

Supporting Information

Effect of Backbone Chemistry on Hybridization Thermodynamics of Oligonucleic Acids: A Coarse-Grained Molecular Dynamics Simulation Study

*Ahmadreza F. Ghobadi and Arthi Jayaraman**

*Department of Chemical and Biomolecular Engineering, Colburn Laboratory, 150
Academy Street, University of Delaware, Newark DE 19711*

*Corresponding author arthij@udel.edu

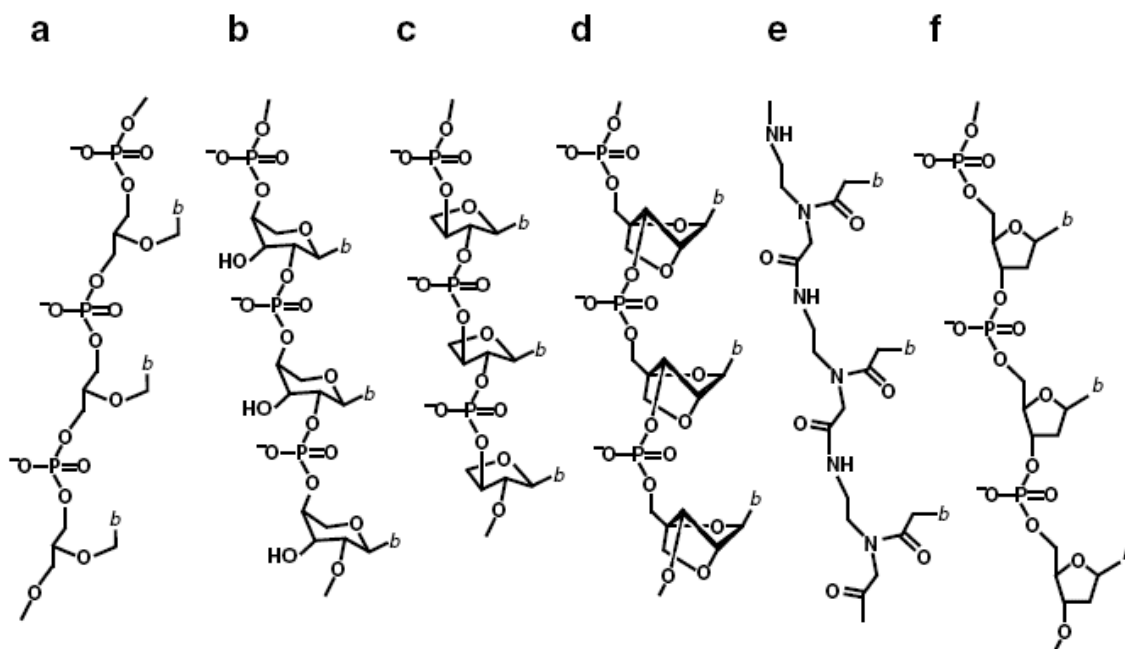


Figure S 1. Schematic representation of the molecular backbones of five relevant nucleic acid analogues (the letter b denotes the position of the nucleobase): glycerolderived nucleic acid, GNA (a); pyranosyl-RNA, p-RNA (b); threose nucleic acid, TNA (c); locked nucleic acid, LNA (d); peptide nucleic acid, PNA (e). *Adapted with permission from Springer Science and Business Media*; C. Brions and M. Moreno, *Analytical and Bioanalytical Chemistry*, 2012, Volume 402, Issue 10, pp 3071-3089, Figure 1.

Table S 1. Effect of nucleobase spacing (S) on dihedral force constant $k_{stacking}^{ij} / \epsilon$ for various neighboring nucleobase combinations

Neighboring nucleobases	$k_{stacking}^{ij} / \epsilon$		
	$S = (r_0^{BB} - 0.16\sigma) / \sigma$	$S = r_0^{BB} / \sigma$	$S = (r_0^{BB} + 0.16\sigma) / \sigma$
CC, CT, TT, AT	2.1	3.0	4.6
GT, GC, AC	4.2	6.0	9.1
GG, AA, GA	6.3	9.0	13.7

Table S 2. Effect of backbone angle force constant on persistence length (L_p) of single-stranded chains with neutral backbone.

Sequence	k_{angle}^{BB} (in units of ϵ/rad^2)	Label	L_p (in units of σ)
GCGCGCGC $T^* = 8.3$	10	flexible (flx)	4.1
	30	Semi-flexible (sflx)	9.8
	100	Semi-rigid (srgd)	30.7
	300	Rigid (rgd)	91.4
ATATATAT $T^* = 6.2$	10	flexible (flx)	5.1
	30	Semi-flexible (sflx)	12.9
	100	Semi-rigid (srgd)	40.8

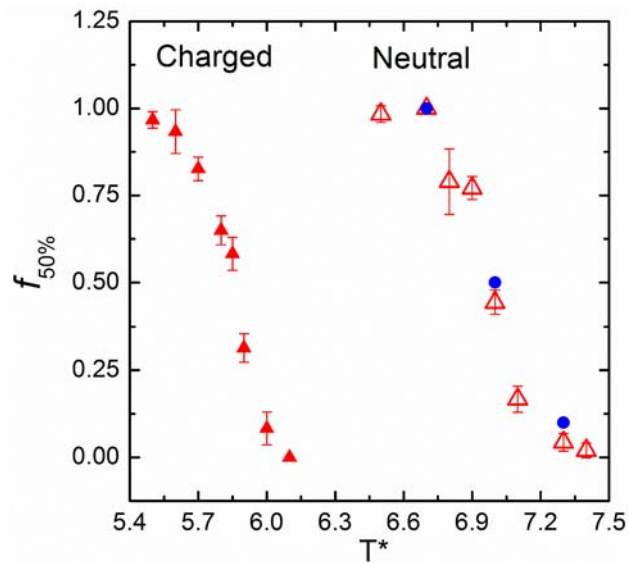
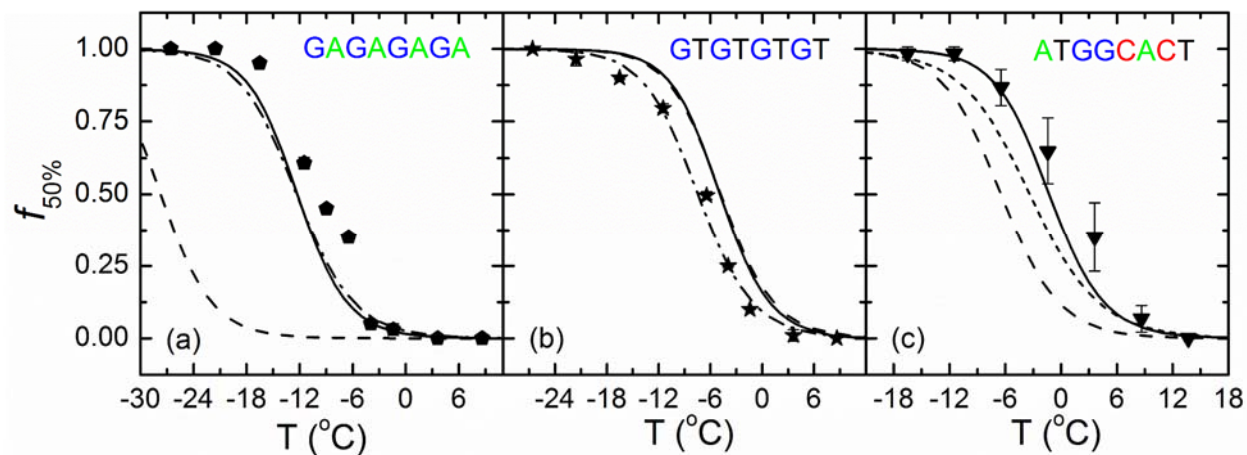


Figure S 2. Effect of salt ions on melting curve of d(GCGCGCGC) duplex with neutral backbone. Unfilled red triangles and filled blue circles represent melting curves with 0 mM and 1 mM salt, respectively. For comparison, the melting curve of corresponding charged backbone in 1 mM salt is also shown with filled triangles.

a)



b)

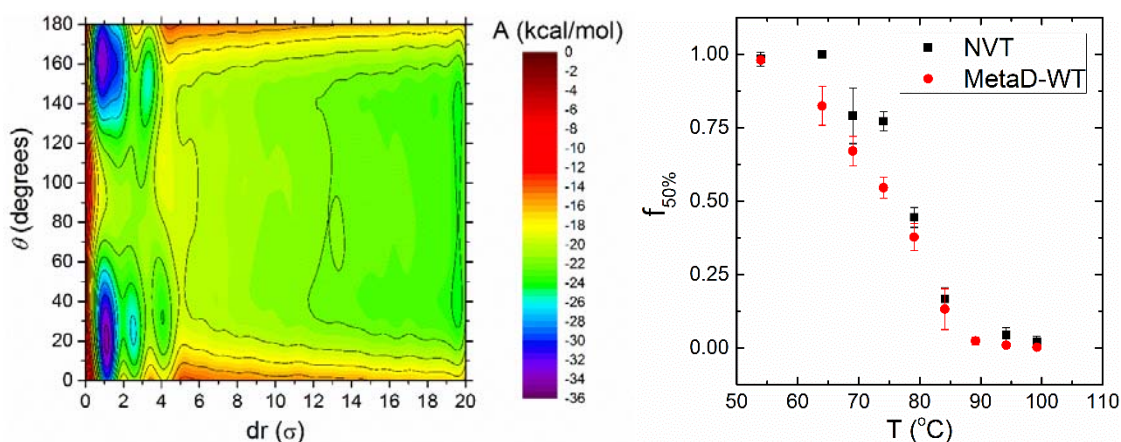


Figure S 3. a) CG simulation results of melting of duplexes with 50% G-C content compared to melting curves from NN methods. DNA melting curves are shown for (a) d(GAGAGAGA), (b) d(GTGTGTGT), and (c) d(ATGGCACT). Symbols are our simulation data and lines are predictions from NN method. Solid, short-dashed, long-dashed, and dash-dotted lines represent melting curves from work of Blake et al¹, Huguet et al², Sugimoto et al³ and SantaLucia⁴, respectively. b) Free energy landscape (left) for hybridization of an 8-mer DNA duplex with sequence GCGCGCGC at T = 54 °C. The two collective variables are the angle (θ) and the distance (dr) between the two hybridizing strands. The corresponding melting curve (right) obtained from our simulation protocol (NVT) and MetaD-WT simulations are in satisfactory agreement.

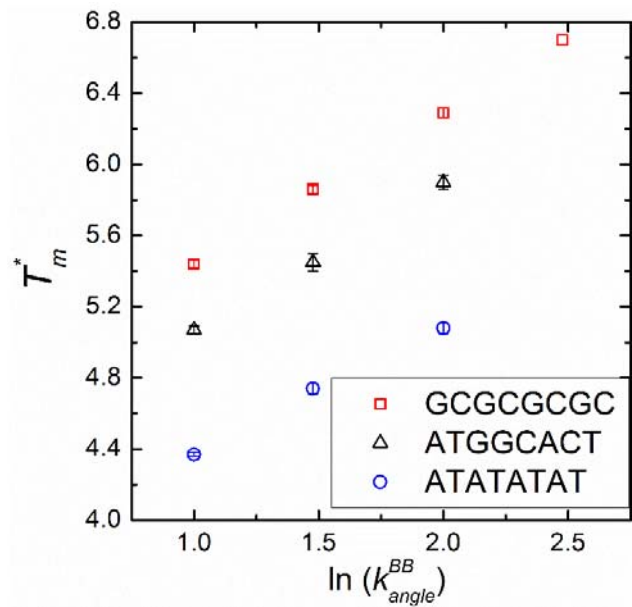


Figure S 4. Effect of backbone angle force constant on melting temperature for charged backbones. Squares, triangles and circles represent data for d(GCGCGCGC), d(ATGGCACT) and d(ATATATAT) duplexes, respectively.

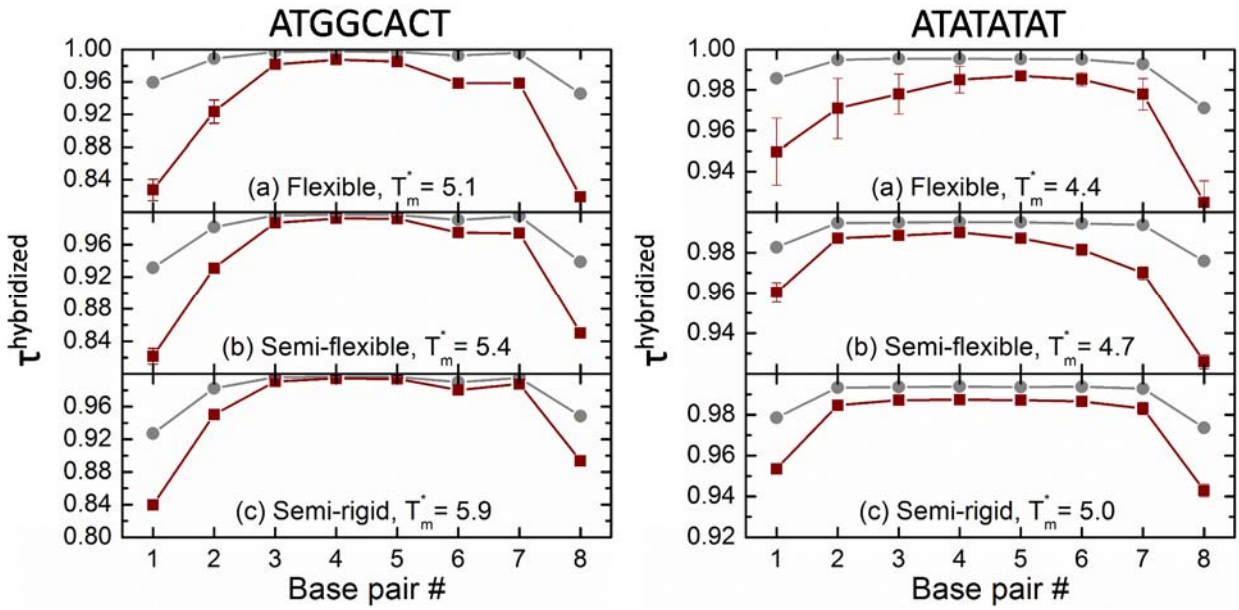


Figure S 5. Effect of backbone flexibility on the ensemble average fraction of configurations that base pairs remain hybridized ($\tau^{\text{hybridized}}$) for ATGGCACT (left) and ATATATAT (right) sequences with (a) flx/flx, (b) sflx/sflx and (c) srgd/srgd duplexes and charged backbones. Circles and squares corresponds to temperatures at which $f_{50\%}$ is greater than 0.9 and smaller than 0.2, respectively

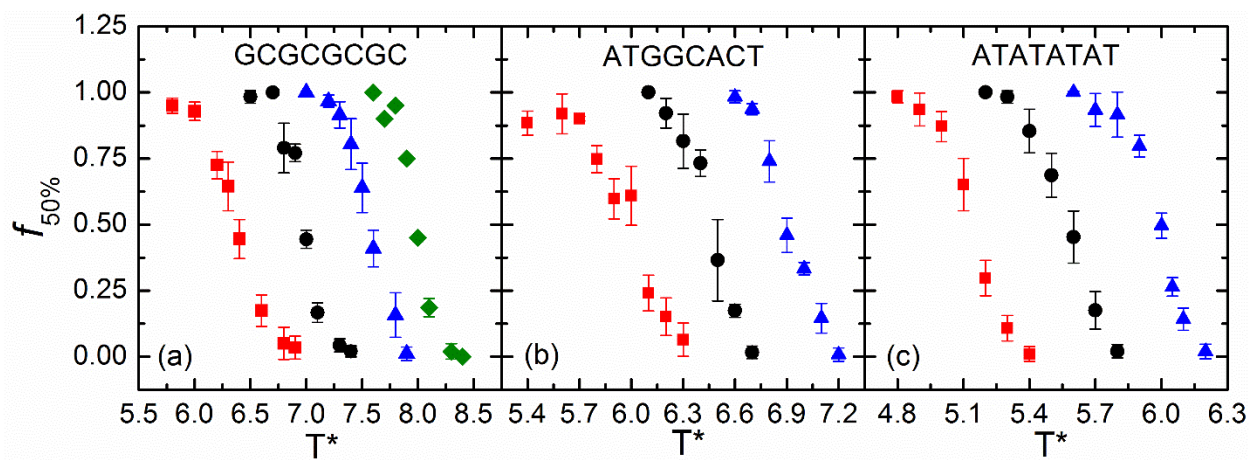


Figure S 6. Effect of backbone flexibility on melting curves of (a) d(GCGCGCGC), (b) d(ATGGCACT) and (c) d(ATATATAT) with neutral backbones. Filled squares, circles, triangles and diamonds correspond to duplexes with flx/flx, sflx/sflx, srgd/srgd and rgd/rgd backbones, respectively.

Table S 3. Effect of intra-strand electrostatic repulsion on persistence length of chains with varying backbone flexibility.

Sequence	k_{angle}^{BB} (ϵ/rad^2)	L_p^e/L_p	L_p/σ of a charged backbone	L_p/σ of a neutral backbone
GCGCGCGC	10	0.32	5.85	4.43
	30	0.11	12.07	10.9
	100	0.03	33.3	32.3
ATGGCACT	10	0.13	6.2	5.47
	30	0.06	13.1	12.3
	100	0.03	36.4	35.3
ATATATAT	10	0.24	6.8	5.47
	30	0.08	14.8	13.7
	100	0.03	42.0	40.8

Table S 4. Effect of nucleobase spacing on persistence length of chains with semi-flexible (DNA-like) backbone.

Sequence	r_0^{BB}/σ	L_p/σ for a charged backbone	L_p/σ for a neutral backbone
GCGCGCGC	0.68	14.6	11.5
	0.84	14.0	10.9
	1.0	13.6	10.8
ATATATAT	0.68	18.3	13.8
	0.84	17.0	13.7
	1.0	16.8	12.9

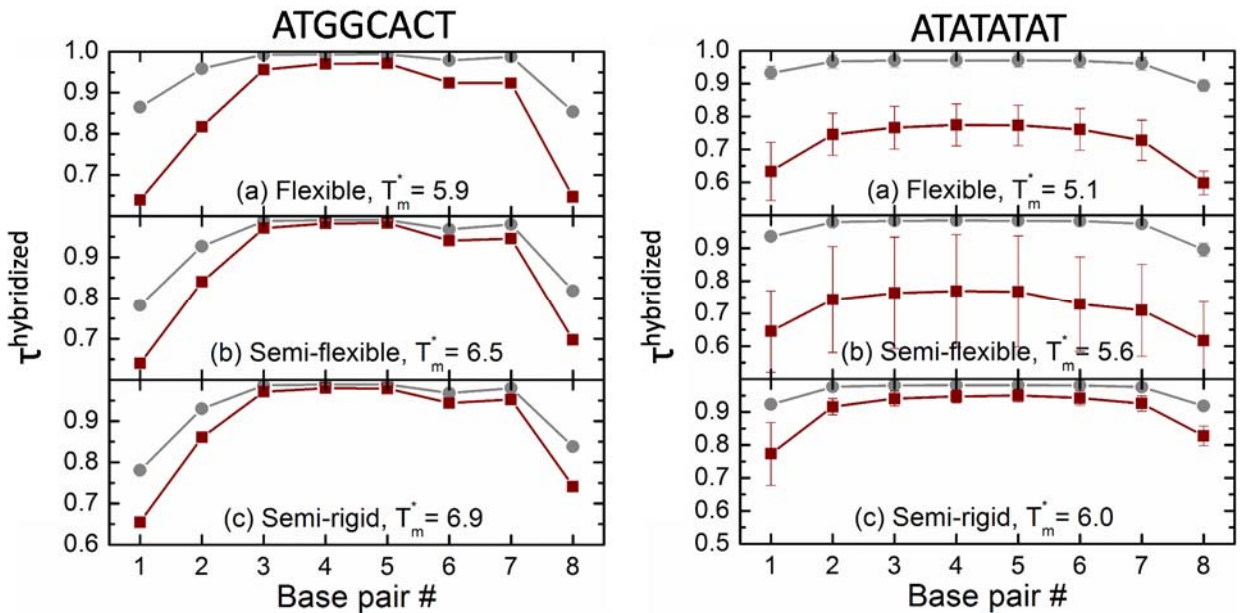


Figure S 7. Effect of backbone flexibility on the ensemble average fraction of configurations that base pairs remain hybridized ($\tau^{\text{hybridized}}$) for ATGGCACT (left) and ATATATAT (right) sequences with (a) flx/flx, (b) sflx/sflx and (c) rgd/rgd duplexes and neutral backbones. Circles and squares corresponds to temperatures at which $f_{50\%}$ is greater than 0.9 and smaller than 0.2, respectively.

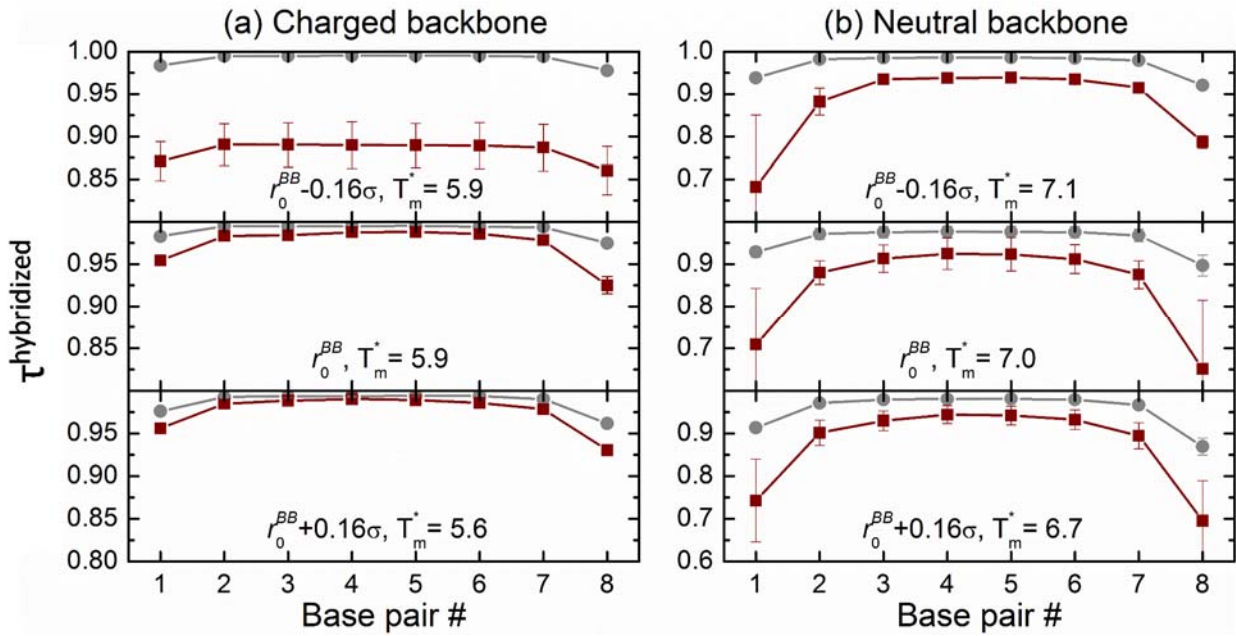


Figure S 8. Effect of nucleobase distance on the ensemble average fraction of configurations that base pairs remain hybridized ($\tau^{\text{hybridized}}$) for GCGCGGC sequence with charged (left) and neutral (right) backbones. Circles and squares corresponds to temperatures at which $f_{50\%}$ is greater than 0.9 and smaller than 0.2, respectively.

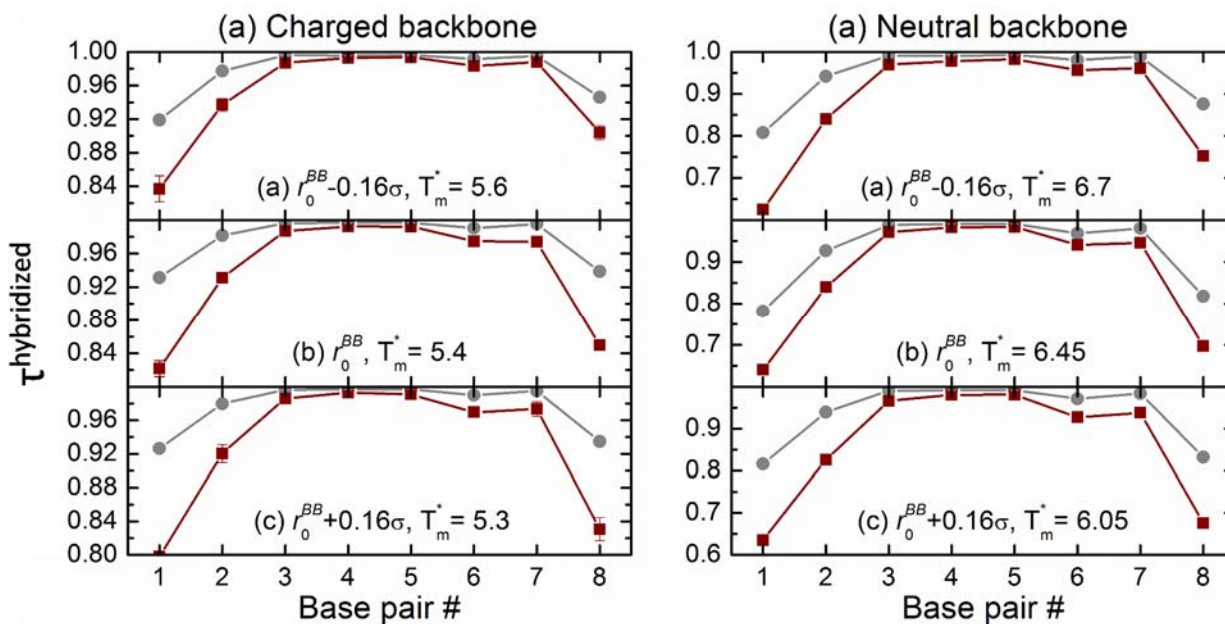


Figure S 9. Effect of nucleobase distance on the ensemble average fraction of configurations that base pairs remain hybridized ($\tau^{\text{hybridized}}$) for ATGGCACT sequence with charged (left) and neutral (right) backbones. Circles and squares corresponds to temperatures at which $f_{50\%}$ is greater than 0.9 and smaller than 0.2, respectively.

References

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