Supporting information

Cationic carbosilane dendrimers and oligonucleotide binding: an energetic affair

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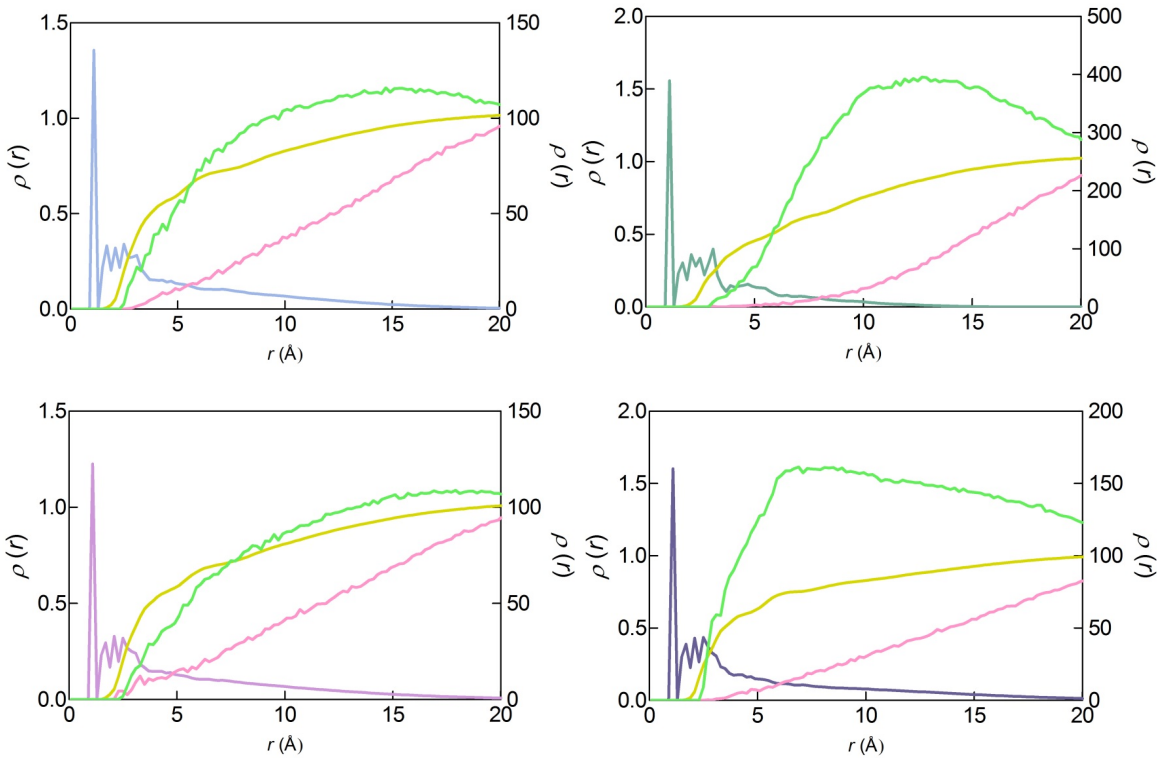

Figure SI1. Density distributions for dendrimers **1** (top left), **2** (top right), **3** (bottom left), and **4** (bottom right). Color legend: **1**, light blue; **2**, dark sea green; **3**, plum; **4**, dark lavender; water, dark yellow; Na^+, pink; Cl^-, green.

Table SI1. Free energy of binding ΔG_{bind} (kcal/mol) for the three equilibrated dendrimer/ODN complex structures generated by the combined SMD/MD approach. End refers to the dendrimer docked by SMD onto the end of the ODN strand, whereas center refers to the configuration in which the dendrimer is approximately in the middle of the ODN sequence (for further explanation see main text and Fig. 5).

	GEM91			SREV		
	END	CENTER	END	END	CENTER	END
1	-17.0 ± 2.6	-16.8 ± 2.9	-15.78 ± 3.1	-15.2 ± 3.3	-16.7 ± 3.4	-16.7 ± 2.9
2	-31.8 ± 4.3	-35.4 ± 4.2	-33.2 ± 4.1	-26.1 ± 4.5	-29.9 ± 4.6	-26.7 ± 4.5
3	-47.0 ± 3.0	-47.5 ± 3.8	-44.5 ± 3.6	-45.7 ± 4.9	-47.2 ± 5.2	-44.3 ± 5.0
4	-53.4 ± 4.6	-54.9 ± 5.0	-53.3 ± 5.1	-49.0 ± 5.3	-52.6 ± 5.5	-48.1 ± 5.5

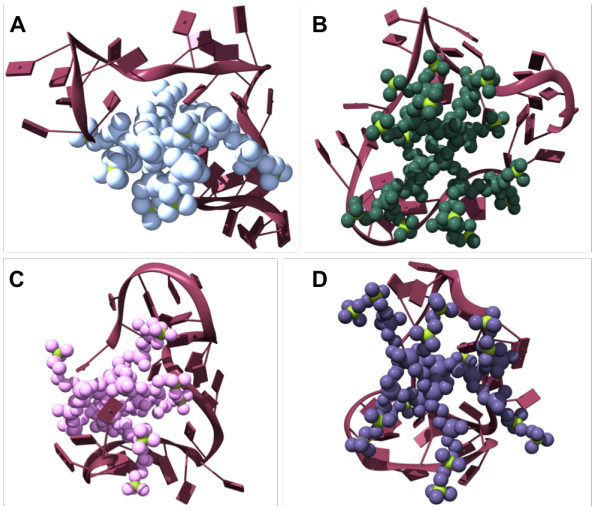

Figure SI2. Equilibrated MD snapshots of dendrimers **1**-**4** in complex with the ODN SREV. Dendrimers **1** (A), **2** (B), **3** (C), and **4** (D) are depicted as light sky blue, dark sea green, plum, and dark lavender sticks and balls, respectively, with terminal charged amine groups highlighted in green. The SREV sequence is portrayed as a red grape ribbon. Water and ions are omitted for clarity.

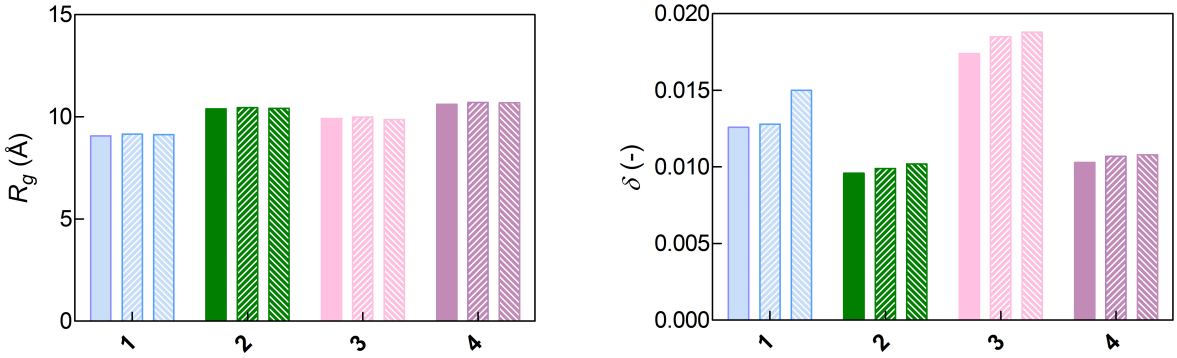

Figure SI3. Comparison of the radius of gyration R_g (Å) (left) and asphericity δ (-) (right) for the dendrimers alone (solid color filled bars), in complex with the ODN GEM91 (left diagonal line bars), and in complex with the ODN SREV (right diagonal line bars).

Table SI2. Per residue contribution to free energy of binding (kcal/mol) of dendrimers **1-4** in complex with ODN GEM91 and SREV. Dendrimer terminal branches are labeled according to Fig. 1 in main text.

GEM91								
1		**2**				**3**		**4**
CTA1	-1.8	CTB1	-2.5	CTB9	-1.1	CTC1	-4.1	CTD1	-6.5
CTA2	-2.1	CTB2	-2.8	CTB10	-1.4	CTC2	-4.0	CTD2	-6.1
CTA3	-1.1	CTB3	-1.2	CTB11	-2.3	CTC3	-4.6	CTD3	-4.4
CTA4	-2.1	CTB4	-2.9	CTB12	-2.8	CTC4	-4.0	CTD4	-6.7
CTA5	-2.2	CTB5	-1.2	CTB13	-0.98	CTC5	-4.3	CTD5	-4.5
CTA6	-1.0	CTB6	-2.6	CTB14	-2.4	CTC6	-4.5	CTD6	-6.6
CTA7	-1.9	CTB7	-0.99	CTB15	-1.0	CTC7	-4.1	CTD7	-6.3
CTA8	-1.8	CTB8	-2.9	CTB16	-2.7	CTC8	-5.0	CTD8	-4.8
SREV								
1		**2**				**3**		**4**
CTA1	-2.1	CTB1	-1.3	CTB9	-2.1	CTC1	-3.9	CTD1	-6.1
CTA2	-1.6	CTB2	-2.5	CTB10	-2.7	CTC2	-3.9	CTD2	-4.2
CTA3	-0.95	CTB3	-2.5	CTB11	-1.2	CTC3	-4.2	CTD3	-5.9
CTA4	-2.0	CTB4	-0.97	CTB12	-2.6	CTC4	-4.2	CTD4	-4.2
CTA5	-1.7	CTB5	-2.4	CTB13	-0.88	CTC5	-3.8	CTD5	-6.3
CTA6	-1.0	CTB6	-1.2	CTB14	-2.5	CTC6	-4.1	CTD6	-4.1
CTA7	-1.8	CTB7	-2.3	CTB15	-2.4	CTC7	-3.9	CTD7	-6.1
CTA8	-2.1	CTB8	-1.1	CTB16	-0.95	CTC8	-4.2	CTD8	-6.2

Table SI3. Components of the free energy of binding (kcal/mol) for the three equilibrated dendrimer/ODN complex structures generated by the combined SMD/MD approach. End refers to the dendrimer docked by SMD onto the end of the ODN strand, whereas center refers to the configuration in which the dendrimer is approximately in the middle of the ODN sequence (for further explanation, see main text and Fig. 5). $\Delta H_{bind} = \Delta E_{int} + \Delta E_{vdW} + \Delta E_{ele} + \Delta G_{PB} + \Delta G_{np}$.

GEM91								
END	ΔE_{int}	ΔE_{vdW}	ΔE_{ele}	ΔG_{PB}	ΔG_{np}	ΔH_{bind}	$-T\Delta S$	ΔG_{bind}
1	1.5	-10.0	-3369.2	3352.1	-4.6	-30.2	-13.2	-17.0
	(0.8)	(0.8)	(64.0)	(57.0)	(0.1)	(1.7)	(2.0)	(2.6)
2	-1.1	-16.9	-7533.1	7498.2	-12.8	-65.7	-33.9	-31.8
	(0.8)	(1.9)	(113.0)	(142.5)	(0.6)	(2.8)	(3.2)	(4.3)
3	-10.8	-21.2	-3506.2	3464.1	-10.0	-84.1	-37.6	-47.4
	(6.5)	(1.3)	(73.6)	(69.3)	(0.8)	(1.8)	(2.4)	(3.0)
4	-11.5	-24.8	-7683.4	7639.2	-13.3	-93.8	-40.4	-53.4
	(8.6)	(2.2)	(146.0)	(114.6)	(3.1)	(3.1)	(3.4)	(4.6)
CENTER	ΔE_{int}	ΔE_{vdW}	ΔE_{ele}	ΔG_{PB}	ΔG_{np}	ΔH_{bind}	$-T\Delta S$	ΔG_{bind}
1	2.4	-10.2	-3339.8	3321.1	-5.0	-31.5	-14.7	-16.8
	(1.5)	(1.0)	(66.8)	(59.8)	(0.3)	(1.9)	(2.2)	(2.9)
2	-2.2	-16.6	-7542.9	7505.3	-12.4	-68.8	-33.4	-35.4
	(1.5)	(1.5)	(135.8)	(127.6)	(1.0)	(2.8)	(3.1)	(4.2)
3	-12.5	-22.3	-3499.5	3459.4	-10.5	-85.4	-37.9	-47.5
	(7.6)	(2.2)	(70.0)	(62.3)	(0.6)	(2.5)	(2.9)	(3.8)
4	-10.6	-26.9	-7706.9	7661.7	-13.9	-96.6	-41.7	-54.9
	(7.1)	(1.9)	(146.4)	(122.6)	(1.1)	(3.4)	(3.6)	(5.0)
END	ΔE_{int}	ΔE_{vdW}	ΔE_{ele}	ΔG_{PB}	ΔG_{np}	ΔH_{bind}	$-T\Delta S$	ΔG_{bind}
1	5.5	-11.1	-3317.4	3298.4	-5.2	-29.8	-14.1	-15.7
	(3.4)	(1.0)	(56.4)	(66.0)	(0.3)	(2.1)	(3.1)	(3.1)
2	-3-3	-15.5	-7555.3	7519.1	-12.0	-66.4	-33.2	-33.2
	(2.5)	(1.1)	(128.4)	(116.6)	(1.2)	(2.7)	(3.1)	(4.1)
3	-4.8	-27.3	-3480.9	3437.2	-10.3	-82.5	-38.0	-44.5
	(3.6)	(1.9	(66.1)	(56.7)	(0.6)	(2.4)	(2.7)	(3.6)
4	-10.0	-25.8	-7669.1	7624.3	-13.6	-94.2	-40.9	-53.3
	(6.9)	(2.6)	(130.4)	(122.0)	(1.2)	(3.2)	(4.0)	(5.1)
SREV								
END	ΔE_{int}	ΔE_{vdW}	ΔE_{ele}	ΔG_{PB}	ΔG_{np}	ΔH_{bind}	$-T\Delta S$	ΔG_{bind}
1	6.8	-11.0	-3277.7	3258.5	-4.7	-28.1	-12.9	-15.2
	(4.8)	(0.9)	(59.0)	(48.9)	(0.5)	(2.2)	(2.4)	(3.3)
2	-3.7	-14.8	-7483.3	7452.9	-10.4	-59.3	-33.2	-26.1
	(2.0)	(1.3)	(119.7)	(126.7)	(0.8)	(2.7)	(3.6)	(4.5)
3	-11.8	-20.8	-3461.8	3420.1	-13.2	-87.5	-41.8	-45.7
	(7.3)	(2.1)	(58.9)	(61.6)	(1.2)	(3.1)	(3.8)	(4.9)
4	-6.4	-25.1	-7633.7	7588.6	-12.9	-89.5	-40.5	-49.0
	(4.4)	(1.5)	(137.4)	(121.4)	(1.4)	(3.1)	(4.3)	(5.3)
CENTER	ΔE_{int}	ΔE_{vdW}	ΔE_{ele}	ΔG_{PB}	ΔG_{np}	ΔH_{bind}	$-T\Delta S$	ΔG_{bind}
1	2.1	-10.1	-3287.9	3269.9	-4.9	-30.9	-14.2	-16.7
	(1.4)	(0.9)	(52.6)	(55.6)	(0.4)	(2.3)	(2.5)	(3.4)
2	-4.1	-15.9	-7465.0	7432.9	-10.1	-62.2	-32.3	-29.9
	(2.6)	(1.1)	(141.8)	(148.7)	(1.1)	(3.0)	(3.5)	(4.6)
3	-12.6	-21.2	-3437.9	3395.2	-13.8	-90.3	-43.1	-47.2
	(8.7)	(1.7)	(65.3)	(64.5)	(1.0)	(3.3)	(4.0)	(5.2)
4	-9.1	-27.3	-7656.1	7612.9	-13.3	-92.9	-40.3	-52.6
	(5.5)	(1.4)	(114.8)	(106.6)	(1.3)	(3.6)	(4.1)	(5.5)
END	ΔE_{int}	ΔE_{vdW}	ΔE_{ele}	ΔG_{PB}	ΔG_{np}	ΔH_{bind}	$-T\Delta S$	ΔG_{bind}
1	5.7	-9.8	-3301.6	3281.3	-5.1	-29.5	-12.8	-16.7
	(3.4)	(0.5)	(66.0)	(58.4)	(0.5)	(1.9)	(2.2)	(2.9)
2	-1.8	-17.2	-7442.	7410.7	-9.9	-60.6	-33.9	-26.7
	(1.4)	(1.9)	(141.4)	(163.0)	(1.0)	(2.9)	(3.4)	(4.5)
3	-9.8	-23.4	-3458.6	3418.2	-13.3	-86.9	-42.6	-44.3
	(6.1)	(2.3)	(58.8)	(61.5)	(1.2)	(3.3)	(3.8)	(5.0)
4	-7.8	-25.9	-7590.2	7546.0	-12.0	-89.9	-41.8	-48.1
	(5.9)	(2.3)	(159.4)	(135.8)	(1.1)	(3.3)	(4.4)	(5.5)

As can be seen from the values of the free energy components reported in Table SI3, for each dendrimer/ODN complex and for each individual simulation starting point these quantities converge to very similar values, well within their standard deviation. As expected, giving the opposite charged nature of the molecular species involved, in all cases the driving force leading to complex formation is mainly electrostatic in nature. Nonetheless, a significant contribution is also afforded by the dispersion/non polar component of ΔG_{bind}, as these quantities also account for the H-bond and π-cation stabilizing interactions which concur, behind purely Coulombic attraction, to anchor the two molecular components within their supermolecular assemblies.

Of note, both the values of the enthalpic (ΔH_{bind}) and entropic ($-T\Delta S$) components of ΔG_{bind} are very well equilibrated and very close to each other for every set of simulation of each ODN/carbosilane nanocarrier complex. This can be taken as an indication that the resulting structures which, as discussed in detail in the dedicated section of the main text, are utterly similar to one another, may well represent a pronounced and stable energy minimum for these systems.