M14 K44 T79 A80 G81 F82 T83 K84 L98	-----

														K84 A85 P86 G87 K88 S89 D90 K91 W93 H232							
5hru				4m6d				4m4o				4zbn				1ooa			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
T8 G10 A11 T12 G23	D35 K44 G81 T83 Y238	G11 S12 G13 M14 F34 D35 K44 T79 A80 G81 F82 T83 K84 L98 Y238	-----	U30 A31 A35 G36 C39 ----- U30 A31 A35 G36 ----- U30 A31 A35 G36	K1 C6 E7 R14 R128 ----- K1 R5 C6 E7 R128 ----- K1 R5 E7 R128	K1 R5 C6 E7 L8 A9 A10 R14 G126 C127 R128 L129 ----- K1 R5 C6 E7 L8 A9 A10 R125 C127 R128 L129 ----- K1	R5 C6 E7 A10 G126 C127 R128	U30 A31 A35 G36	K1 R5 E7 R128	K1 R5 C6 E7 A10 R125 G126 C127 R128 L129	R5 C6 E7 A10 G126 C127 R128	Duz10 Duz11 Duz18 C21 C22 G23 Duz24 Duz27 ----- Duz10 Duz11 Duz18 C21 C22 G23 Duz24 Duz27	S17 S19 W21 K32 R59 R69 R103 ----- S17 S19 W21 K32 R59 R69 R103	F12 D16 S17 V18 S19 V20 W21 V22 D30 Ile31 K32 G33 F54 R59 R69 H84 R103 ----- F12 D16 S17 V18 S19 V20 W21 V22	-----	G8 A9 A11 C12 G14 A17 G19 U20 U21 G22 G23 C24 G25 ----- G8 A9 A11 C12 U15 A17 G19 U20 U21 G22 G23 C24	R54 R56 Y57 E60 P62 S63 H64 K77 K144 K145 K241 K249 R305 ----- R54 R56 Y57 E60 S63 K77 K144 K145 K241	R54 R56 Y57 E60 G61 P62 S63 H64 G65 K77 H141 V142 T143 K144 K145 K241 K249 R305 ----- R54 R56 Y57 E60 G61 P62 S63	Y57 H141 T143 K144

						R5 C6 E7 A10 R125 C127 R128 L129								D30 Ile31 K32 G33 F54 R59 R69 H84 R103		G25		H64 G65 K77 H141 T143 K144 K145 K241	
4hqx				4hqu				3dd2				5do4				4i7y			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
Duz1 Ubi8 Upe17 A19	V39 R73 K80 F84	L38 V39 W40 R73 K80 K81 P82 I83 F84 K85	L38 V39 W40 R73 I75 F84	Duz1 Duz8 Upe17 A19	V39 R73 K80 F84	L38 V39 W40 R73 K80 K81 P82 I83 F84 K85	L38 V39 W40 R73 I75 F84	Cfl6 A7 A8 A9 Cfl11 G13 A15 G16 Uft17	H91 R101 R126 Q131 R165 K169 D178 N179 R233 K236 K240	H91 P92 R93 D100 R101 R126 E127 A129 L130 Q131 V163 E164 R165 P166 K169 D178 N179 M180 H230 R233 L234 K235 K236 W237 I238 K240	H91 R93 R101 N179 R233 L234 K236 W237	A7 A8 Cfz11 G13 A14 A15 G16	D34 R36 R98 Q131 R170 K174 D183 N184 R245 W249	D34 G35 R36 D97 R98 A127 L130 Q131 A132 V168 E169 R170 P171 K174 D183 N184 M185 H242 R245 L246 K247 K248 W249 I250	H87 R89 R98 N184 R245 L246 K248 W249	T9 T18 G20 G21 G23 T24 G25 C27	P92 R93 N95 R97 R101 R126 K169 H230 R233 W237	I90 H91 P92 R93 Y94 N95 R97 E97A N98 R101 R126 K169 H230 R233 W237 V241	P92 R93 Y94 N95 W96 R97 R101
6eo6				6eo7				3qlp				5cmx				4dii			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS

77y4				8dt4				G2				T11				T3			
G5	T432	R425	I371	T12	R433	H429	I371	T4	R75	H71	I24	T12	R75	H71	R75	T4	H71	I24	T74
T12	R433	H429	H429	T13	Y434	S430	H429	T12	Y76	S72	T74	G13	Y76	S72	Y76	G5	R75	H71	R75
T13	Y434	S430	R433	G14	E435	T432	R433	T13	E77	T74	R75	T21	E77	T74	R77A	T13	Y76	T74	Y76
G14	E435	T432	E435		R436	R433	Y434	G14	R77A	R75	Y76		R77A	R75			R77A	R75	R77A
	R436	R433	R436		N437	Y434	E435		N78	Y76	E77		Y117	Y76			N78	Y76	N78
	N437	Y434	N437		Y477	E435	R436		Y117	E77	R77A			E77			Y117	R77A	I79
	Y477	E435	I438			R436	N437			R77A	N78			R77A				N78	
		R436	Y477			N437	Y477			N78	I79			N78				I79	
		N437				Y477				Y117	Y117			Y117				Y117	
		I438																	
		Y477																	
4dih				4lz4				4lz1				3hxq				3hxo			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
T3	R75	H71	I24	T4	R75	H71	I24	T3	R75	H71	I24	C7	R524	R524	Q625	C7	E626	K599	Q625
T4	Y76	S72	R75	T12	Y76	S72	R75	T4	Y76	S72	R75	A8	Q625	K599	Q628	A8	Q628	Q625	Q628
G5	E77	T74	E77	T13	E77	T74	E77	G5	E77	T74	E77	G9	E626	F603	R629	T10	R629	E626	R629
T13	R77A	R75	R77A	G14	R77A	R75	R77A	T13	R77A	R75	R77A	T10	Q628	Q625	S631	G21	R632	P627	S631
G14	Y117	Y76	N78	-----	N78	Y76	N78	G14	N78	Y76	N78	G11	R629	E626	R632	T22	N633	Q628	R632
		E77	I79	T4	Y117	E77	I79		Y117	E77	I79	G21	R632	P627	F655	C24	Y637	R629	F655
		R77A	Y117	T12	-----	R77A	Y117			R77A	Y117	T22	N633	Q628	H656	G25	P655	M630	H656
		N78		T13	R75	N78				N78		C24	R636	R629	A657	G26	A657	S631	A657
		I79		G14	Y76	Y117				Y117		G25	Y637	M630	N658	T27	L659	R632	N658
		Y117			E77	-----						G26	P655	S631	L659	G28	K660	N633	L659
					R77A	H71						T27	A657	R632	K660	C29		Y637	K660
					N78	S72						G28	L659	N633		T31		P655	
					Y117	T74						C29	K660	R636		C32		H656	
						R75						C30		Y637				A657	
						Y76						C32		P655				N658	
						E77								H656				L659	
						R77A								A657				K660	
						N78								N658				Q661	
						Y117								L659				L664	
														K660					
														Q661					
5msf				1u1y				6msf				6gn7				6evv			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
C2	K43	K43	V29	C2	K43	K43	V29	C8	T45	T45	V29	G8	R75	I24	R75	T10	R75	H71	R75
C10	T45	T45	K43	C10	T45	T45	K43	A9	S47	C46	K43	T10	Y76	H71	Y76	G13	Y76	S72	Y76
A11	S47	C46	T45	A11	S47	C46	T45	-----	T59	S47	T45	G13	E77	S72	R77A	G18	E77	T74	R77A

----- C10 A11	R49 T59 K61 E63 Y85 N87 ----- K43 T45 S47 T59 E63 Y85	S47 V48 R49 S51 K57 T59 I60 K61 E63 R83 Y85 N87 ----- K43 T45 C46 S47 V48 T59 I60 K61 E63 R83 Y85	C46 S47 T59 K61 E63 Y85 N87		R49 T59 K61 E63 Y85 ----- K43 T45 S47 T59 K61 E63 Y85	S47 V48 R49 S51 K57 T59 I60 K61 E63 R83 Y85 N87 ----- K43 T45 C46 S47 V48 T59 I60 K61 E63 R83 Y85	C46 S47 T59 K61 E63 Y85 N87	U7 C8 A9	E63 Y85 N85 ----- K43 T45 S47 T59 Y85	V48 T59 I60 K61 E63 R83 Y85 N87 ----- K43 T45 C46 S47 V48 T59 I60 K61 E63 R83 Y85	C46 S47 T59 K61	G18 T19 G20	R77A	T74 R75 Y76 E77 R77A N78 I79	N78 I79	T19 G20	R77A Y117	R75 Y76 E77 R77A N78 Y117	

Table S2. Data from literature (ΔG_b) and calculated data (other parameters) for the set of aptamer-protein complexes that were used to find correlations: changes in Gibbs free energy during binding (ΔG_b) and characteristics of interfaces: number of polar contacts (PC), number of amino acids (AA) and hydrophobic amino acids (HP AA) within 4 Å vicinity of PC, mean length of sidechain (SC) in AA and HP AA, total atoms in AA and HP AA, proportion of HP AA, number of aliphatic and aromatic carbon atoms ('carbons') in AA and HP AA, proportion of 'carbons' in HP AA versus total AA, mean number of 'carbons' in AA and HP AA. Hydrogen atoms were not counted. Results for alternative conformations were averaged.

PDB id	$-\Delta G_b$, kJ/mol	Number of polar contacts	Number of AA	Mean length of sidechain	Number of HP AA	Mean length of SC of HP AA	% of HP AA	Total atoms in AA	Total atoms in HP AA	Carbons in AA	Carbons in HP AA	% of carbons in HP AA	Mean carbons in AA	Mean carbons in HP AA
4pdb	36.9	16	19	3.05	5	2.40	26.3	58	12	38	12	31.6	2.00	2.40
4wb2	63.5	20	15.5	4.74	5	4.58	32.5	73.5	23	47.5	22	45.9	3.10	4.38
5hrt	50.2	14	18	4.39	6	4.50	33.3	79	27	55	26	47.3	3.06	4.33
4r8i	52.5	18	13	4.92	4	5.25	30.8	64	21	41	20	48.8	3.15	5.00
3agv	40.5	7	10.5	3.75	3.5	4.67	33.2	39.5	16.5	26.5	16	59.4	2.51	4.50
4ni7-4ni9	57.6	13.7	13.3	4.90	4.7	4.40	35.2	65.3	20.7	42	19.3	46.0	3.15	4.12
5uc6	46.4	9	14	4.21	3	5.00	21.4	59	15	39	14	35.9	2.79	4.67
3zh2	42.2	18.5	14.5	3.86	7	3.93	48.3	56	27.5	44	27	61.5	3.03	3.86
5hto-5hru	44.4	5.3	12.3	3.64	5.3	4.95	42.1	45	26.7	37.7	25	64.1	3.05	4.65
4m6d	41.3	10	10.7	4.10	5.3	2.31	49.7	43.3	12.3	25.3	10.3	40.2	2.38	1.92
4m4o	44.0	7	10	4.50	4	2.25	40.0	45	9	24	7	29.2	2.40	1.75
4zbn	57.6	11	16.5	4.73	7	5.29	42.4	78	37	55	36	65.5	3.33	5.14
1ooa	47.2	18.5	16.5	4.51	2.5	5.08	15.0	74.5	12.5	50	11.5	22.9	3.03	4.67
4hqx	50.9	7	10	5.30	6	5.17	60.0	53	31	45	30	66.7	4.50	5.00
4hqu	61.0	7	10	5.30	6	5.17	60.0	53	31	45	30	66.7	4.50	5.00
3hxq-3hxo	52.6	25	20	4.72	7	4.07	35.1	94.5	28.5	58.5	26.5	45.4	2.92	3.79
5msf	48.8	9.5	13.5	4.29	4	4.25	30.0	58	17	38	15.5	41.4	2.82	3.88
1u1y	51.7	10	13	4.30	4	4.25	31.5	56	17	37.5	15	40.6	2.90	3.75
6msf	48.2	7	11	4.41	4	4.25	36.4	48.5	17	32	15	47.1	2.91	3.75

3dd2	50.6	18	26	5.00	9	4.00	34.6	130	36	82	34	41.5	3.15	3.78
5do4	67.9	14	24	4.54	9	3.78	37.5	109	34	68	32	47.1	2.83	3.56
4i7y	42.6	16	16	5.81	5	5.60	31.3	93	28	57	26	45.6	3.56	5.20
6eo6	52.2	15	11	5.55	3	6.67	27.3	61	20	37	18	48.6	3.36	6.00
6eo7	54.6	13	9	5.56	2	8.00	22.2	50	16	30	14	46.7	3.33	7.00
3qlp	43.4	12	9	5.56	2	8.00	22.2	50	16	30	14	46.7	3.33	7.00
5cmx	52.8	9	9	5.56	2	8.00	22.2	50	16	30	14	46.7	3.33	7.00
4dii	44.5	11.5	9.5	5.58	4	6.00	42.1	53	24	35	22	62.9	3.68	5.50
4dih	43.3	11	10	5.40	3	6.67	30.0	54	20	34	18	52.9	3.40	6.00
4lz4	41.4	12.5	9	5.56	2	8.00	22.2	50	16	30	14	46.7	3.33	7.00
4lz1	42.1	14	9	5.56	2	8.00	22.2	50	16	30	14	46.7	3.33	7.00
6gn7	44.3	9	10	5.00	3	5.33	30.0	50	16	31	15	48.4	3.10	5.00
6evv	52.8	9.5	9	5.56	2	8.00	22.2	50	16	30	14	46.7	3.33	7.00

Table S3. Calculated data for the set of aptamer-protein complexes that were used to find correlations: characteristics of amino acids participated in polar contacts (AA in PC) and amino acids within 4 Å vicinity of hot spots (HS) that are nucleotides with ≥3 PC. The characteristics are number of amino acids (AA), mean length of sidechain (SC) in AA, total atoms in AA, sum of positively charged and aromatic amino acids (F, Y, W, H, R, K). Hydrogen atoms were not counted. Results for alternative conformations were averaged. Parameter C_y' was calculated using equation (5), mean length of SC and number of amino acids in 4Å vicinity of PC; the values used for linearization are colored. The efficiency of the complexes was calculated using equation (8); low efficient complexes (efficiency < 55%) are colored with red, highly efficient complex (efficiency >80%) is colored with green.

PDB id	Mean length of SC of AA in PC	Number of AA in PC	Total atoms in AA in PC	Mean length of SC of AA in HS	Number of AA in HS vicinity	Total atoms in HS vicinity	Sum of F, Y, W, H, R, K	C_y'	Efficiency, %
4pdb	3.00	10	30	2.13	8	17	3	308	45.6
4wb2	4.74	8.5	40.5	4.60	10	46	7	413	71.8
5hrt	5.25	8	42	5.67	3	17	9	405	57.1
4r8i	4.56	9	41	4.67	3	14	5	350	62.5
3agv	5.00	5.5	27.5	4.00	6	24	3.5	164	57.4
4ni7-4ni9	5.34	7.3	39.3	4.75	8	38	6.7	332	69.7
5uc6	5.14	7	36	4.30	10	43	5	266	59.6
3zh2	3.52	9.5	33.5	2.86	7	20	5.3	309	52.1
5hto-5hru	3.56	3.3	12	-	-	-	4.3	170	62.6
4m6d	5.47	4.7	25.3	3.43	7	24	4	204	56.2
4m4o	6.00	4	24	3.43	7	24	4	187	60.9
4zbn	5.71	7	40	-	-	-	7.5	374	67.3
1ooa	5.41	11	59.5	5.50	4	22	10	411	53.5
4hqx	5.50	4	22	5.83	6	35	6	221	68.2
4hqu	5.50	4	22	5.83	6	35	6	221	81.7
3hxq-3hxo	5.07	11.5	58.5	4.82	11	53	7.5	561	53.1
5msf	4.22	8	34	3.90	10	39	5.5	266	62.7
1u1y	4.59	7.5	34.5	3.80	10	38	5	260	66.7

6msf	3.83	6	23	3.14	7	22	3.5	202	65.8
3dd2	5.64	11	62	6.11	9	55	12	712	46.0
5do4	6.00	10	60	6.25	8	50	9	558	68.7
4i7y	6.30	10	63	6.71	7	47	10	494	45.2
6eo6	6.00	7	42	5.60	10	56	6	319	63.9
6eo7	6.50	6	39	5.63	8	45	5	251	71.1
3qlp	6.50	6	39	5.56	9	50	5	246	56.8
5cmx	7.00	5	35	7.33	3	22	5	226	70.4
4dii	6.80	5	34	5.50	6	33	4.5	257	57.6
4dih	7.00	5	35	5.57	7	39	5	259	56.0
4lz4	6.50	6	39	5.57	7	39	5	249	54.0
4lz1	6.50	6	39	6.25	8	50	5	256	54.5
6gn7	6.75	4	27	6.00	5	30	4	226	59.1
6evv	6.30	5	31.5	7.33	3	22	5	229	70.2

Table S4. HTH-type proteins complexed with DNA duplexes. A list of nucleotides forming polar contacts (N), amino acids forming polar contacts (PC), amino acids within 4 Å vicinity of atoms in polar contacts (4Å) and amino acids in 4 Å vicinity to nucleotides forming ≥3 polar contacts (HS). If more than one conformation of complex was reported, the alternative variants of interfaces are divided with dashes.

4Z58				4R24				4WLW				3IV5				5D8C			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
A3	R21	R21	Q28	T12	S15	S15	I16	C14	S4	N2	R18	T5	N73	G72	G72	A11	T5	T5	T5
T2	Q28	W26	Q39	C13	G17	I16	S26	T15	T13	I3	R31	T6	Q74	N73	N73	C12	R20	A6	R20
A12'	K38	T27	T41	T14	S26	G17	R28	G16	K15	S4	G35	G7	T75	Q74	Q74	C1'	Y23	A16	R33
C13'	Q39	Q28	S43	G1'	R28	I18	R31	G17	R18	D5	R37	T8	N84	T75	T75	T2'	K24	T18	G37
G14'	T41	S29	N47	T2'	Q29	S26	Y32	G21	Y20	T13		T16'	R85	R76	R85	T3'	R33	R20	N38
G15'	S43	I37	T52	G3'	R31	E27	R43	T22	R31	S14		C17'	T87	I83	R89	A4'	R39	Y22	R39
G16'	N47	K38	T53	A10'	Y32	R28	G47	C23	N34	K15		A18'	R89	N84	-----	G5'	L62	D23	-----
	N51	Q39	T54	T11'	Y33	Q29	I48	C3'	Y36	A16		T5'	K90	R85	G72	-----	-----	K24	T5
	T53	A40			R43	R31	R49	C4'	R37	R18		T6'	-----	T87	N73	A11	T5	R33	R20
	T56	T41			T46	Y32	Q71	T5'	R54	Y20		G7'	N73	L88	Q74	C12	R20	G37	R33
		S43			R49	Y33	T72	T6'		E21		T16	Q74	R89	T75	C1'	Y23	N38	G37
		N44			T72	R36				R31		T17	T75	K90	R85	T2'	K24	R39	N38
		Q46				R43				N34		G18	N84	-----	R89	T3'	R33	R40	R39
		N47				T44				G35			R85	E59		G5'	R39	F41	
		N48				T46				Y36			T87	G72			L62	K56	

		N51 T52 T53 L54 T55 T56				G47 I48 R49 K50 I66 V70 Q71 T72 S73				R37 T38 R54 L60			R89 K90 K91	N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 K91				M60 S61 L62 K63 ----- T4 T5 A6 A16 T18 R20 Y22 D23 K24 R33 G37 N38 R39 R40 F41 K56 M60 S61 L62 K63	
3ZKC				3O9X				5H3R				4WWC				3H0D			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
A3 G4 T5 T6 A13' G14' A15' G16' A17' ----- T3 G4 T5	R10 S16 L17 S18 A27 S29 Y30 S32 R36 Q39 S43 ----- S16	N41' R10 K11 Y15 S16 L17 S18 E19 V26 A27 K28 S29 Y30	N41' R10 S16 L17 S18 K28 S29 Y30 S32 R36 Q39 P42 S43	T14 T15 A16 G17 G18 T19 A5' T6' A7' A15' G16'	R23 Q85 G94 N97 S100 R101 Y102 Q108 H110	Y102' H110' P111' T113' T21 F22 R23 G24 N65 R78 T84 Q85 K86	N97 R101	G12 G13 G14 C15 A3' A5' T6' G8' G14'	Q23 T39 Q42 V58 D67 R73 R77 R86 R94 V96	S65' Q23 T39 A40 A41 Q42 T56 P57 V58 E59 V66 D67 L68	Q23' T39 A41 Q42 V66 D67 R73 M74 R77	G3 T4 G5 G6 T7' C8' T9' A10' ----- G3 T4 G5 G6	I11 Y12 S36 E37 R38 S47 R48 T50 R52 R66 G69 T72 -----	I9 P10 I11 Y12 Y13 P35 S36 E37 R38 E39 I46 S47 R48	S36 E37 R38 R48 R52 R66 G71 T72 ----- S36 E37 R38 R48	T16 A17 G18 T5' T6' G8' A12' T15' ----- A25 T15 T16 G18	N3 I4 S5 K27 R28 S29 S40 Q41 N43 Y44 R49 S60 K61	N3' R49' N3 I4 S5 D6 I26 K27 R28 S29 E30 V38 P39	N3 I4 S5 K27 R28 S29 Q41 N43 Y44 R49 S60 K61 R62

T6 A13' G14' A15' G16' A17'	L17 S18 A27 K28 S29 Y30 S32 R36 Q39 S43	S32 S33 I34 R36 L38 Q39 P42 S43 I44 Q45 F46 ----- N41' R10 S16 L17 S18 E19 V26 A27 K28 S29 Y30 S32 S33 I34 R36 L38 Q39 P42 S43 I44 F46	----- N41' R10 S16 L17 S18 K28 S29 Y30 R36 Q39 P42 S43			G93 G94 G95 V96 N97 A98 S100 R101 Y102 E103 A107 Q108 P109 H110				G69 A70 T72 R73 M74 L75 D76 R77 R86 N89 R94 G95 V96 L97		T7 C8' T9' A10' T7'	I11 Y12 S36 E37 R38 S47 R48 T50 R52 Q53 G69 T72	T50 R52 Q53 S56 R66 G69 R70 G71 T72 ----- I9 P10 I11 Y12 Y13 P35 S36 E37 R38 E39 I46 S47 R48 M49 T50 R52 Q53 V51 R66 G69 R70 G71 T72	R52 R66 G71 T72	T22 A6' G7' G8' T9' T10'	R62 G63 G65 ----- I4 S5 K27 R28 S29 S40 N43 Y44 R49 S60 K61 R62 G63	S40 Q41 N43 Y44 V45 T48 R49 E59 S60 K61 R62 G63 G64 G65 Q41 N43 Y44 R49 S60 K61 R62 G66 Y67 I68 ----- K61' N3 I4 S5 D6 I26 K27 R28 S29 E30 P39 S40 Q41 N43 Y44 T48 R49 E59 S60 K61 R62 G63	G63 G64 G65 G66 Y67 I68 ----- N3 I4 S5 K27 R28 S29 Q41 N43 Y44 R49 S60 K61 R62 G66 Y67 I68 K61' G64'

																		G64 G65 G66 Y67 I68	
4HF1				3JR9				3JRA				3JRB				3JRC			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
T6 C7 C8 T17' G18' T19' G20' T25' ----- A6 C7 A8 T17' G18' T19' G20' T25'	R2 T4 L28 S38 S40 Y41 E43 Q44 S57 R59 Y65 ----- R2 T4 S5 L28 S38 S40 Y41 E43 Q44 R50 S57 R59 Y65	R2 T4 S5 K6 G7 V26 P27 L28 A29 I37 S38 L39 S40 Y41 E43 Q44 R50 S57 V58 R59 G64 Y65 D84 ----- R2 T4 S5 K6 Y9 V26 P27 L28 A29	R2 T4 K6 I37 S38 S40 Y41 E43 Q44 R50 S57 R59 Y65 ----- R2 T4 S5 K6 Y9 G36 I37 S38 S40 Y41 E43 Q44 R50 S57 R59 Y65	T5 T6 G7 T8 T16' T17' A18' ----- T5' T6' G7' T16 T17 G18 G20	N73 Q74 T75 N84 R85 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R85 R89 ----- G72 N73 Q74 T75 R85 R89	T5 T6 G7 A16' T17' G18' ----- T5' T6' A7' T16 T17 A18	N73 Q74 T75 N84 R85 T87 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89 K90 K91	G72 N73 Q74 T75 R76 I83 N84 R85 T87 L88 R89 K90 ----- E59 G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 K91	G72 N73 Q74 T75 R85 R89	T5 T6 G7 T8 C17' A18' ----- T5' T6' G7' T16 C17 A18 G20	N73 Q74 T75 N84 R85 T87 R89 ----- N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85 T87 L88 R89 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 L88 R89 K90 N98	G72 N73 Q74 T75 R85 R89 ----- G72 N73 Q74 T75 R85 R89	T6 G7 C16' C17' A18' ----- T5' T6' G7' C16 T17 G18	N73 Q74 T75 N84 R85 T87 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 ----- M67 G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R85 R89 ----- G72 N73 Q74 T75 R85 R89

		G36 I37 S38 L39 S40 Y41 E43 Q44 R50 S57 V58 R59 G64 Y65 D84																	
3JRD				3JRE				3JRF				3JRG				3JRH			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
T5 T6 G7 A16' C17' A18' ----- T5' T6' G7' A16 T17 G18 G20	N73 Q74 T75 N84 R85 T87 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89 K90 K91	G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 ----- E59 G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89	G72 N73 Q74 T75 R85 R89 ----- G72 N73 Q74 T75 R85 R89	T5 T6 G7 T16' C17' A18' ----- T5' T6' G7' A16 T17 G18 G20	N73 Q74 T75 N84 R85 T87 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89	G72 N73 Q74 T75 R85 R89 ----- G72 N73 Q74 T75 R85 R89	T5 T6 G7 T16' C17' ----- T5' T6' G7' T17 G18 G20	N73 Q74 T75 N84 R85 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89	G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89	G72 N73 Q74 T75 R85 R89 ----- G72 N73 Q74 T75 R85 R89	T5 T6 G7 T8 T16' C17' C18' ----- T5' T6' G7' T16 T17 G20	N73 Q74 T75 N84 R85 T87 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89 K90 K91	G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 ----- E59 G72 N73 Q74 T75 R76 I83 N84 R85 T87	G72 N73 Q74 T75 R85 R89 ----- G72 N73 Q74 T75 R85 R89	T5 T6 G7 T16' G17' A18' ----- T5' T6' G7' T15 G17 G18	N73 Q74 T75 N84 R85 T87 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 G86	G72 N73 Q74 T75 R85 R89 ----- G72 N73 Q74 T75 R85 R89

		K90 K91				K90								R89 K90 K91				R89 K90	
3JRI				5E3O				5E3N				5E3M				5E3L			
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS
T5 T6 G7 A17' ----- T5' T6' G7' T16 G17	N73 Q74 T75 N84 R85 T87 R89 ----- N73 Q74 T75 N84 R85 T87 R89 K90 K91	G72 N73 Q74 T75 R76 I83 N84 R85 L88 T87 R89 ----- E59 G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 K91	G72 N73 Q74 T75 R85 R89 ------ G72 N73 Q74 T75 R85 R89	T5 T6 G7 G8 T16' C17' ----- T5' T6' G7' G8' T16 T17	N73 Q74 T75 N84 R85 T87 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85 G86 T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R85 ----- G72 N73 Q74 T75 R85 R89	T5 T6 G7 T8 T16' C17' ----- T5' T6' G7' T16 T17	N73 Q74 T75 N84 R85 T87 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R85 R89	T5 A6 G7 T8 T16' C17' A18' ----- T5' A6' G7' T16 C17 G18 G20	N73 Q74 T75 N84 R85 T87 R89 K90 ----- Q74 T75 R76 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R85 R89	T5 G6 G7 T8 T16' C17' A18' ----- T5' G6' G7' T16 C17 G18	N73 Q74 T75 N84 R85 T87 R89 K90 ----- N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R85 R89
5DTD				5DS9				4IHV											
N	PC	4Å	HS	N	PC	4Å	HS	N	PC	4Å	HS								
T5 C6 G7 T8 T16' C17' A18' -----	N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85	G72 N73 Q74 T75 R85 R89 ----- G72	T5 A6 G7 T8 T16' C17' A18' -----	N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85	G72 N73 Q74 T75 R85 R89 ----- G72	T5 T6 G7 T8 T16' C17' A18' -----	N73 Q74 T75 N84 R85 T87 R89 K90	G72 N73 Q74 T75 R76 I83 N84 R85	G72 N73 Q74 T75 R85 R89 ----- G72								

T5' C6' G7' T16 T17 G18 G20	----- N73 Q74 T75 N84 R85 T87 R89 K90	T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90	N73 Q74 T75 R85 R89	T5' A6' G7' T16 T17 G18	----- N73 Q74 T75 N84 R85 T87 R89 K90	T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90	N73 Q74 T75 R85 R89	T5' T6' G7' T16 T17 G18	----- N73 Q74 T75 N84 R85 T87 R89 K90	L88 T87 R89 K90 ----- G72 N73 Q74 T75 R76 I83 N84 R85 T87 R89 K90	N73 Q74 T75 R85 R89								

Table S5. Data from literature (ΔG_b) and calculated data (other parameters) for the set of HTH-type proteins complexed with DNA duplexes that were used to find correlations: changes in Gibbs free energy during binding (ΔG_b) and characteristics of interfaces: number of polar contacts (PC), characteristics of amino acids within 4 Å vicinity of PC, amino acids participated in polar contacts (AA in PC) and amino acids within 4 Å vicinity of hot spots (HS) that are nucleotides with ≥3 PC. The characteristics are number of amino acids (AA), mean length of sidechain (SC) in AA, total atoms in AA, sum of positively charged and aromatic amino acids (F, Y, W, H, R, K). Hydrogen atoms were not counted. Results for alternative conformations were averaged; the values refer to 1 domain. Parameter C_y' was calculated using equation (5), mean length of SC and number of amino acids within 4 Å vicinity of PC; the values used for linearization are colored. The efficiency of the complexes was calculated using equation (8); low efficient complexes (efficiency < 55%) are colored with red.

PDB id	-ΔG_b, kJ/mol	Number of polar contacts	Mean length of SC of AA in PC	Total atoms in AA in PC	Number of AA in PC	Mean length of SC	Total atoms in AA	Number of AA in 4Å vicinity	Mean length of SC of AA in HS	Total atoms in HS vicinity	Number of AA in HS vicinity	C_y'	Efficiency, %
4Z58	50	15	4.10	41	10	4.00	84	21	3.50	28	8	439	55.4
4R24	45.3	20	4.92	59	12	4.38	105	24	4.91	54	11	591	44.7
4WLW	44.6	21	5.80	58	10	4.47	85	19	5.25	21	4	484	47.7
3IV5	51.4	14.5	4.76	40.5	8.5	4.48	56	12.5	4.33	26	6	290	64.6
5D8C	43.3	15	5.86	41	7	4.38	85.5	19.5	4.67	28	6	446	47.7
3ZKC	37.5	17	3.87	44.5	11.5	4.09	92	22.5	4.16	52	12.5	497	39.7
3O9X	48.2	18	4.89	44	9	3.93	106	27	5.50	11	2	581	48.0
5H3R	51.3	16	5.10	51	10	3.59	97	27	4.22	38	9	515	53.5
4WWC	60.2	20	4.50	54	12	4.38	98.5	22.5	4.75	38	8	554	61.0
3H0D	44.4	23	4.10	59.5	14.5	3.89	111	28.5	4.14	76.5	18.5	647	42.2
4HF1	43.9	18.5	4.79	57.5	12	3.96	93	23.5	4.83	70	14.5	513	45.9
3IV5	51.4	14.5	4.76	40.5	8.5	4.48	56	12.5	4.33	26	6	290	64.6
3JR9	51.4	14	4.87	36.5	7.5	4.45	49	11	4.33	26	6	251	66.9
3JRA	42.9	14.5	4.76	40.5	8.5	4.48	56	12.5	4.33	26	6	290	53.9
3JRB	49.3	14.5	4.73	35.5	7.5	4.38	52.5	12	4.33	26	6	272	63.0

3JRC	36.3	14.5	4.75	38	8	4.43	51	11.5	4.33	26	6	264	46.7
3JRD	47.7	15	4.76	40.5	8.5	4.50	54	12	4.33	26	6	282	60.3
3JRE	49.3	14	4.75	38	8	4.43	51	11.5	4.33	26	6	261	63.6
3JRF	48.9	11.5	4.86	34	7	4.43	46.5	10.5	4.33	26	6	226	65.2
3JRG	46.1	13.5	4.76	40.5	8.5	4.48	56	12.5	4.33	26	6	284	58.2
3JRH	39.2	13	4.75	38	8	4.08	49	12	4.33	26	6	246	51.3
3JRI	39.7	13	4.75	38	8	4.46	53.5	12	4.33	26	6	269	50.8
4IHV	40.1	14	4.75	38	8	4.43	51	11.5	4.33	26	6	261	51.7
5E3O	40.1	12.5	4.75	38	8	4.26	49	11.5	4.09	22.5	5.5	243	52.6
5E3N	40.7	13	4.75	38	8	4.45	49	11	4.33	26	6	246	53.2
5E3M	41.5	16	4.75	38	8	4.45	49	11	4.33	26	6	260	53.6
5E3L	39.9	15	4.75	38	8	4.45	49	11	4.33	26	6	256	51.7
5DTD	46	14.5	4.75	38	8	4.45	49	11	4.33	26	6	254	59.7
5DS9	48.5	15.5	4.75	38	8	4.45	49	11	4.33	26	6	258	62.7

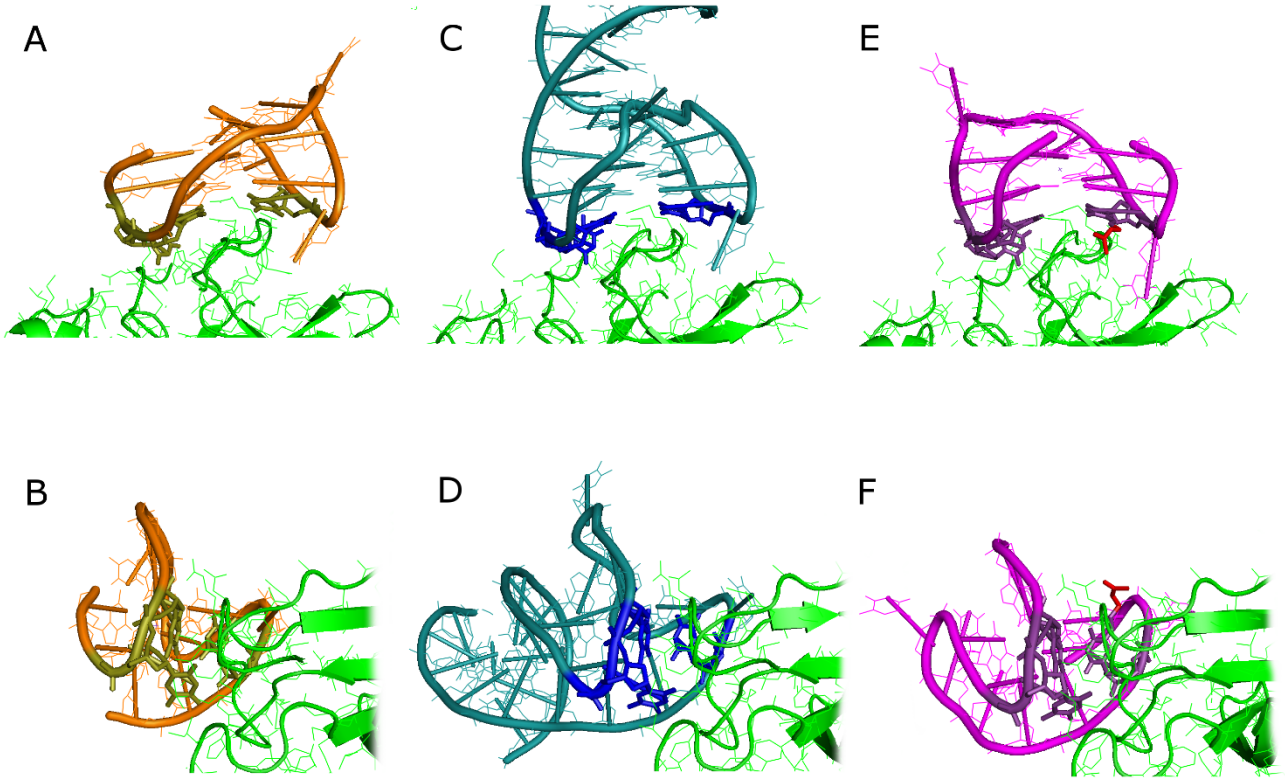

Figure S1. Thrombin complexes with DNA aptamers: HD1 (A,B), RE31 (C,D), and T4K (E,F) in two different views: front view (A,C, and E) and side view (B,D, and F). Thrombin is colored in green. The substituent in thymine (T4) is colored in red. The positioning of recognizing loops is common in all three complexes.

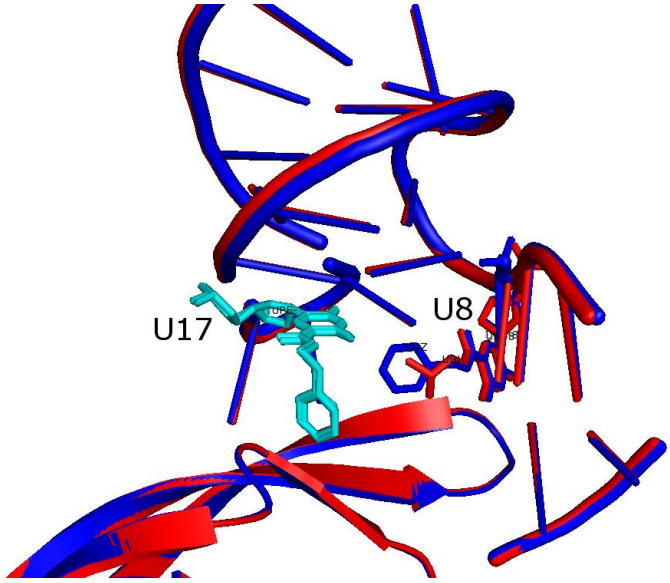

Figure S2. PDGFB complexes with modified DNA aptamers SL4 (in red color) and SL5 (in blue color) aligned together. 'Hot spot' residue (U17, benzyl modified uridine; in light blue) and the sole differing residue (U8, i-butyl or benzyl modified uridine) are shown in details. U17 is in contact with benzyl substituent but not with i-butyl substituent.