

Supplementary Materials

Supplementary figures

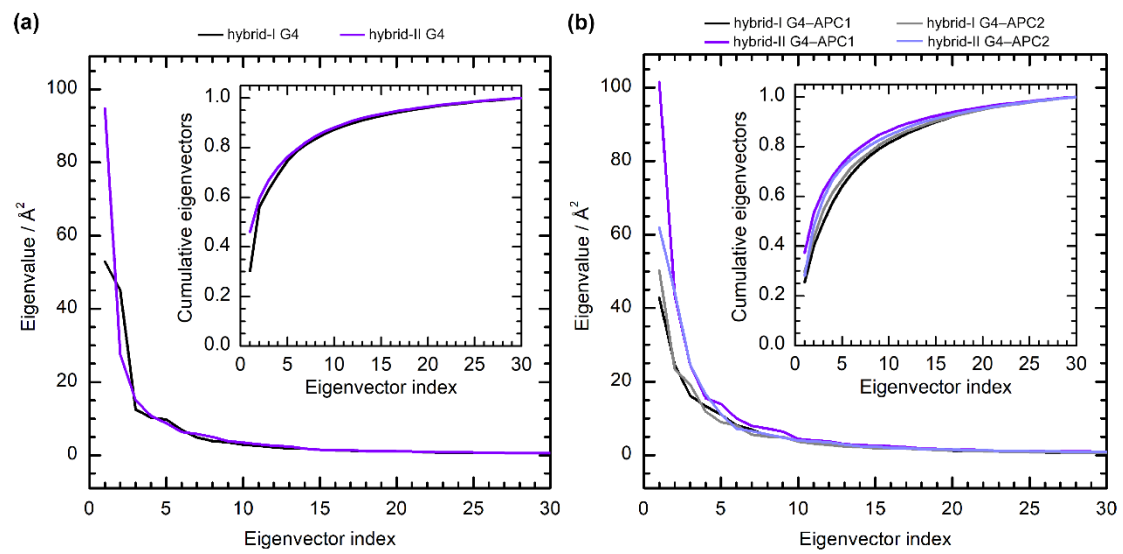


Fig. S1 Eigenvalue profiles constructed by the first 30 eigenvectors from PCA analyses of the apo (a) and APC bound telomere G4s (b)

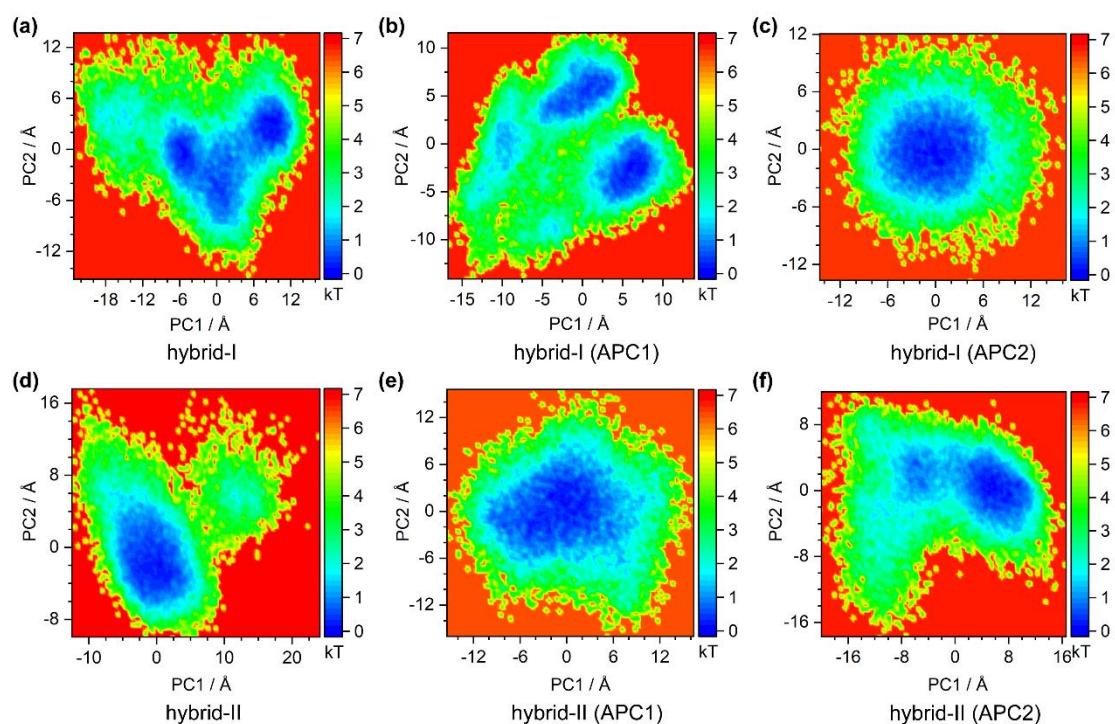


Fig. S2 Free energy landscapes (FELs) of the apo and the APC bound hybrid G4s. Energies are in kT

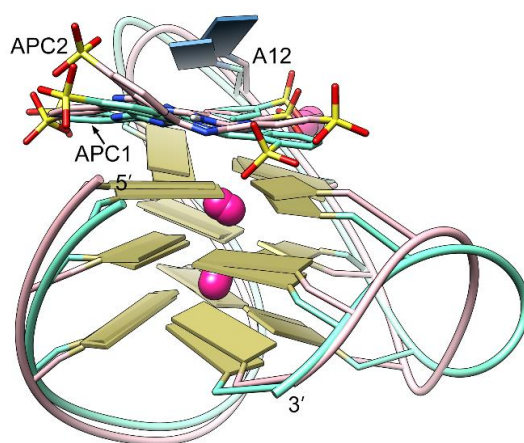


Fig. S3 Structure alignment of the MD-equilibrated binding complex of hybrid-II G4–APC1 and hybrid-II G4–APC2. The ribbons of hybrid-II G4s in the hybrid-II G4–APC1 and hybrid-II G4–APC2 binding complexes are colored in aquamarine and pink, respectively. Carbon atoms and bonds in APC1 and APC2 are colored in aquamarine and pink as well

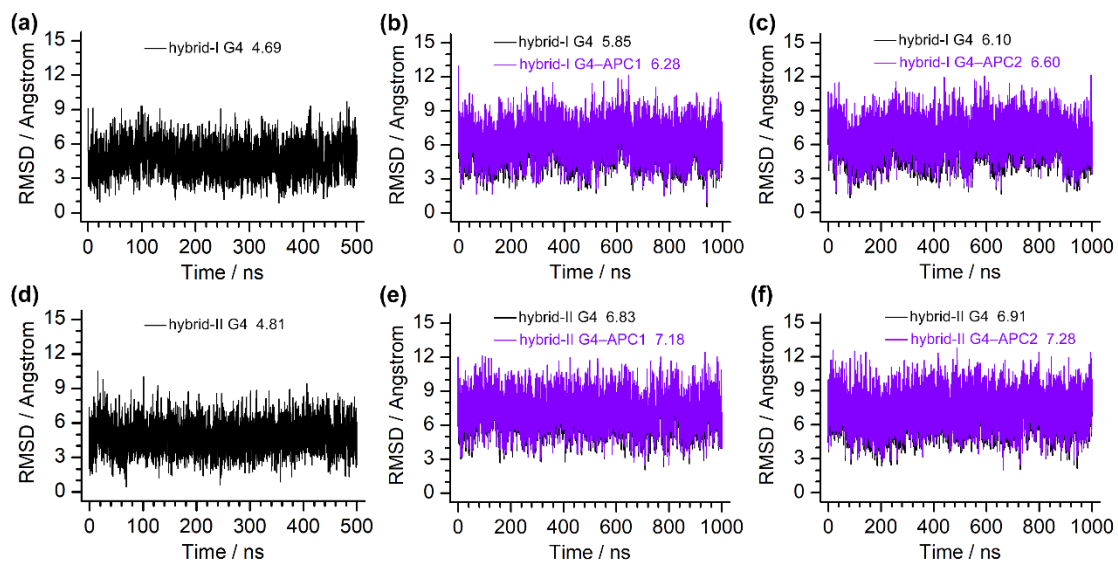


Fig. S4 Number of the environmental K^+ ions located within 3.5 \AA of the apo and APC bound telomere G4s. The average number of environmental K^+ around hybrid G4s and hybrid G4-APC binding complexes are presented

Supplementary tables

Table S1 Hoogsteen hydrogen bonds in the telomere hybrid G4s^a

Model	Acceptor	Donor	Ocpy ^b	Dist ^c	Ang ^d	
Hybrid-I G4	G1@O6	G7@H1 G7@N1	99.54	2.94	158.99	
	G7@O6	G15@H1 G15@N1	99.89	2.93	162.17	
	G15@O6	G19@H1 G19@N1	99.88	2.90	157.32	
	G19@O6	G1@H1 G1@N1	99.64	2.94	155.75	
	G1@N7	G7@H21 G7@N2	99.23	2.97	159.46	
	G7@N7	G15@H21 G15@N2	99.79	2.97	156.94	
	G15@N7	G19@H21 G19@N2	99.82	3.02	161.37	
	G19@N7	G1@H21 G1@N2	99.56	2.99	159.20	
	G2@O6	G20@H1 G20@N1	93.32	3.15	143.24	
	G8@O6	G2@H1 G2@N1	90.49	3.16	139.94	
	G14@O6	G8@H1 G8@N1	95.90	3.10	144.94	
	G20@O6	G14@H1 G14@N1	90.71	3.17	144.16	
	G2@N7	G20@H21 G20@N2	99.86	2.94	159.85	
	G8@N7	G2@H21 G2@N2	98.76	3.00	157.71	
	G14@N7	G8@H21 G8@N2	99.26	3.01	163.21	
	G20@N7	G14@H21 G14@N2	99.78	2.97	162.34	
	G3@O6	G21@H1 G21@N1	99.75	2.97	159.23	
	G9@O6	G3@H1 G3@N1	99.85	2.97	161.16	
	G13@O6	G9@H1 G9@N1	99.94	2.93	157.85	
	G21@O6	G13@H1 G13@N1	99.04	3.00	161.43	
	G3@N7	G21@H21 G21@N2	99.78	2.97	160.10	
	G9@N7	G3@H21 G3@N2	99.79	2.96	156.98	
	G13@N7	G9@H21 G9@N2	99.64	2.97	158.65	
	G21@N7	G13@H21 G13@N2	99.92	2.96	159.67	
	Hybrid-I G4– APC1	G1@O6	G7@H1 G7@N1	99.96	2.89	158.72
		G7@O6	G15@H1 G15@N1	99.93	2.94	160.42
		G15@O6	G19@H1 G19@N1	99.62	2.98	161.67
		G19@O6	G1@H1 G1@N1	98.64	2.93	149.35
G1@N7		G7@H21 G7@N2	99.15	3.00	160.33	
G7@N7		G15@H21 G15@N2	99.92	2.96	160.60	
G15@N7		G19@H21 G19@N2	99.82	2.97	158.50	
G19@N7		G1@H21 G1@N2	99.85	2.98	157.25	
G2@O6		G20@H1 G20@N1	96.29	3.12	143.29	
G8@O6		G2@H1 G2@N1	95.37	3.12	141.22	
G14@O6		G8@H1 G8@N1	97.18	3.11	146.33	

Model	Acceptor	Donor	Ocpy ^b	Dist ^c	Ang ^d
	G20@O6	G14@H1 G14@N1	93.36	3.16	143.48
	G2@N7	G20@H21 G20@N2	99.86	2.96	160.80
	G8@N7	G2@H21 G2@N2	99.35	2.99	160.26
	G14@N7	G8@H21 G8@N2	99.85	2.96	163.49
	G20@N7	G14@H21 G14@N2	99.93	2.96	163.04
	G3@O6	G21@H1 G21@N1	99.40	3.01	156.48
	G9@O6	G3@H1 G3@N1	99.81	2.97	160.45
	G13@O6	G9@H1 G9@N1	99.82	2.94	158.73
	G21@O6	G13@H1 G13@N1	99.92	2.93	162.77
	G3@N7	G21@H21 G21@N2	99.85	2.96	161.97
	G9@N7	G3@H21 G3@N2	99.72	2.97	156.96
	G13@N7	G9@H21 G9@N2	99.04	3.03	157.92
	G21@N7	G13@H21 G13@N2	99.94	2.94	158.36
Hybrid-I G4- APC2	G1@O6	G7@H1 G7@N1	99.68	2.94	159.22
	G7@O6	G15@H1 G15@N1	99.80	2.92	161.55
	G15@O6	G19@H1 G19@N1	99.73	2.93	155.83
	G19@O6	G1@H1 G1@N1	99.76	2.93	156.71
	G1@N7	G7@H21 G7@N2	99.01	2.99	158.31
	G7@N7	G15@H21 G15@N2	99.28	3.02	158.37
	G15@N7	G19@H21 G19@N2	99.92	2.99	161.79
	G19@N7	G1@H21 G1@N2	99.50	2.98	158.15
	G2@O6	G20@H1 G20@N1	94.24	3.14	143.30
	G8@O6	G2@H1 G2@N1	90.75	3.17	140.52
	G14@O6	G8@H1 G8@N1	94.54	3.13	142.90
	G20@O6	G14@H1 G14@N1	91.31	3.18	142.22
	G2@N7	G20@H21 G20@N2	99.77	2.96	159.83
	G8@N7	G2@H21 G2@N2	99.21	2.98	156.95
	G14@N7	G8@H21 G8@N2	99.64	2.98	161.95
	G20@N7	G14@H21 G14@N2	99.76	2.98	160.98
	G3@O6	G21@H1 G21@N1	99.41	3.00	158.91
	G9@O6	G3@H1 G3@N1	99.38	2.99	160.69
	G13@O6	G9@H1 G9@N1	98.91	2.98	154.73
	G21@O6	G13@H1 G13@N1	99.91	2.93	159.25
	G3@N7	G21@H21 G21@N2	99.70	2.97	159.15
	G9@N7	G3@H21 G3@N2	99.71	2.96	156.77
	G13@N7	G9@H21 G9@N2	99.77	2.96	159.93
G21@N7	G13@H21 G13@N2	99.91	2.96	159.91	
Hybrid-II G4	G1@O6	G9@H1 G9@N1	99.74	2.94	158.81
	G9@O6	G13@H1 G13@N1	99.71	2.92	158.33
	G13@O6	G19@H1 G19@N1	99.75	2.95	156.26

Model	Acceptor	Donor	Ocpy ^b	Dist ^c	Ang ^d
	G19@O6	G1@H1 G1@N1	99.55	2.96	155.68
	G1@N7	G9@H21 G9@N2	99.57	2.96	158.30
	G9@N7	G13@H21 G13@N2	98.63	3.06	159.70
	G13@N7	G19@H21 G19@N2	99.87	2.97	162.80
	G19@N7	G1@H21 G1@N2	99.57	2.96	159.13
	G2@O6	G20@H1 G20@N1	91.15	3.12	145.81
	G8@O6	G2@H1 G2@N1	95.65	3.06	149.59
	G14@O6	G8@H1 G8@N1	88.55	3.14	146.12
	G20@O6	G14@H1 G14@N1	96.82	3.05	147.64
	G2@N7	G20@H21 G20@N2	99.60	2.97	158.90
	G8@N7	G2@H21 G2@N2	98.16	3.02	161.95
	G14@N7	G8@H21 G8@N2	99.81	2.97	160.86
	G20@N7	G14@H21 G14@N2	99.75	2.97	161.89
	G3@O6	G21@H1 G21@N1	78.87	2.94	163.16
	G7@O6	G3@H1 G3@N1	90.93	2.99	155.48
	G15@O6	G7@H1 G7@N1	78.41	2.94	158.55
	G21@O6	G15@H1 G15@N1	89.97	3.02	154.16
	G3@N7	G21@H21 G21@N2	78.48	3.00	155.49
	G7@N7	G3@H21 G3@N2	99.54	2.98	157.04
	G15@N7	G7@H21 G7@N2	78.71	2.98	156.43
G21@N7	G15@H21 G15@N2	99.26	3.00	160.62	
Hybrid-II G4- APC1	G1@O6	G9@H1 G9@N1	99.93	2.90	161.74
	G9@O6	G13@H1 G13@N1	99.93	2.91	158.90
	G13@O6	G19@H1 G19@N1	99.96	2.89	161.34
	G19@O6	G1@H1 G1@N1	99.97	2.90	158.60
	G1@N7	G9@H21 G9@N2	99.48	3.01	157.39
	G9@N7	G13@H21 G13@N2	99.79	3.02	160.73
	G13@N7	G19@H21 G19@N2	96.05	3.01	154.46
	G19@N7	G1@H21 G1@N2	99.75	2.99	159.50
	G2@O6	G20@H1 G20@N1	92.93	3.15	142.78
	G8@O6	G2@H1 G2@N1	96.77	3.07	145.64
	G14@O6	G8@H1 G8@N1	90.90	3.18	142.47
	G20@O6	G14@H1 G14@N1	97.13	3.07	144.70
	G2@N7	G20@H21 G20@N2	99.48	2.98	158.95
	G8@N7	G2@H21 G2@N2	99.54	2.99	162.83
	G14@N7	G8@H21 G8@N2	99.83	2.97	160.41
	G20@N7	G14@H21 G14@N2	99.76	2.98	162.38
	G3@O6	G21@H1 G21@N1	99.73	2.96	161.52
	G7@O6	G3@H1 G3@N1	99.31	2.93	155.63
	G15@O6	G7@H1 G7@N1	99.37	2.94	157.45

Model	Acceptor	Donor	Ocpy ^b	Dist ^c	Ang ^d
	G21@O6	G15@H1 G15@N1	99.57	2.98	159.95
	G3@N7	G21@H21 G21@N2	99.66	2.97	156.91
	G7@N7	G3@H21 G3@N2	99.38	2.96	157.38
	G15@N7	G7@H21 G7@N2	99.71	2.99	158.36
	G21@N7	G15@H21 G15@N2	99.42	2.99	157.61
Hybrid-II G4- APC2	G1@O6	G9@H1 G9@N1	99.94	2.90	161.19
	G9@O6	G13@H1 G13@N1	99.84	2.92	156.95
	G13@O6	G19@H1 G19@N1	99.94	2.86	160.52
	G19@O6	G1@H1 G1@N1	99.95	2.90	158.36
	G1@N7	G9@H21 G9@N2	99.60	3.01	159.10
	G9@N7	G13@H21 G13@N2	99.46	3.02	161.19
	G13@N7	G19@H21 G19@N2	91.75	3.05	154.29
	G19@N7	G1@H21 G1@N2	99.83	2.97	160.63
	G2@O6	G20@H1 G20@N1	95.91	3.12	143.98
	G8@O6	G2@H1 G2@N1	98.45	3.03	147.16
	G14@O6	G8@H1 G8@N1	92.30	3.17	142.50
	G20@O6	G14@H1 G14@N1	97.68	3.04	144.59
	G2@N7	G20@H21 G20@N2	99.63	2.98	160.38
	G8@N7	G2@H21 G2@N2	99.78	2.98	163.95
	G14@N7	G8@H21 G8@N2	99.82	2.96	160.09
	G20@N7	G14@H21 G14@N2	98.28	3.01	162.21
	G3@O6	G21@H1 G21@N1	99.86	2.96	160.15
	G7@O6	G3@H1 G3@N1	99.72	2.92	157.96
	G15@O6	G7@H1 G7@N1	99.62	2.96	156.14
	G21@O6	G15@H1 G15@N1	99.69	2.96	161.08
	G3@N7	G21@H21 G21@N2	99.27	2.99	156.66
	G7@N7	G3@H21 G3@N2	99.57	2.97	157.87
	G15@N7	G7@H21 G7@N2	99.90	2.97	161.54
G21@N7	G15@H21 G15@N2	99.27	2.99	156.65	

^a The Hoogsteen hydrogen bond parameters of the top, central, and bottom G-tetrads of hybrid G4s are colored in green, blue, and purple, respectively

^b Hydrogen bond occupancy during MD (%)

^c Time averaged hydrogen bond length (Å)

^d Time averaged hydrogen bond angle (°)