# Electronic Supplementary Information 

# Structural properties and influence of solvent in the stability of telomeric four-stranded i-motif DNA 

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## Table and Figure legends:

Table S1: Base pair orientational parameters in model $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structure (ABC/DEF) as derived from the NMR structure of i-motif DNA (PDB id: 1EL2).

Table S2: Configurational entropy of the core and loop regions of the i-motif in $3^{\prime} \mathrm{E}$ and $5^{\prime} \mathrm{E}$-form structure with hemi-protonated cytosines, derived from the normal mode analysis of equilibrated MD simulated trajectory at 300 K .

Table S3: Average value along with standard deviation of the base pair parameters as found in experimental dataset and MD simulation of 3 ' E and $5^{\prime}$ 'E-form structure under acidic pH with hemiprotonated cytosines having two different topologies.

Table S4: Average value along with standard deviation of the backbone dihedral angles for the bases as found in MD simulation of $5^{\prime} \mathrm{E}$-form i-motif structure under acidic pH with hemi-protonated cytosines.

Table S5: Average value along with standard deviation of the backbone dihedral angles for the bases as found in MD simulation of 3'E-form i-motif structure under acidic pH with hemi-protonated cytosines.

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Table S7: Average value along with standard deviation of the backbone dihedral angles for the bases as found in MD simulation of $5^{\prime} \mathrm{E}$-form structure in deprotonated state with normal cytosines.

Table S8: Average hydrogen bonding geometry and occupancy (considering C-O distance $\leq 3.4 \AA$ and $\mathrm{C}-\mathrm{H} . . . \mathrm{O}$ angle $>120^{\circ}$ ) of possible C-H...O mediated hydrogen bond between sugar moieties of the antiparallel strands along the narrow grooves of i-motif DNA.

Table S9: Base pairing and stacking energy between the stacked base pairs in model $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structure (ABC/DEF) as derived from the NMR structure of i-motif DNA (PDB id: 1EL2).

Table S10: Variation of stacking energy between the stacked base pairs in model $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structure ( $\mathrm{ABC} / \mathrm{DEF}$ ) with stacking interval between the consecutive base pairs.

Table S11: Average hydrogen bonding geometry and occupancy (considering C - O distance $\leq 3.4$ $\AA$ and $\mathrm{C}-\mathrm{H} . . . \mathrm{O}$ angle $>120^{\circ}$ ) of possible C-H...O mediated hydrogen bond between sugar moieties of the antiparallel strands along the narrow grooves of i-motif DNA at elevated temperatures.

Table S12: Average value along with standard deviation of the base pair step parameters as found in MD simulation of $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ and $5^{\prime} \mathrm{E}_{\mathrm{CGG}}$ form structure ( ${ }^{\prime}$ ' denotes base pair and ' $\because$ ' denotes base pairs stack).

Table S13: Average value along with standard deviation of stacking interval and twist between consecutive stacked base pair within i-motif core as found in MD simulation of $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ and $5^{\prime} \mathrm{E}_{\mathrm{CGG}}{ }^{-}$ form structure ( $\because ’$ denotes base pair and ' $:: ’$ denotes base pairs stack).

Table S14: Average value along with standard deviation of the backbone dihedral angles for the bases as found in MD simulation of $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$-form structure.

Table S15: Average value along with standard deviation of the backbone dihedral angles for the bases as found in MD simulation of $5{ }^{\prime} \mathrm{E}_{\mathrm{CGG}}$-form structure.

Table S16: Average hydrogen bonding geometry and occupancy (considering $\mathrm{C}-\mathrm{O}$ distance $\leq 3.4$ $\AA$ and C-H...O angle $>120^{\circ}$ ) of possible C-H...O mediated hydrogen bond between sugar moieties of the antiparallel strands along the narrow grooves of $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ and $5^{\prime} \mathrm{E}_{\mathrm{CGG}}$ i-motif DNA.

Fig. S1: Variation of RMSD with respect to the initial energy minimized structure in case of studied i-motif systems: (a) $3^{\prime} E-$ form structure with hemi-protonated cytosines and normal cytosines at 300 K , (b) 3 'E-form structure with hemi-protonated cytosines at elevated temperatures, (c) $5^{\prime} \mathrm{E}-$ form structure with hemi-protonated cytosines and normal cytosines at 300 K , (d) $5^{\prime}$ 'E-form structure with hemi-protonated cytosines at elevated temperatures, (e) $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ and $5{ }^{\prime} \mathrm{E}_{\mathrm{CGG}}$-form structure with hemi-protonated cytosines at 300 K and (f) 5 'E-form structure with hemi-protonated cytosines and normal cytosine at 300 K with TIP3P water model.

Fig. S2: Representative backbone refined conformations of model (a)-(h) $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structures having different rotational orientation of intercalated base pair about its base pair helix axis and (i)-(p) tetranucleotide structures of two intercalated $\mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CC}$ dinuceotides with different helical rotations around their base pair helix axis.

Fig. S3: Root mean square fluctuation (RMSF) of the nucleotides in (a) $3^{\prime} \mathrm{E}$ and (b) $5^{\prime} \mathrm{E}$-form i motif structure under acidic pH with hemi-protonated cytosines.

Fig. S4: Distribution of distance between the N3 atoms of paired bases in equilibrated MD trajectory of 3 ' E (a) and $5^{\prime} \mathrm{E}$-form (b) i-motif structure with hemi-protonated cytosines, and distance matrix for the nucleobases in equilibrated conformation of $3^{\prime} \mathrm{E}$ (c) and $5^{\prime} \mathrm{E}$-form (d) i-motif structure with hemi-protonated cytosines.

Fig. S5: Variation of distance between the N3 atoms of paired bases along the MD simulated trajectory of $3^{\prime} \mathrm{E}$ (a)-(b) and $5^{\prime} \mathrm{E}$-form (c)-(d) structure in deprotonated state with normal cytosines.

Fig. S6: Average conformation of (a) $3^{\prime} E$ and (b) $5^{\prime} E$-form structure, and distance matrix for the nucleobases in equilibrated conformation of (c) $3^{\prime} \mathrm{E}$ and (d) $5^{\prime} \mathrm{E}$-form structure under neutral pH with deprotonated cytosines.

Fig. S7: Variation of distance between the N3 atoms of paired bases along the MD simulated trajectory of $3^{\prime} \mathrm{E}$ (a) and $5^{\prime} \mathrm{E}$-form (b) structure in deprotonated state with normal cytosine considering larger simulation box, and considering TIP3P water model in case of 5'E-form structure (c).

Fig. S8: $1^{\text {st }}$ and $2^{\text {nd }}$ normal mode of motions in the equilibrated MD trajectory of (a)-(b) $3^{\prime} E$ and (c)(d) $5^{\prime} \mathrm{E}$-form structure under neutral pH with deprotonated cytosines.

Fig. S9: Average structure of i-motif core in the equilibrated MD trajectory of (a) 3'E and (b) $5^{\prime} \mathrm{E}-$ form topology under acidic pH with hemi-protonted cytosines.

Fig. S10: Average values along with standard deviations of narrow grooves and wide grooves backbone phosphate-phosphate distances in (a)-(b) 3'E and (c)-(d) 5'E-form i-motif structure under acidic pH with hemi-protonted cytosines.

Fig. S11: Variation of energy of the sugar-phosphate backbone refined conformation of model (a) $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structure with helical rotations $(\theta)$ of the intercalated base pair around their base pair helix axis, and (b) tetranucleotide conformations of two intercalated $\mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CC}$ dinuceotides with helical rotations $(\theta)$ around their base pair helix axis.

Fig. S12: Radial distributions of the oxygen ( O ) atom of solvent water molecule around backbone phosphate group of bases $\left(g\left(r_{P-O}\right)\right)$ within i-motif core with hemi-protonated cytosines under acidic pH for (a) $3^{\prime} \mathrm{E}$ and (b) $5^{\prime} \mathrm{E}$-form structure, and in deprotonated state of cytosines under neutral pH for (c) $3^{\prime} E$ and (d) $5^{\prime} E$-form structure.

Fig. S13: Radial distributions of the oxygen (O) atoms of solvent water molecule around N 4 atom of cytosines $(g(r))$ within i-motif core in hemi-protonated and deprotonated state of cytosines for (a) 3'E and (b) 5'E-form structure considering SPC/E water model, and (c) 5'E-form structure considering TIP3P water model.

Fig. S14: Radial distributions of the oxygen (O) atoms of solvent water molecule around N 4 atom of cytosines $\left(g\left(r_{N 4-O}\right)\right.$ ) within i-motif core at elevated temperatures with hemi-protonated cytosines under acidic pH for (a) $3^{\prime} \mathrm{E}$ and (b) $5^{\prime} \mathrm{E}$-form i-motif structure.

Fig. S15: (a) DFT optimized geometry of six water molecules in wider grooves first solvation cell considering MD average model conformation of $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide within the i-motif core and fixing all the non-hydrogen atoms of the bases. (b) DFT optimized structure of a water molecule along with cytosine base.

Fig. S16: First normal mode of motions at different temperature in the equilibrated MD trajectory of (a)-(c) $3^{\prime} \mathrm{E}$ and (d)-(f) $5^{\prime} \mathrm{E}$-form i-motif structure under acidic pH with hemi-protonated cytosines.

Fig. S17: Root mean square fluctuation (RMSF) of the nucleotides at different temperature in (a) $3^{\prime} \mathrm{E}$ and (b) $5^{\prime} \mathrm{E}$-form i-motif structure with hemi-protonated cytosines under acidic pH .

Fig. S18: At different temperature distribution of wide grooves width in (a) $3^{\prime} \mathrm{E}$ and (b) $5^{\prime} \mathrm{E}$-form structure, narrow grooves width in (c) $3^{\prime} E$ and (d) $5^{\prime} E-$ form structure, and hydrogen bonding distance and angle between sugar oxygen O 4 ' of one strand and C 1 ' on the anti-parallel strand across the narrow grooves in (e) $3^{\prime} \mathrm{E}$ and (f) $5^{\prime} \mathrm{E}$-form structure, as derived from the equilibrated

MD trajectory of i-motif DNA under acidic pH with hemi-protonated cytosines.

Fig. S19: Temperature dependent grid water density distribution ( $\rho_{\text {wat }}$ ) around the i-motif core in (a)-(c) $3^{\prime} \mathrm{E}$ and (d)-(f) $5^{\prime} \mathrm{E}$-form structure under acidic pH having probability of water molecules stay in that grid points greater than 0.5 . Grid points are represented with a sphere of color tints wheat.

Fig. S20: (a) At different temperature distribution of number of water molecules forming hydrogen bonds with the N 4 atom of cytosines in the wide grooves of $5^{\prime}$ 'E-form i-motif DNA in equilibrated trajectory under acidic pH . (b) Distribution of hydrogen bonded life time at different temperature for the hydrogen bonded water molecules in the wide grooves of $5^{\prime} \mathrm{E}$-form structure with hemiprotonated cytosines.

Fig. S21: In case of $5^{\prime} \mathrm{E}_{\mathrm{CGG}}$ (a)-(b) and $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ (c)-(d) form structure first two normal modes of motions in the equilibrated trajectory. Distribution of (e) narrow grooves width and (f) hydrogen bonding distance and angle between sugar oxygen O 4 ' of one strand and $\mathrm{C1}^{\prime}$ on the anti-parallel strand across the narrow minor grooves in $5^{\prime} \mathrm{E}$ (TAA), $5^{\prime} \mathrm{E}_{\mathrm{CGG}}$ (CGG) and $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ (GCC) form structure, as derived from the equilibrated MD trajectory of i-motif DNA under acidic pH with hemi-protonted cytosines.

## Tables:

Table S1: Base pair orientational parameters in model $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structure (ABC/DEF) as derived from the NMR structure of i-motif DNA (PDB id: 1EL2).

| System | Base pair step parameters |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Base pair step | Shift <br> (Å) | Slide <br> (Å) | Rise <br> (Å) | Tilt <br> $\left({ }^{\circ}\right)$ | Roll <br> ( ${ }^{\circ}$ ) | Twist $\left({ }^{\circ}\right)$ |
| ABC/DEF ( $\left.\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}\right)$ trinucleotide conformation | $\begin{gathered} \mathrm{AB} / \mathrm{EF} \\ (\mathrm{~A}: \mathrm{F}:: \mathrm{B}: \mathrm{E}) \end{gathered}$ | -0.89 | 0.47 | 3.37 | 1.34 | 1.49 | 93.97 |
|  | $\begin{gathered} \mathrm{BC} / \mathrm{DE} \\ (\mathrm{~B}: \mathrm{E}:: \mathrm{C}: \mathrm{D}) \end{gathered}$ | 0.17 | 0.72 | 2.81 | 6.37 | 0.10 | 106.89 |
|  | Base pair parameters |  |  |  |  |  |  |
|  | Base pair | Shear <br> (A) | Stagger <br> (A) | Stretch <br> (A) | Buckle <br> $\left({ }^{\circ}\right)$ | Open <br> ${ }^{\circ}$ ) | Propeller <br> $\left({ }^{\circ}\right)$ |
|  | A:F | -0.13 | -0.42 | 2.76 | -6.78 | -0.11 | -0.64 |
|  | B:E | -0.55 | -0.12 | 2.75 | -12.79 | 0.85 | 1.08 |
|  | C:D | 0.69 | 0.06 | 2.73 | -7.25 | -0.47 | 3.13 |

Table S2: Configurational entropy of the core and loop regions of the i-motif in $3^{\prime} \mathrm{E}$ and $5^{\prime} \mathrm{E}$-form structure with hemi-protonated cytosines, derived from the normal mode analysis of equilibrated MD simulated trajectory at 300 K .

| System | Structural region | Configurational Entropy <br> (cal/mol-K) |
| :---: | :---: | :---: |
| 3'E-form structure <br> (3'E topology) | Core | 690.68 |
|  | Loop1 | 378.08 |
|  | Loop2 | 415.92 |
|  | Loop3 | 368.56 |
| 5'E-form structure |  |  |
|  |  |  |$\quad$ Core $\quad 607.20$

Table S3: Average value along with standard deviation of the base pair parameters as found in experimental dataset and MD simulation of $3^{\prime} \mathrm{E}$ and $5^{\prime} \mathrm{E}-$ form structure under acidic pH with hemiprotonated cytosines having two different topologies.

| System | Base pair | Shear <br> (A) | Stagger <br> (A) | Stretch <br> (A) | Buckle <br> $\left({ }^{\circ}\right)$ | Open <br> ${ }^{\circ}$ ) | Propeller $\left({ }^{\circ}\right)$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Experimental Dataset | $\mathrm{C}: \mathrm{C}^{+}$ | $\begin{gathered} -0.33 \\ {[0.60]} \end{gathered}$ | $\begin{gathered} 0.07 \\ {[0.35]} \end{gathered}$ | $\begin{gathered} 2.62 \\ {[0.20]} \end{gathered}$ | $\begin{gathered} 0.95 \\ {[8.79]} \end{gathered}$ | $\begin{gathered} 0.83 \\ {[2.97]} \end{gathered}$ | $\begin{gathered} 0.86 \\ {[8.80]} \end{gathered}$ |
| 3'E-form structure (3'E topology) | $\mathrm{C} 1: \mathrm{C}^{+} 12$ | $\begin{gathered} -0.22 \\ {[0.35]} \end{gathered}$ | $\begin{gathered} -0.18 \\ {[0.44]} \end{gathered}$ | $\begin{gathered} 2.88 \\ {[0.12]} \end{gathered}$ | $\begin{gathered} 13.19 \\ {[9.78]} \end{gathered}$ | $\begin{gathered} -3.44 \\ {[4.11]} \end{gathered}$ | $\begin{gathered} -4.49 \\ {[7.33]} \end{gathered}$ |
|  | $\mathrm{C} 2: \mathrm{C}^{+} 13$ | $\begin{gathered} -0.58 \\ {[0.25]} \end{gathered}$ | $\begin{gathered} 0.05 \\ {[0.29]} \end{gathered}$ | $\begin{gathered} 2.80 \\ {[0.09]} \end{gathered}$ | $\begin{gathered} 5.37 \\ {[9.12]} \end{gathered}$ | $\begin{gathered} -2.09 \\ {[3.16]} \end{gathered}$ | $\begin{gathered} 2.82 \\ {[5.85]} \end{gathered}$ |
|  | C6:C ${ }^{+} 17$ | $\begin{gathered} -0.57 \\ {[0.25]} \end{gathered}$ | $\begin{gathered} 0.09 \\ {[0.29]} \end{gathered}$ | $\begin{gathered} 2.81 \\ {[0.09]} \end{gathered}$ | $\begin{gathered} 13.11 \\ {[8.75]} \end{gathered}$ | $\begin{gathered} -2.71 \\ {[3.06]} \end{gathered}$ | $\begin{gathered} 3.42 \\ {[5.43]} \end{gathered}$ |
|  | C7:C ${ }^{+} 18$ | $\begin{gathered} -0.35 \\ {[0.25]} \end{gathered}$ | $\begin{gathered} 0.06 \\ {[0.30]} \end{gathered}$ | $\begin{gathered} 2.85 \\ {[0.08]} \end{gathered}$ | $\begin{gathered} 11.67 \\ {[8.63]} \end{gathered}$ | $\begin{gathered} -2.86 \\ {[2.95]} \end{gathered}$ | $\begin{gathered} -3.21 \\ {[6.05]} \end{gathered}$ |
|  | T5:T16 | $\begin{gathered} -2.06 \\ {[0.43]} \end{gathered}$ | $\begin{gathered} 0.27 \\ {[0.55]} \end{gathered}$ | $\begin{gathered} 2.95 \\ {[0.18]} \end{gathered}$ | $\begin{gathered} -16.41 \\ {[10.18]} \end{gathered}$ | $\begin{gathered} -0.62 \\ {[7.11]} \end{gathered}$ | $\begin{aligned} & 15.64 \\ & {[9.94]} \end{aligned}$ |
| 5'E-form structure (5'E topology) | $\mathrm{C} 1: \mathrm{C}^{+} 13$ | $\begin{gathered} -0.45 \\ {[0.27]} \end{gathered}$ | $\begin{gathered} 0.02 \\ {[0.31]} \end{gathered}$ | $\begin{gathered} 2.82 \\ {[0.09]} \end{gathered}$ | $\begin{gathered} -3.82 \\ {[8.34]} \end{gathered}$ | $\begin{gathered} -2.41 \\ {[3.28]} \end{gathered}$ | $\begin{gathered} 6.10 \\ {[6.47]} \end{gathered}$ |
|  | C2: $\mathrm{C}^{+} 14$ | $\begin{gathered} -0.56 \\ {[0.25]} \end{gathered}$ | $\begin{gathered} 0.02 \\ {[0.29]} \end{gathered}$ | $\begin{gathered} 2.80 \\ {[0.08]} \end{gathered}$ | $\begin{aligned} & 10.33 \\ & {[8.29} \end{aligned}$ | $\begin{gathered} -1.87 \\ {[2.96]} \end{gathered}$ | $\begin{gathered} 2.72 \\ {[5.69]} \end{gathered}$ |
|  | C3:C ${ }^{+} 15$ | $\begin{gathered} -0.36 \\ {[0.29]} \end{gathered}$ | $\begin{gathered} 0.05 \\ {[0.31]} \end{gathered}$ | $\begin{gathered} 2.84 \\ {[0.09]} \end{gathered}$ | $\begin{aligned} & 15.77 \\ & {[9.12]} \end{aligned}$ | $\begin{gathered} -2.50 \\ {[3.06]} \end{gathered}$ | $\begin{gathered} -0.77 \\ {[6.78]} \end{gathered}$ |
|  | $\mathrm{C}^{+}:$C19 | $\begin{gathered} -0.18 \\ {[0.31]} \end{gathered}$ | $\begin{gathered} 0.05 \\ {[0.36]} \end{gathered}$ | $\begin{gathered} 2.86 \\ {[0.09]} \end{gathered}$ | $\begin{gathered} -12.15 \\ {[14.11]} \end{gathered}$ | $\begin{gathered} 2.67 \\ {[3.43]} \end{gathered}$ | $\begin{gathered} 7.71 \\ {[9.49]} \end{gathered}$ |
|  | C8 ${ }^{+}$: C 20 | $\begin{gathered} -0.70 \\ {[0.24]} \end{gathered}$ | $\begin{gathered} 0.05 \\ {[0.27]} \end{gathered}$ | $\begin{gathered} 2.78 \\ {[0.09]} \end{gathered}$ | $\begin{gathered} 3.77 \\ {[8.73]} \end{gathered}$ | $\begin{gathered} 2.71 \\ {[3.23]} \end{gathered}$ | $\begin{gathered} 0.93 \\ {[5.82]} \end{gathered}$ |
|  | $\mathrm{C} 9^{+}: \mathrm{C} 21$ | $\begin{gathered} -0.52 \\ {[0.25]} \end{gathered}$ | $\begin{gathered} -0.01 \\ {[0.29]} \end{gathered}$ | $\begin{gathered} 2.83 \\ {[0.09]} \end{gathered}$ | $\begin{gathered} 14.15 \\ {[8.19]} \end{gathered}$ | $\begin{gathered} 2.66 \\ {[3.14]} \end{gathered}$ | $\begin{gathered} -1.68 \\ {[5.47]} \end{gathered}$ |
|  | T10:T22 | $\begin{gathered} 2.47 \\ {[0.28]} \end{gathered}$ | $\begin{gathered} 0.00 \\ {[0.42]} \end{gathered}$ | $\begin{gathered} 2.84 \\ {[0.12]} \end{gathered}$ | $\begin{gathered} 20.19 \\ {[8.85]} \end{gathered}$ | $\begin{gathered} -1.40 \\ {[5.61]} \end{gathered}$ | $\begin{gathered} -16.57 \\ {[7.45]} \end{gathered}$ |

Table S4: Average value along with standard deviation of the backbone dihedral angles for the bases as found in MD simulation of $5^{\prime} \mathrm{E}$-form i-motif structure under acidic pH with hemi-protonated cytosines.

| Nucleotide | $\alpha\left({ }^{\circ}\right)$ | $\beta\left({ }^{\circ}\right)$ | $\gamma\left({ }^{\circ}\right)$ | $\delta\left({ }^{\circ}\right)$ | $\varepsilon\left(^{\circ}\right)$ | $\zeta\left({ }^{\circ}\right)$ | $\chi\left({ }^{\circ}\right)$ | Phase ( ${ }^{\circ}$ ) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| C1 | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 65.50 \\ & {[22.5]} \end{aligned}$ | $\begin{aligned} & 88.79 \\ & {[21.4]} \end{aligned}$ | $\begin{gathered} 200.27 \\ {[19.1]} \end{gathered}$ | $\begin{gathered} 275.07 \\ {[9.9]} \end{gathered}$ | $\begin{gathered} -127.60 \\ {[10.7]} \end{gathered}$ | $\begin{aligned} & 51.68 \\ & {[41.6]} \end{aligned}$ |
| C2 | $\begin{gathered} 293.27 \\ {[15.8]} \end{gathered}$ | $\begin{aligned} & 174.64 \\ & {[21.5]} \end{aligned}$ | $\begin{gathered} 73.19 \\ {[27.2]} \end{gathered}$ | $\begin{gathered} 86.59 \\ {[10.3]} \end{gathered}$ | $\begin{aligned} & 192.10 \\ & {[10.4]} \end{aligned}$ | $\begin{gathered} 277.85 \\ {[8.2]} \end{gathered}$ | $\begin{gathered} -127.94 \\ {[8.4]} \end{gathered}$ | $\begin{aligned} & 35.64 \\ & {[27.2]} \end{aligned}$ |
| C3 | $\begin{gathered} 293.31 \\ {[26.0]} \end{gathered}$ | $\begin{aligned} & 176.78 \\ & {[10.6]} \end{aligned}$ | $\begin{gathered} 71.73 \\ {[23.3]} \end{gathered}$ | $\begin{gathered} 94.08 \\ {[19.5]} \end{gathered}$ | $\begin{gathered} 214.75 \\ {[15.4]} \end{gathered}$ | $\begin{gathered} 294.15 \\ {[10.4]} \end{gathered}$ | $\begin{gathered} -125.34 \\ {[13.2]} \end{gathered}$ | $\begin{aligned} & 53.57 \\ & {[43.6]} \end{aligned}$ |
| T4 | $\begin{gathered} 276.27 \\ {[27.1]} \end{gathered}$ | $\begin{gathered} 220.08 \\ {[36.7]} \end{gathered}$ | $\begin{aligned} & 301.10 \\ & {[14.1]} \end{aligned}$ | $\begin{aligned} & 142.80 \\ & {[12.6]} \end{aligned}$ | $\begin{gathered} 188.65 \\ {[9.5]} \end{gathered}$ | $\begin{gathered} 277.37 \\ {[9.2]} \end{gathered}$ | $\begin{gathered} -114.40 \\ {[14.7]} \end{gathered}$ | $\begin{aligned} & 154.97 \\ & {[16.6]} \end{aligned}$ |
| A5 | $\begin{gathered} 288.72 \\ {[9.7]} \end{gathered}$ | $\begin{gathered} 171.07 \\ {[8.7]} \end{gathered}$ | $\begin{gathered} 55.65 \\ {[9.7]} \end{gathered}$ | $\begin{aligned} & 136.17 \\ & {[12.1]} \end{aligned}$ | $\begin{gathered} 230.14 \\ {[17.2]} \end{gathered}$ | $\begin{gathered} 289.39 \\ {[25.5]} \end{gathered}$ | $\begin{aligned} & -99.12 \\ & {[14.5]} \end{aligned}$ | $\begin{aligned} & 145.52 \\ & {[19.8]} \end{aligned}$ |
| A6 | $\begin{aligned} & 190.18 \\ & {[66.9]} \end{aligned}$ | $\begin{aligned} & 180.24 \\ & {[11.6]} \end{aligned}$ | $\begin{gathered} 58.34 \\ {[13.4]} \end{gathered}$ | $\begin{gathered} 150.02 \\ {[9.3]} \end{gathered}$ | $\begin{gathered} 209.52 \\ {[19.2]} \end{gathered}$ | $\begin{gathered} 280.66 \\ {[10.5]} \end{gathered}$ | $\begin{gathered} -132.61 \\ {[26.8]} \end{gathered}$ | $\begin{aligned} & 177.43 \\ & {[23.3]} \end{aligned}$ |
| $\mathrm{C}^{+} 7$ | $\begin{gathered} 294.27 \\ {[9.36]} \end{gathered}$ | $\begin{aligned} & 182.68 \\ & {[12.4]} \end{aligned}$ | $\begin{gathered} 66.40 \\ {[9.5]} \end{gathered}$ | $\begin{aligned} & 86.06 \\ & {[8.6]} \end{aligned}$ | $\begin{aligned} & 190.20 \\ & {[11.6]} \end{aligned}$ | $\begin{gathered} 272.54 \\ {[11.9]} \end{gathered}$ | $\begin{gathered} -124.71 \\ {[14.5]} \end{gathered}$ | $\begin{aligned} & 24.34 \\ & {[13.2]} \end{aligned}$ |
| $\mathrm{C}^{+} 8$ | $\begin{gathered} 295.76 \\ {[10.6]} \end{gathered}$ | $\begin{aligned} & 181.26 \\ & {[10.6]} \end{aligned}$ | $\begin{gathered} 68.52 \\ {[9.3]} \end{gathered}$ | $\begin{aligned} & 100.41 \\ & {[20.8]} \end{aligned}$ | $\begin{gathered} 188.32 \\ {[8.9]} \end{gathered}$ | $\begin{gathered} 275.30 \\ {[10.7]} \end{gathered}$ | $\begin{gathered} -121.21 \\ {[11.0]} \end{gathered}$ | $\begin{aligned} & 46.06 \\ & {[45.3]} \end{aligned}$ |
| $\mathrm{C}^{+} 9$ | $\begin{gathered} 292.61 \\ {[28.6]} \end{gathered}$ | $\begin{aligned} & 180.31 \\ & {[10.2]} \end{aligned}$ | $\begin{gathered} 76.32 \\ {[18.8]} \end{gathered}$ | $\begin{aligned} & 125.24 \\ & {[21.8]} \end{aligned}$ | $\begin{aligned} & 195.91 \\ & {[14.4]} \end{aligned}$ | $\begin{gathered} 253.92 \\ {[24.4]} \end{gathered}$ | $\begin{gathered} -111.04 \\ {[13.7]} \end{gathered}$ | $\begin{aligned} & 122.74 \\ & {[40.7]} \end{aligned}$ |
| T10 | $\begin{gathered} 290.17 \\ {[11.9]} \end{gathered}$ | $\begin{aligned} & 184.19 \\ & {[22.4]} \end{aligned}$ | $\begin{gathered} 56.88 \\ {[10.8]} \end{gathered}$ | $\begin{aligned} & 137.96 \\ & {[10.0]} \end{aligned}$ | $\begin{aligned} & 193.81 \\ & {[14.6]} \end{aligned}$ | $\begin{gathered} 271.52 \\ {[20.5]} \end{gathered}$ | $\begin{gathered} -96.76 \\ {[14.0]} \end{gathered}$ | $\begin{aligned} & 149.41 \\ & {[15.1]} \end{aligned}$ |
| A11 | $\begin{gathered} 280.32 \\ {[13.5]} \end{gathered}$ | $\begin{gathered} 69.59 \\ {[9.49]} \end{gathered}$ | $\begin{gathered} 179.67 \\ {[8.2]} \end{gathered}$ | $\begin{aligned} & 146.36 \\ & {[11.7]} \end{aligned}$ | $\begin{gathered} 243.07 \\ {[28.4]} \end{gathered}$ | $\begin{aligned} & 168.20 \\ & {[11.4]} \end{aligned}$ | $\begin{gathered} -133.02 \\ {[23.5]} \end{gathered}$ | $\begin{aligned} & 158.36 \\ & {[18.0]} \end{aligned}$ |
| A12 | $\begin{gathered} 75.59 \\ {[15.8]} \end{gathered}$ | $\begin{aligned} & 182.29 \\ & {[24.1]} \end{aligned}$ | $\begin{gathered} 60.11 \\ {[13.1]} \end{gathered}$ | $\begin{gathered} 148.06 \\ {[9.1]} \end{gathered}$ | $\begin{gathered} 228.80 \\ {[34.0]} \end{gathered}$ | $\begin{gathered} 70.33 \\ {[34.2]} \end{gathered}$ | $\begin{gathered} -121.14 \\ {[22.4]} \end{gathered}$ | $\begin{aligned} & 167.81 \\ & {[18.8]} \end{aligned}$ |
| $\mathrm{C}^{+} 13$ | $\begin{gathered} 269.83 \\ {[17.9]} \end{gathered}$ | $\begin{aligned} & 168.71 \\ & {[30.3]} \end{aligned}$ | $\begin{gathered} 61.10 \\ {[13.7]} \end{gathered}$ | $\begin{aligned} & 96.81 \\ & {[21.5]} \end{aligned}$ | $\begin{gathered} 209.87 \\ {[25.1]} \end{gathered}$ | $\begin{gathered} 272.57 \\ {[14.4]} \end{gathered}$ | $\begin{gathered} -138.58 \\ {[11.4]} \end{gathered}$ | $\begin{gathered} 64.07 \\ {[38.3]} \end{gathered}$ |
| $\mathrm{C}^{+} 14$ | $\begin{gathered} 292.28 \\ {[21.3]} \end{gathered}$ | $\begin{aligned} & 173.53 \\ & {[30.3]} \end{aligned}$ | $\begin{gathered} 72.02 \\ {[18.0]} \end{gathered}$ | $\begin{aligned} & 130.66 \\ & {[19.6]} \end{aligned}$ | $\begin{aligned} & 198.58 \\ & {[15.1]} \end{aligned}$ | $\begin{gathered} 260.62 \\ {[23.6]} \end{gathered}$ | $\begin{gathered} -108.23 \\ {[16.2]} \end{gathered}$ | $\begin{aligned} & 135.25 \\ & {[31.0]} \end{aligned}$ |
| $\mathrm{C}^{+} 15$ | $\begin{gathered} 276.40 \\ {[24.8]} \end{gathered}$ | $\begin{aligned} & 181.50 \\ & {[17.5]} \end{aligned}$ | $\begin{aligned} & 69.62 \\ & {[34.7]} \end{aligned}$ | $\begin{aligned} & 109.65 \\ & {[19.8]} \end{aligned}$ | $\begin{gathered} 236.59 \\ {[27.9]} \end{gathered}$ | $\begin{gathered} 273.22 \\ {[18.4]} \end{gathered}$ | $\begin{gathered} -106.18 \\ {[14.4]} \end{gathered}$ | $\begin{aligned} & 103.76 \\ & {[34.1]} \end{aligned}$ |
| T16 | $\begin{gathered} 237.20 \\ {[46.4]} \end{gathered}$ | $\begin{aligned} & 193.16 \\ & {[32.3]} \end{aligned}$ | $\begin{gathered} 60.26 \\ {[14.91]} \end{gathered}$ | $\begin{gathered} 145.69 \\ {[7.9]} \end{gathered}$ | $\begin{aligned} & 199.96 \\ & {[9.86]} \end{aligned}$ | $\begin{gathered} 282.87 \\ {[10.8]} \end{gathered}$ | $\begin{gathered} -130.09 \\ {[14.6]} \end{gathered}$ | $\begin{aligned} & 163.42 \\ & {[13.7]} \end{aligned}$ |
| A17 | $\begin{gathered} 277.24 \\ {[12.0]} \end{gathered}$ | $\begin{gathered} 172.33 \\ {[8.9]} \end{gathered}$ | $\begin{aligned} & 48.86 \\ & {[12.8]} \end{aligned}$ | $\begin{aligned} & 136.15 \\ & {[10.7]} \end{aligned}$ | $\begin{aligned} & 223.42 \\ & {[20.31]} \end{aligned}$ | $\begin{gathered} 289.68 \\ {[9.8]} \end{gathered}$ | $\begin{gathered} -92.19 \\ {[15.4]} \end{gathered}$ | $\begin{aligned} & 146.04 \\ & {[15.9]} \end{aligned}$ |
| A18 | $\begin{aligned} & 262.73 \\ & {[41.4]} \end{aligned}$ | $\begin{aligned} & 173.27 \\ & {[18.0]} \end{aligned}$ | $\begin{aligned} & 81.32 \\ & {[25.4]} \end{aligned}$ | $\begin{gathered} 156.09 \\ {[7.3]} \end{gathered}$ | $\begin{gathered} 214.10 \\ {[30.0]} \end{gathered}$ | $\begin{aligned} & 164.33 \\ & {[21.8]} \end{aligned}$ | $\begin{gathered} -94.10 \\ {[25.2]} \end{gathered}$ | $\begin{aligned} & 179.20 \\ & {[13.5]} \end{aligned}$ |
| C19 | $\begin{aligned} & 224.15 \\ & {[29.8]} \end{aligned}$ | $\begin{aligned} & 177.66 \\ & {[16.0]} \end{aligned}$ | $\begin{aligned} & 69.53 \\ & {[38.6]} \end{aligned}$ | $\begin{aligned} & 104.92 \\ & {[24.1]} \end{aligned}$ | $\begin{gathered} 203.87 \\ {[12.6]} \end{gathered}$ | $\begin{gathered} 280.29 \\ {[9.9]} \end{gathered}$ | $\begin{gathered} -117.05 \\ {[11.0]} \end{gathered}$ | $\begin{aligned} & 38.22 \\ & {[51.9]} \end{aligned}$ |
| C20 | $\begin{gathered} 287.79 \\ {[27.6]} \end{gathered}$ | $\begin{aligned} & 172.51 \\ & {[18.1]} \end{aligned}$ | $\begin{gathered} 86.28 \\ {[30.8]} \end{gathered}$ | $\begin{aligned} & 83.23 \\ & {[9.6]} \end{aligned}$ | $\begin{aligned} & 190.37 \\ & {[10.5]} \end{aligned}$ | $\begin{gathered} 276.32 \\ {[8.6]} \end{gathered}$ | $\begin{gathered} -126.45 \\ {[9.3]} \end{gathered}$ | $\begin{aligned} & 39.80 \\ & {[24.8]} \end{aligned}$ |
| C21 | $\begin{gathered} 295.25 \\ {[20.1]} \end{gathered}$ | $\begin{aligned} & 177.06 \\ & {[8.42]} \end{aligned}$ | $\begin{gathered} 69.24 \\ {[16.15]} \end{gathered}$ | $\begin{aligned} & 82.31 \\ & {[8.0]} \end{aligned}$ | $\begin{aligned} & 197.30 \\ & {[18.5]} \end{aligned}$ | $\begin{gathered} 278.44 \\ {[10.5]} \end{gathered}$ | $\begin{gathered} -127.35 \\ {[8.6]} \end{gathered}$ | $\begin{gathered} 38.64 \\ {[19.8]} \end{gathered}$ |
| T22 | $\begin{gathered} 289.40 \\ {[21.5]} \end{gathered}$ | $\begin{aligned} & 152.57 \\ & {[45.7]} \end{aligned}$ | $\begin{aligned} & 88.33 \\ & {[33.2]} \end{aligned}$ | $\begin{aligned} & 120.28 \\ & {[40.0]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{gathered} -122.07 \\ {[15.8]} \end{gathered}$ | $\begin{aligned} & 108.77 \\ & {[46.8]} \end{aligned}$ |

Table S5: Average value along with standard deviation of the backbone dihedral angles for the bases as found in MD simulation of $3^{\prime} \mathrm{E}$-form i-motif structure under acidic pH with hemi-protonated cytosines.

| Nucleotide | $\alpha{ }^{\circ}$ ) | $\beta\left({ }^{\circ}\right.$ | $\gamma\left({ }^{\circ}\right)$ | $\delta\left({ }^{\circ}\right)$ | $\varepsilon\left(^{\circ}\right)$ | $\zeta\left({ }^{\circ}\right)$ | $\chi\left({ }^{\circ}\right)$ | Phase ( ${ }^{\circ}$ ) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| C1 | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 65.09 \\ & {[25.4]} \end{aligned}$ | $\begin{aligned} & 124.92 \\ & {[21.0]} \end{aligned}$ | $\begin{aligned} & 235.57 \\ & {[23.2]} \end{aligned}$ | $\begin{gathered} 288.78 \\ {[11.6]} \end{gathered}$ | $\begin{gathered} -129.75 \\ {[11.7]} \end{gathered}$ | $\begin{aligned} & 137.75 \\ & {[22.5]} \end{aligned}$ |
| C2 | $\begin{gathered} 231.57 \\ {[50.3]} \end{gathered}$ | $\begin{aligned} & 110.39 \\ & {[52.3]} \end{aligned}$ | $\begin{aligned} & 188.77 \\ & {[10.8]} \end{aligned}$ | $\begin{aligned} & 119.18 \\ & {[21.6]} \end{aligned}$ | $\begin{aligned} & 227.06 \\ & {[25.9]} \end{aligned}$ | $\begin{aligned} & 268.75 \\ & {[21.9]} \end{aligned}$ | $\begin{gathered} -127.23 \\ {[14.2]} \end{gathered}$ | $\begin{aligned} & 135.11 \\ & {[14.8]} \end{aligned}$ |
| T3 | $\begin{aligned} & 76.43 \\ & {[27.0]} \end{aligned}$ | $\begin{aligned} & 159.50 \\ & {[20.7]} \end{aligned}$ | $\begin{aligned} & 62.43 \\ & {[17.3]} \end{aligned}$ | $\begin{gathered} 147.46 \\ {[7.1]} \end{gathered}$ | $\begin{aligned} & 236.96 \\ & {[36.5]} \end{aligned}$ | $\begin{aligned} & 284.11 \\ & {[12.5]} \end{aligned}$ | $\begin{gathered} -128.42 \\ {[16.9]} \end{gathered}$ | $\begin{aligned} & 165.00 \\ & {[11.8]} \end{aligned}$ |
| T4 | $\begin{gathered} 94.94 \\ {[39.0]} \end{gathered}$ | $\begin{aligned} & 175.01 \\ & {[13.7]} \end{aligned}$ | $\begin{gathered} 300.14 \\ {[12.0]} \end{gathered}$ | $\begin{gathered} 150.13 \\ {[9.1]} \end{gathered}$ | $\begin{aligned} & 266.45 \\ & {[24.2]} \end{aligned}$ | $\begin{gathered} 71.59 \\ {[26.0]} \end{gathered}$ | $\begin{gathered} -128.53 \\ {[14.8]} \end{gathered}$ | $\begin{aligned} & 163.81 \\ & {[13.9]} \end{aligned}$ |
| T5 | $\begin{aligned} & 246.77 \\ & {[14.5]} \end{aligned}$ | $\begin{aligned} & 168.95 \\ & {[14.4]} \end{aligned}$ | $\begin{aligned} & 55.35 \\ & {[9.5]} \end{aligned}$ | $\begin{gathered} 94.51 \\ {[14.7]} \end{gathered}$ | $\begin{gathered} 186.82 \\ {[9.1]} \end{gathered}$ | $\begin{gathered} 276.13 \\ {[8.2]} \end{gathered}$ | $\begin{gathered} -107.45 \\ {[9.9]} \end{gathered}$ | $\begin{gathered} 2.97 \\ {[21.8]} \end{gathered}$ |
| C6 | $\begin{gathered} 300.37 \\ {[9.1]} \end{gathered}$ | $\begin{gathered} 173.03 \\ {[8.8]} \\ \hline \end{gathered}$ | $\begin{gathered} 65.10 \\ {[8.4]} \end{gathered}$ | $\begin{aligned} & 84.94 \\ & {[7.7]} \end{aligned}$ | $\begin{gathered} 193.94 \\ {[8.9]} \end{gathered}$ | $\begin{gathered} 279.25 \\ {[8.2]} \\ \hline \end{gathered}$ | $\begin{gathered} -131.57 \\ {[7.9]} \end{gathered}$ | $\begin{aligned} & 26.84 \\ & {[17.9]} \end{aligned}$ |
| C7 | $\begin{gathered} 301.01 \\ {[9.6]} \end{gathered}$ | $\begin{aligned} & 180.15 \\ & {[10.3]} \end{aligned}$ | $\begin{gathered} 72.17 \\ {[10.4]} \end{gathered}$ | $\begin{aligned} & 88.59 \\ & {[7.2]} \end{aligned}$ | $\begin{aligned} & 202.71 \\ & {[17.8]} \end{aligned}$ | $\begin{gathered} 287.51 \\ {[12.6]} \end{gathered}$ | $\begin{gathered} -120.42 \\ {[15.2]} \end{gathered}$ | $\begin{gathered} 34.61 \\ {[14.9]} \end{gathered}$ |
| T8 | $\begin{gathered} 291.39 \\ {[9.5]} \end{gathered}$ | $\begin{gathered} 175.0 \\ {[10.2]} \end{gathered}$ | $\begin{aligned} & 62.25 \\ & {[9.9]} \end{aligned}$ | $\begin{gathered} 141.51 \\ {[9.9]} \end{gathered}$ | $\begin{aligned} & 211.02 \\ & {[29.4]} \end{aligned}$ | $\begin{gathered} 255.65 \\ {[30.8]} \end{gathered}$ | $\begin{gathered} -116.73 \\ {[17.6]} \end{gathered}$ | $\begin{aligned} & 156.40 \\ & {[16.7]} \end{aligned}$ |
| T9 | $\begin{aligned} & 122.35 \\ & {[31.9]} \end{aligned}$ | $\begin{aligned} & 184.18 \\ & {[21.5]} \end{aligned}$ | $\begin{gathered} 56.49 \\ {[12.6]} \end{gathered}$ | $\begin{gathered} 146.84 \\ {[8.6]} \end{gathered}$ | $\begin{gathered} 201.78 \\ {[11.8]} \end{gathered}$ | $\begin{gathered} 285.70 \\ {[8.7]} \end{gathered}$ | $\begin{gathered} -137.67 \\ {[16.9]} \end{gathered}$ | $\begin{aligned} & 161.70 \\ & {[13.5]} \end{aligned}$ |
| T10 | $\begin{gathered} 279.48 \\ {[11.0]} \end{gathered}$ | $\begin{aligned} & 174.19 \\ & {[11.3]} \end{aligned}$ | $\begin{aligned} & 46.60 \\ & {[17.7]} \end{aligned}$ | $\begin{aligned} & 127.15 \\ & {[18.2]} \end{aligned}$ | $\begin{aligned} & 187.85 \\ & {[11.2]} \end{aligned}$ | $\begin{gathered} 274.81 \\ {[10.5]} \end{gathered}$ | $\begin{gathered} -109.24 \\ {[16.5]} \end{gathered}$ | $\begin{aligned} & 135.49 \\ & {[27.6]} \end{aligned}$ |
| A11 | $\begin{gathered} 285.95 \\ {[10.9]} \\ \hline \end{gathered}$ | $\begin{gathered} 171.38 \\ {[9.7]} \end{gathered}$ | $\begin{aligned} & 54.08 \\ & {[8.8]} \end{aligned}$ | $\begin{aligned} & 104.06 \\ & {[26.8]} \end{aligned}$ | $\begin{aligned} & 195.83 \\ & {[11.2]} \end{aligned}$ | $\begin{gathered} 275.77 \\ {[10.4]} \end{gathered}$ | $\begin{gathered} -121.30 \\ {[14.5]} \\ \hline \end{gathered}$ | $\begin{aligned} & 85.32 \\ & {[35.2]} \end{aligned}$ |
| $\mathrm{C}^{+} 12$ | $\begin{gathered} 298.31 \\ {[10.4]} \end{gathered}$ | $\begin{gathered} 180.33 \\ {[9.9]} \end{gathered}$ | $\begin{aligned} & 66.73 \\ & {[10.3]} \end{aligned}$ | $\begin{aligned} & 115.58 \\ & {[24.4]} \end{aligned}$ | $\begin{aligned} & 193.94 \\ & {[13.1]} \end{aligned}$ | $\begin{aligned} & 261.79 \\ & {[19.5]} \end{aligned}$ | $\begin{gathered} -116.53 \\ {[15.6]} \end{gathered}$ | $\begin{aligned} & 101.53 \\ & {[38.5]} \end{aligned}$ |
| $\mathrm{C}^{+} 13$ | $\begin{gathered} 297.38 \\ {[15.3]} \\ \hline \end{gathered}$ | $\begin{aligned} & 182.67 \\ & {[11.7]} \end{aligned}$ | $\begin{gathered} 56.49 \\ {[12.6]} \\ \hline \end{gathered}$ | $\begin{aligned} & 126.90 \\ & {[17.3]} \\ & \hline \end{aligned}$ | $\begin{gathered} 214.86 \\ {[30.2]} \end{gathered}$ | $\begin{gathered} 222.81 \\ {[28.8]} \end{gathered}$ | $\begin{gathered} -106.94 \\ {[11.5]} \end{gathered}$ | $\begin{aligned} & 131.48 \\ & {[32.4]} \\ & \hline \end{aligned}$ |
| T14 | $\begin{aligned} & 59.28 \\ & {[14.3]} \end{aligned}$ | $\begin{aligned} & 172.06 \\ & {[18.3]} \end{aligned}$ | $\begin{gathered} 289.35 \\ {[17.4]} \end{gathered}$ | $\begin{aligned} & 147.60 \\ & {[11.2]} \end{aligned}$ | $\begin{gathered} 213.24 \\ {[18.5]} \end{gathered}$ | $\begin{aligned} & 172.73 \\ & {[15.1]} \end{aligned}$ | $\begin{aligned} & 62.92 \\ & {[12.3]} \end{aligned}$ | $\begin{aligned} & 158.90 \\ & {[15.0]} \end{aligned}$ |
| T15 | $\begin{aligned} & 68.28 \\ & {[13.1]} \end{aligned}$ | $\begin{aligned} & 200.86 \\ & {[21.0]} \end{aligned}$ | $\begin{aligned} & 55.57 \\ & {[10.2]} \end{aligned}$ | $\begin{aligned} & 136.71 \\ & {[11.0]} \end{aligned}$ | $\begin{aligned} & 219.95 \\ & {[24.8]} \end{aligned}$ | $\begin{aligned} & 45.73 \\ & {[13.7]} \end{aligned}$ | $\begin{gathered} -126.65 \\ {[21.8]} \end{gathered}$ | $\begin{aligned} & 151.39 \\ & {[20.2]} \end{aligned}$ |
| T16 | $\begin{gathered} 74.60 \\ {[11.9]} \end{gathered}$ | $\begin{aligned} & 179.60 \\ & {[14.5]} \end{aligned}$ | $\begin{gathered} 301.43 \\ {[9.1]} \end{gathered}$ | $\begin{gathered} 83.05 \\ {[12.0]} \end{gathered}$ | $\begin{aligned} & 188.78 \\ & {[10.0]} \end{aligned}$ | $\begin{gathered} 269.89 \\ {[8.8]} \end{gathered}$ | $\begin{gathered} -129.73 \\ {[9.5]} \end{gathered}$ | $\begin{aligned} & 38.06 \\ & {[24.5]} \end{aligned}$ |
| $\mathrm{C}^{+} 17$ | $\begin{aligned} & 304.72 \\ & {[10.3]} \end{aligned}$ | $\begin{gathered} 180.11 \\ {[9.4]} \end{gathered}$ | $\begin{aligned} & 73.49 \\ & {[9.2]} \end{aligned}$ | $\begin{aligned} & 135.09 \\ & {[20.6]} \end{aligned}$ | $\begin{aligned} & 195.11 \\ & {[14.4]} \end{aligned}$ | $\begin{gathered} 256.00 \\ {[21.2]} \end{gathered}$ | $\begin{gathered} -110.25 \\ {[13.5]} \end{gathered}$ | $\begin{aligned} & 164.42 \\ & {[24.5]} \end{aligned}$ |
| $\mathrm{C}^{+} 18$ | $\begin{gathered} 289.52 \\ {[24.3]} \end{gathered}$ | $\begin{aligned} & 181.62 \\ & {[23.5]} \end{aligned}$ | $\begin{gathered} 66.92 \\ {[29.6]} \end{gathered}$ | $\begin{aligned} & 129.90 \\ & {[18.1]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{gathered} 0.00 \\ {[0.0]} \end{gathered}$ | $\begin{gathered} -102.23 \\ {[15.4]} \end{gathered}$ | $\begin{aligned} & 136.48 \\ & {[27.1]} \end{aligned}$ |

Table S6: Average value along with standard deviation of the base pair parameters as found in MD simulation of $5^{\prime} \mathrm{E}$-form structure in deprotonated state with normal cytosines.

| System | Base pair | Shear <br> (Å) | Stagger <br> (Å) | Stretch <br> (A) | Buckle <br> $\left({ }^{\circ}\right)$ | Open <br> $\left({ }^{\circ}\right)$ | Propeller $\left({ }^{\circ}\right)$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 5'E-form structure with normal cytosine | C1:C13 | $\begin{aligned} & 6.50 \\ & {[1.5]} \end{aligned}$ | $\begin{gathered} -1.47 \\ {[1.9]} \end{gathered}$ | $\begin{aligned} & 3.92 \\ & {[2.3]} \end{aligned}$ | $\begin{aligned} & -55.86 \\ & {[15.7]} \end{aligned}$ | $\begin{aligned} & -30.62 \\ & {[19.3]} \end{aligned}$ | $\begin{aligned} & 12.66 \\ & {[15.5]} \end{aligned}$ |
|  | C2:C14 | $\begin{aligned} & 1.99 \\ & {[2.4]} \end{aligned}$ | $\begin{gathered} -0.35 \\ {[1.8]} \end{gathered}$ | $\begin{aligned} & 3.70 \\ & {[1.2]} \end{aligned}$ | $\begin{gathered} 17.30 \\ {[37.2]} \end{gathered}$ | $\begin{aligned} & 30.90 \\ & {[24.5]} \end{aligned}$ | $\begin{aligned} & 40.21 \\ & {[20.0]} \end{aligned}$ |
|  | C3:C15 | $\begin{aligned} & 2.46 \\ & {[0.4]} \end{aligned}$ | $\begin{gathered} 2.40 \\ {[0.7]} \end{gathered}$ | $\begin{aligned} & 2.88 \\ & {[0.7]} \end{aligned}$ | $\begin{gathered} 53.26 \\ {[14.0]} \end{gathered}$ | $\begin{gathered} -40.98 \\ {[10.3]} \end{gathered}$ | $\begin{gathered} 74.92 \\ {[9.0]} \end{gathered}$ |
|  | C7:C19 | $\begin{aligned} & -2.35 \\ & {[0.8]} \end{aligned}$ | $\begin{gathered} 6.13 \\ {[0.7]} \end{gathered}$ | $\begin{gathered} 5.44 \\ {[0.7]} \end{gathered}$ | $\begin{aligned} & -31.45 \\ & {[11.8]} \end{aligned}$ | $\begin{gathered} -13.84 \\ {[8.3]} \end{gathered}$ | $\begin{gathered} -30.43 \\ {[8.1]} \end{gathered}$ |
|  | C8:C20 | $\begin{aligned} & -2.47 \\ & {[1.1]} \end{aligned}$ | $\begin{aligned} & 9.25 \\ & {[1.0]} \end{aligned}$ | $\begin{aligned} & 1.52 \\ & {[1.3]} \end{aligned}$ | $\begin{aligned} & 36.62 \\ & {[20.6]} \end{aligned}$ | $\begin{aligned} & 48.27 \\ & {[10.9]} \end{aligned}$ | $\begin{gathered} 2.95 \\ {[13.5]} \end{gathered}$ |
|  | C9:C21 | $\begin{aligned} & 0.26 \\ & {[1.4]} \end{aligned}$ | $\begin{aligned} & 0.78 \\ & {[1.7]} \end{aligned}$ | $\begin{aligned} & 3.13 \\ & {[0.9]} \end{aligned}$ | $\begin{aligned} & 47.57 \\ & {[30.8]} \end{aligned}$ | $\begin{aligned} & 17.88 \\ & {[25.5]} \end{aligned}$ | $\begin{aligned} & 67.98 \\ & {[44.1]} \end{aligned}$ |

Table S7: Average value along with standard deviation of the backbone dihedral angles for the bases as found in MD simulation of $5^{\prime} \mathrm{E}$-form structure in deprotonated state with normal cytosines.

| Nucleotide | $\alpha\left({ }^{\circ}\right)$ | $\beta\left({ }^{\circ}\right)$ | $\gamma\left({ }^{\circ}\right)$ | $\delta\left({ }^{\circ}\right)$ | $\varepsilon\left(^{\circ}\right)$ | $\zeta\left({ }^{\circ}\right)$ | $\chi\left({ }^{\circ}\right)$ | Phase ( ${ }^{\circ}$ ) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| C1 | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 63.69 \\ & {[19.4]} \end{aligned}$ | $\begin{aligned} & 79.84 \\ & {[7.3]} \end{aligned}$ | $\begin{aligned} & 211.00 \\ & {[17.3]} \end{aligned}$ | $\begin{gathered} 277.02 \\ {[12.1]} \end{gathered}$ | $\begin{gathered} -133.11 \\ {[15.0]} \end{gathered}$ | $\begin{aligned} & 29.72 \\ & {[15.2]} \end{aligned}$ |
| C2 | $\begin{gathered} 290.06 \\ {[13.0]} \end{gathered}$ | $\begin{gathered} 192.02 \\ {[9.9]} \end{gathered}$ | $\begin{aligned} & 59.17 \\ & {[11.1]} \end{aligned}$ | $\begin{aligned} & 85.88 \\ & {[9.1]} \end{aligned}$ | $\begin{gathered} 225.28 \\ {[11.8]} \end{gathered}$ | $\begin{gathered} 294.27 \\ {[9.3]} \end{gathered}$ | $\begin{gathered} -131.08 \\ {[16.4]} \end{gathered}$ | $\begin{aligned} & 53.46 \\ & {[18.3]} \end{aligned}$ |
| C3 | $\begin{gathered} 296.83 \\ {[10.0]} \end{gathered}$ | $\begin{gathered} 196.61 \\ {[9.8]} \end{gathered}$ | $\begin{aligned} & 63.57 \\ & {[9.9]} \end{aligned}$ | $\begin{gathered} 139.20 \\ {[7.8]} \end{gathered}$ | $\begin{gathered} 233.00 \\ {[14.1]} \end{gathered}$ | $\begin{gathered} 280.10 \\ {[12.1]} \end{gathered}$ | $\begin{gathered} -71.12 \\ {[7.6]} \end{gathered}$ | $\begin{aligned} & 146.80 \\ & {[10.9]} \end{aligned}$ |
| T4 | $\begin{aligned} & 94.13 \\ & {[20.2]} \end{aligned}$ | $\begin{aligned} & 184.43 \\ & {[12.4]} \end{aligned}$ | $\begin{gathered} 62.38 \\ {[8.9]} \end{gathered}$ | $\begin{gathered} 143.84 \\ {[7.0]} \end{gathered}$ | $\begin{gathered} 193.17 \\ {[7.9]} \end{gathered}$ | $\begin{gathered} 278.78 \\ {[6.9]} \end{gathered}$ | $\begin{gathered} -121.52 \\ {[12.4]} \end{gathered}$ | $\begin{aligned} & 159.68 \\ & {[11.8]} \end{aligned}$ |
| A5 | $\begin{gathered} 292.94 \\ {[8.1]} \end{gathered}$ | $\begin{gathered} 169.94 \\ {[8.3]} \end{gathered}$ | $\begin{aligned} & 54.00 \\ & {[7.6]} \end{aligned}$ | $\begin{gathered} 141.97 \\ {[7.0]} \end{gathered}$ | $\begin{gathered} 222.32 \\ {[11.3]} \end{gathered}$ | $\begin{gathered} 293.27 \\ {[9.7]} \end{gathered}$ | $\begin{gathered} -90.40 \\ {[13.1]} \end{gathered}$ | $\begin{aligned} & 152.10 \\ & {[10.7]} \end{aligned}$ |
| A6 | $\begin{aligned} & 184.86 \\ & {[18.4]} \end{aligned}$ | $\begin{aligned} & 183.22 \\ & {[11.1]} \end{aligned}$ | $\begin{aligned} & 57.45 \\ & {[13.9]} \end{aligned}$ | $\begin{gathered} 148.53 \\ {[6.8]} \end{gathered}$ | $\begin{gathered} 193.86 \\ {[8.3]} \end{gathered}$ | $\begin{gathered} 274.02 \\ {[7.6]} \end{gathered}$ | $\begin{gathered} -156.84 \\ {[11.6]} \end{gathered}$ | $\begin{aligned} & 191.30 \\ & {[14.5]} \end{aligned}$ |
| C7 | $\begin{gathered} 291.57 \\ {[9.3]} \end{gathered}$ | $\begin{gathered} 172.95 \\ {[8.8]} \end{gathered}$ | $\begin{gathered} 57.89 \\ {[7.9]} \end{gathered}$ | $\begin{gathered} 82.43 \\ {[6.6]} \end{gathered}$ | $\begin{gathered} 216.61 \\ {[11.5]} \end{gathered}$ | $\begin{gathered} 283.14 \\ {[8.4]} \end{gathered}$ | $\begin{gathered} -135.63 \\ {[9.2]} \end{gathered}$ | $\begin{aligned} & 21.18 \\ & {[11.4]} \end{aligned}$ |
| C8 | $\begin{gathered} 295.29 \\ {[15.7]} \end{gathered}$ | $\begin{aligned} & 193.91 \\ & {[14.2]} \end{aligned}$ | $\begin{aligned} & 59.25 \\ & {[11.4]} \end{aligned}$ | $\begin{aligned} & 84.01 \\ & {[17.5]} \end{aligned}$ | $\begin{aligned} & 196.14 \\ & {[13.7]} \end{aligned}$ | $\begin{gathered} 268.37 \\ {[20.7]} \end{gathered}$ | $\begin{gathered} -94.58 \\ {[11.8]} \end{gathered}$ | $\begin{aligned} & 62.35 \\ & {[27.8]} \end{aligned}$ |
| C9 | $\begin{array}{r} 284.37 \\ {[14.8]} \end{array}$ | $\begin{aligned} & 185.57 \\ & {[10.4]} \end{aligned}$ | $\begin{gathered} 55.06 \\ {[9.1]} \end{gathered}$ | $\begin{aligned} & 84.63 \\ & {[7.7]} \end{aligned}$ | $\begin{gathered} 218.23 \\ {[15.6]} \end{gathered}$ | $\begin{gathered} 281.98 \\ {[20.9]} \end{gathered}$ | $\begin{gathered} \hline-132.35 \\ {[14.5]} \end{gathered}$ | $\begin{gathered} 24.25 \\ {[12.4]} \end{gathered}$ |
| T10 | $\begin{aligned} & 89.53 \\ & {[9.8]} \end{aligned}$ | $\begin{aligned} & 185.03 \\ & {[29.2]} \end{aligned}$ | $\begin{gathered} 291.47 \\ {[8.7]} \end{gathered}$ | $\begin{gathered} 135.13 \\ {[11.3]} \end{gathered}$ | $\begin{gathered} 227.87 \\ {[21.1]} \end{gathered}$ | $\begin{aligned} & 161.25 \\ & {[13.8]} \end{aligned}$ | $\begin{gathered} -119.65 \\ {[17.3]} \end{gathered}$ | $\begin{aligned} & 146.62 \\ & {[17.2]} \end{aligned}$ |
| A11 | $\begin{aligned} & 81.90 \\ & {[17.1]} \end{aligned}$ | $\begin{aligned} & 182.79 \\ & {[15.1]} \end{aligned}$ | $\begin{aligned} & 62.13 \\ & {[10.9]} \end{aligned}$ | $\begin{aligned} & 141.67 \\ & {[11.8]} \end{aligned}$ | $\begin{gathered} 201.09 \\ {[14.0]} \end{gathered}$ | $\begin{gathered} 274.19 \\ {[17.0]} \end{gathered}$ | $\begin{aligned} & 140.93 \\ & {[19.8]} \end{aligned}$ | $\begin{aligned} & 155.45 \\ & {[26.5]} \end{aligned}$ |
| A12 | $\begin{aligned} & 197.76 \\ & {[17.5]} \end{aligned}$ | $\begin{aligned} & 168.74 \\ & {[13.6]} \end{aligned}$ | $\begin{aligned} & 61.38 \\ & {[10.7]} \end{aligned}$ | $\begin{gathered} 151.05 \\ {[6.4]} \end{gathered}$ | $\begin{gathered} 223.60 \\ {[11.4]} \end{gathered}$ | $\begin{gathered} 288.20 \\ {[8.6]} \end{gathered}$ | $\begin{gathered} -145.67 \\ {[21.5]} \end{gathered}$ | $\begin{aligned} & 178.26 \\ & {[13.7]} \end{aligned}$ |
| C13 | $\begin{gathered} 288.96 \\ {[9.0]} \end{gathered}$ | $\begin{gathered} 174.60 \\ {[9.1]} \end{gathered}$ | $\begin{aligned} & 59.74 \\ & {[7.3]} \end{aligned}$ | $\begin{gathered} 144.02 \\ {[8.9]} \end{gathered}$ | $\begin{gathered} 232.71 \\ {[17.4]} \end{gathered}$ | $\begin{gathered} 288.64 \\ {[9.9]} \end{gathered}$ | $\begin{gathered} -129.29 \\ {[13.6]} \end{gathered}$ | $\begin{aligned} & 163.73 \\ & {[19.9]} \end{aligned}$ |
| C14 | $\begin{gathered} 279.43 \\ {[13.4]} \end{gathered}$ | $\begin{aligned} & 177.84 \\ & {[10.7]} \end{aligned}$ | $\begin{aligned} & 53.58 \\ & {[10.3]} \end{aligned}$ | $\begin{gathered} 140.60 \\ {[8.2]} \end{gathered}$ | $\begin{gathered} 209.13 \\ {[23.3]} \end{gathered}$ | $\begin{gathered} 216.95 \\ {[57.4]} \end{gathered}$ | $\begin{gathered} -121.94 \\ {[26.4]} \end{gathered}$ | $\begin{aligned} & 159.64 \\ & {[14.8]} \end{aligned}$ |
| C15 | $\begin{gathered} 279.38 \\ {[22.8]} \end{gathered}$ | $\begin{gathered} 221.30 \\ {[40.4]} \end{gathered}$ | $\begin{aligned} & 55.43 \\ & {[12.0]} \end{aligned}$ | $\begin{aligned} & 147.24 \\ & {[10.2]} \end{aligned}$ | $\begin{gathered} 232.72 \\ {[15.4]} \end{gathered}$ | $\begin{gathered} 294.03 \\ {[12.0]} \end{gathered}$ | $\begin{gathered} \hline-140.38 \\ {[16.2]} \end{gathered}$ | $\begin{aligned} & 159.27 \\ & {[15.2]} \end{aligned}$ |
| T16 | $\begin{gathered} 236.44 \\ {[60.7]} \end{gathered}$ | $\begin{aligned} & 184.11 \\ & {[13.9]} \end{aligned}$ | $\begin{aligned} & 53.52 \\ & {[11.3]} \end{aligned}$ | $\begin{gathered} 145.98 \\ {[8.6]} \end{gathered}$ | $\begin{gathered} 200.98 \\ {[11.8]} \end{gathered}$ | $\begin{gathered} 283.64 \\ {[7.7]} \end{gathered}$ | $\begin{gathered} \hline-132.40 \\ {[14.8]} \end{gathered}$ | $\begin{aligned} & 160.93 \\ & {[13.5]} \end{aligned}$ |
| A17 | $\begin{gathered} 282.86 \\ {[10.8]} \end{gathered}$ | $\begin{gathered} 169.85 \\ {[8.2]} \end{gathered}$ | $\begin{gathered} 46.28 \\ {[9.4]} \end{gathered}$ | $\begin{gathered} 141.74 \\ {[8.9]} \end{gathered}$ | $\begin{gathered} 231.10 \\ {[24.1]} \end{gathered}$ | $\begin{aligned} & 188.81 \\ & {[23.9]} \end{aligned}$ | $\begin{aligned} & \hline-92.06 \\ & {[14.2]} \end{aligned}$ | $\begin{aligned} & 148.46 \\ & {[11.0]} \end{aligned}$ |
| A18 | $\begin{gathered} 286.44 \\ {[12.3]} \end{gathered}$ | $\begin{aligned} & 152.39 \\ & {[15.3]} \end{aligned}$ | $\begin{aligned} & 52.95 \\ & {[10.5]} \end{aligned}$ | $\begin{gathered} 142.96 \\ {[9.2]} \end{gathered}$ | $\begin{gathered} 185.88 \\ {[9.5]} \end{gathered}$ | $\begin{gathered} 270.83 \\ {[8.6]} \\ \hline \end{gathered}$ | $\begin{gathered} \hline-112.60 \\ {[11.9]} \\ \hline \end{gathered}$ | $\begin{aligned} & 170.30 \\ & {[21.7]} \end{aligned}$ |
| C19 | $\begin{gathered} 291.24 \\ {[10.0]} \end{gathered}$ | $\begin{gathered} 168.87 \\ {[8.5]} \end{gathered}$ | $\begin{gathered} 57.39 \\ {[8.6]} \end{gathered}$ | $\begin{aligned} & 131.14 \\ & {[14.9]} \end{aligned}$ | $\begin{gathered} 219.56 \\ {[10.6]} \end{gathered}$ | $\begin{gathered} 288.42 \\ {[9.3]} \end{gathered}$ | $\begin{gathered} -107.65 \\ {[12.0]} \end{gathered}$ | $\begin{aligned} & 136.21 \\ & {[22.8]} \end{aligned}$ |
| C20 | $\begin{array}{r} 285.97 \\ {[10.5]} \end{array}$ | $\begin{aligned} & 172.68 \\ & {[10.1]} \end{aligned}$ | $\begin{gathered} 59.71 \\ {[8.2]} \end{gathered}$ | $\begin{gathered} 145.59 \\ {[8.7]} \end{gathered}$ | $\begin{gathered} 210.28 \\ {[23.5]} \end{gathered}$ | $\begin{aligned} & 162.90 \\ & {[10.8]} \end{aligned}$ | $\begin{gathered} -112.82 \\ {[17.4]} \end{gathered}$ | $\begin{aligned} & 166.53 \\ & {[17.5]} \end{aligned}$ |
| C21 | $\begin{gathered} 257.27 \\ {[36.0]} \end{gathered}$ | $\begin{aligned} & 162.32 \\ & {[18.1]} \end{aligned}$ | $\begin{gathered} 50.0 \\ {[11.0]} \end{gathered}$ | $\begin{aligned} & 143.13 \\ & {[11.9]} \end{aligned}$ | $\begin{aligned} & 219.45 \\ & {[24.9]} \end{aligned}$ | $\begin{aligned} & 152.12 \\ & {[15.8]} \end{aligned}$ | $\begin{gathered} -136.73 \\ {[17.0]} \end{gathered}$ | $\begin{aligned} & 162.91 \\ & {[24.6]} \end{aligned}$ |
| T22 | $\begin{gathered} 235.44 \\ {[85.2]} \end{gathered}$ | $\begin{aligned} & 182.70 \\ & {[17.7]} \end{aligned}$ | $\begin{gathered} 60.03 \\ {[11.0]} \\ \hline \end{gathered}$ | $\begin{aligned} & 146.33 \\ & {[11.7]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{gathered} -135.94 \\ {[20.6]} \end{gathered}$ | $\begin{aligned} & 168.70 \\ & {[23.6]} \end{aligned}$ |

Table S8: Average hydrogen bonding geometry and occupancy (considering C-O distance $\leq 3.4 \AA$ and $\mathrm{C}-\mathrm{H} . . . \mathrm{O}$ angle $>120^{\circ}$ ) of possible C-H...O mediated hydrogen bond between sugar moieties of the antiparallel strands along the narrow grooves of i-motif DNA.

| Structure | C-H...O mediated hydrogen bond between sugar moiety | Distance between C and O (A) | $\underset{\left({ }^{\circ}\right)}{\text { C-H... }}$ | Occupancy <br> (\%) |
| :---: | :---: | :---: | :---: | :---: |
| 5'E i-motif | (C1) C1'-H...O4' (T22) | 3.30 | 138.03 | 51.33 |
|  | (T22) C1'-H...O4' (C1) | 3.32 | 137.86 | 32.24 |
|  | (C2) C1'-H...O4' (C21) | 3.27 | 132.14 | 71.00 |
|  | (C21) C1'-H...O4' (C2) | 3.26 | 131.71 | 72.11 |
|  | (C3) C1'-H...O4' (C20) | 3.29 | 131.07 | 55.74 |
|  | (C20) C1'-H...O4' (C3) | 3.25 | 131.16 | 70.29 |
|  | ( $\mathrm{C}^{+} 8$ ) $\mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4{ }^{\prime}\left(\mathrm{C}^{+} 15\right)$ | 3.29 | 136.34 | 65.10 |
|  | ( $\mathrm{C}^{+} 15$ ) $\mathrm{C} 1{ }^{\prime}-\mathrm{H} . . . \mathrm{O} 4{ }^{\prime}\left(\mathrm{C}^{+} 8\right)$ | 3.36 | 131.12 | 18.31 |
|  | ( $\left.\mathrm{C}^{+} 9\right) \mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4{ }^{\prime}\left(\mathrm{C}^{+} 14\right)$ | 3.29 | 131.14 | 47.22 |
|  | ( $\mathrm{C}^{+} 14$ ) $\mathrm{C} 1{ }^{\prime}-\mathrm{H} . . . \mathrm{O} 4{ }^{\prime}\left(\mathrm{C}^{+} 9\right)$ | 3.30 | 130.74 | 43.15 |
|  | (T10) C1'-H...O4' ( $\mathrm{C}^{+} 13$ ) | 3.38 | 126.16 | 10.0 |
|  | ( $\left.\mathrm{C}^{+} 13\right) \mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4{ }^{\prime}(\mathrm{T} 10)$ | 3.30 | 149.18 | 82.10 |
| 3'E i-motif | (C1) C 1 '- $\mathrm{H} . . . \mathrm{O} 4$ '(C7) | 3.27 | 134.46 | 56.75 |
|  | (C7) C 1 '- $\mathrm{H} . . . \mathrm{O} 4$ '(C1) | 3.31 | 130.51 | 17.70 |
|  | (C2) C 1 '-H...O4'(C6) | 3.29 | 135.51 | 64.64 |
|  | (C6) C 1 '-H...O4 ${ }^{\text {(C2) }}$ | 3.28 | 133.41 | 67.24 |
|  | ( $\left.\mathrm{C}^{+} 12\right) \mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4^{\prime}\left(\mathrm{C}^{+} 18\right)$ | 3.30 | 139.27 | 51.27 |
|  | ( $\left.\mathrm{C}^{+} 18\right) \mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4^{\prime}\left(\mathrm{C}^{+} 12\right)$ | 3.32 | 134.16 | 23.59 |
|  | ( $\mathrm{C}^{+} 13$ ) C1' $-\mathrm{H} . . . \mathrm{O} 4^{\prime}\left(\mathrm{C}^{+} 17\right)$ | 3.29 | 133.26 | 54.27 |
|  | ( $\left.\mathrm{C}^{+} 17\right) \mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4^{\prime}\left(\mathrm{C}^{+} 13\right)$ | 3.31 | 131.11 | 37.35 |

Table S9: Base pairing and stacking energy between the stacked base pairs in model $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structure (ABC/DEF) as derived from the NMR structure of i-motif DNA (PDB id: 1EL2).

| System | Quantum chemical method | Base pairing energy ( $\mathrm{kcal} / \mathrm{mol}$ ) |  |  | Stacking energy between consecutive base pairs ( $\mathrm{kcal} / \mathrm{mol}$ ) |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | A:F | B:E | C:D | AB/EF | BC/DE |  |
| Partial optimized geometry of $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structure | $\begin{aligned} & \omega \text { B97X-D/ } \\ & \text { cc-pVDZ } \end{aligned}$ | -55.51 | -54.50 | -50.31 | 28.93 | 27.77 | 91.18 |
|  | B3LYP-D3/cc- <br> pVDZ | -57.06 | -55.97 | -51.49 | 26.64 | 25.80 | 87.09 |
|  | $\begin{gathered} \text { MO6-2X/cc- } \\ \text { pVDZ } \end{gathered}$ | -53.92 | -53.86 | -49.53 | 28.16 | 28.22 | 90.75 |
| Full optimized geometry of $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structure | $\begin{aligned} & \omega \text { B97X-D/ } \\ & \text { cc-pVDZ } \end{aligned}$ | -57.59 | -59.01 | -58.04 | 20.77 | 17.64 | 70.56 |
|  | $\begin{gathered} \text { B3LYP-D3/cc- } \\ \text { pVDZ } \end{gathered}$ | -56.09 | -57.50 | -56.57 | 22.48 | 21.74 | 75.02 |
|  | $\begin{gathered} \text { MO6-2X/cc- } \\ \text { pVDZ } \end{gathered}$ | -54.62 | -55.96 | -54.98 | 22.09 | 20.94 | 73.91 |
| Full optimized geometry of CCC/CCC trinucleotide structure | $\begin{aligned} & \omega \text { B97X-D/ } \\ & \text { cc-pVDZ } \end{aligned}$ | -28.80 | -28.48 | -28.06 | -24.66 | -34.72 | -61.04 |
|  | $\begin{gathered} \text { B3LYP-D3/cc- } \\ \text { pVDZ } \end{gathered}$ | -27.74 | -27.43 | -27.04 | -21.82 | -30.17 | -53.49 |
|  | $\begin{gathered} \text { MO6-2X/cc- } \\ \text { pVDZ } \end{gathered}$ | -26.42 | -26.17 | -25.80 | -23.83 | -31.55 | -56.71 |

Table S10: Variation of stacking energy between the stacked base pairs in model $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structure ( $\mathrm{ABC} / \mathrm{DEF}$ ) with stacking interval between the consecutive base pairs.

| Stacking interval between consecutive base pairs (Å) | $\omega$ B97X-D/cc-pVDZ |  |  | B3LYP-D3/cc-pVDZ |  |  | MO6-2X/cc-pVDZ |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Stacking energy between consecutive base pairs (kcal/mol) |  | Stacking energy between the stacked base pairs in trinucleoti de step ( $\mathrm{kcal} / \mathrm{mol}$ ) | Stacking energy between consecutive base pairs (kcal/mol) |  | Stacking energy between the stacked base pairs in trinucleoti de step ( $\mathrm{kcal} / \mathrm{mol}$ ) | Stacking energy between consecutive base pairs (kcal/mol) |  | Stacking energy between the stacked base pairs in trinucleotid e step (kcal/mol) |
|  | AB/EF | BC/DE |  | AB/EF | BC/DE |  | AB/EF | BC/DE |  |
| $(1.98,4.20)$ | 868.255 | 38.606 | 941.101 | 865.115 | 37.606 | 937.884 | 861.514 | 39.372 | 934.973 |
| $(2.18,4.00)$ | 496.518 | 38.453 | 569.747 | 493.990 | 37.993 | 566.989 | 486.713 | 39.219 | 560.861 |
| $(2.38,3.80)$ | 291.921 | 36.538 | 363.848 | 289.163 | 35.849 | 360.630 | 281.197 | 37.840 | 354.349 |
| $(2.58,3.60)$ | 166.604 | 34.546 | 236.999 | 163.923 | 33.474 | 233.628 | 156.799 | 36.308 | 228.879 |
| (2.78, 3.40) | 93.988 | 32.248 | 162.391 | 91.613 | 31.099 | 159.021 | 85.945 | 34.010 | 156.263 |
| (2.98, 3.20) | 55.918 | 30.257 | 122.100 | 53.237 | 28.495 | 118.116 | 49.943 | 31.789 | 118.270 |
| (3.18, 3.00) | 37.074 | 27.959 | 101.265 | 34.546 | 26.044 | 97.128 | 34.087 | 29.414 | 99.733 |
| (3.38, 2.80) | 29.49 | 26.886 | 92.685 | 27.116 | 24.742 | 88.396 | 28.342 | 26.886 | 91.919 |
| (3.58, 2.60) | 27.346 | 29.108 | 92.839 | 25.201 | 26.657 | 88.549 | 27.806 | 27.576 | 92.073 |
| (3.78, 2.40) | 27.959 | 37.917 | 102.337 | 26.274 | 35.466 | 98.201 | 29.338 | 34.163 | 100.039 |
| $(3.98,2.20)$ | 29.644 | 59.211 | 125.164 | 28.265 | 56.530 | 121.180 | 31.406 | 52.624 | 120.414 |
| $(4.18,2.00)$ | 31.482 | 101.877 | 169.591 | 30.333 | 99.196 | 165.914 | 33.091 | 92.915 | 162.391 |
| $(4.38,1.80)$ | 33.397 | 180.315 | 249.561 | 32.478 | 177.941 | 246.497 | 34.700 | 169.898 | 240.522 |
| $(4.58,1.60)$ | 34.929 | 315.207 | 385.755 | 34.546 | 314.594 | 384.836 | 36.078 | 304.943 | 376.410 |
| (4.78, 1.40) | 35.849 | 537.345 | 608.813 | 35.849 | 540.409 | 611.724 | 36.921 | 527.694 | 600.080 |

Table S11: Average hydrogen bonding geometry and occupancy (considering C - O distance $\leq 3.4$ $\AA$ and C-H...O angle > $120^{\circ}$ ) of possible C-H...O mediated hydrogen bond between sugar moieties of the antiparallel strands along the narrow grooves of i-motif DNA at elevated temperatures.

| C-H...O mediated hydrogen bond between sugar moiety | 320K |  |  | 340K |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Distance between C and O (Å) | C-H...O angle $\left({ }^{\circ}\right)$ | $\begin{gathered} \text { Occupanc } \\ y \\ (\%) \end{gathered}$ | Distance between C and O (A) | C-H...O angle $\left({ }^{\circ}\right)$ | Occupancy <br> (\%) |
| 5'E i-motif |  |  |  |  |  |  |
| (C1) C1'-H...O4' (T22) | 3.29 | 136.72 | 42.21 | 3.31 | 137.44 | 14.41 |
| (T22) C1'-H...O4' (C1) | 3.32 | 139.89 | 30.51 | 3.32 | 139.76 | 10.27 |
| (C2) C1'-H...O4' (C21) | 3.26 | 131.68 | 68.21 | 3.26 | 132.98 | 69.01 |
| (C21) C1'-H...O4' (C2) | 3.26 | 131.10 | 66.51 | 3.27 | 131.76 | 60.13 |
| (C3) C1'-H...O4' (C20) | 3.30 | 129.49 | 40.40 | 3.29 | 130.16 | 42.93 |
| (C20) C1'-H...O4' (C3) | 3.25 | 130.55 | 64.22 | 3.25 | 131.10 | 63.16 |
| ( $\left.\mathrm{C}^{+} 8\right) \mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4{ }^{\left(\mathrm{C}^{+} 15\right)}$ | 3.29 | 134.92 | 56.72 | 3.29 | 134.43 | 56.15 |
| ( $\mathrm{C}^{+} 15$ ) C1'-H...O4' ( $\mathrm{C}^{+} 8$ ) | 3.34 | 130.00 | 10.82 | 3.33 | 129.85 | 12.40 |
| ( $\left.\mathrm{C}^{+} 9\right) \mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4{ }^{\prime}\left(\mathrm{C}^{+} 14\right)$ | 3.29 | 131.52 | 43.10 | 3.29 | 131.45 | 31.57 |
| ( $\mathrm{C}^{+} 14$ ) $\mathrm{C} 1{ }^{\prime}-\mathrm{H} . . . \mathrm{O} 4{ }^{\prime}\left(\mathrm{C}^{+} 9\right)$ | 3.30 | 133.58 | 38.51 | 3.30 | 134.83 | 44.39 |
| (T10) C1'-H...O4' (C'13) | 3.35 | 131.72 | 1.90 | 3.35 | 131.78 | 18.46 |
| ( $\left.\mathrm{C}^{+} 13\right) \mathrm{C1}$ '-H...O4' (T10) | 3.28 | 141.63 | 66.12 | 3.28 | 134.52 | 40.93 |
| 3'E i-motif |  |  |  |  |  |  |
| (C1) $\mathrm{C} 1{ }^{\prime}-\mathrm{H} . . . \mathrm{O} 4^{\prime}(\mathrm{C} 7)$ | 3.23 | 130.04 | 52.25 | 3.24 | 135.30 | 65.52 |
| (C7) $\mathrm{C1}{ }^{\prime}-\mathrm{H} . . . \mathrm{O} 4$ '(C1) | 3.34 | 128.42 | 2.6 | 3.33 | 128.31 | 1.31 |
| (C2) $\mathrm{C} 1{ }^{\prime}-\mathrm{H} . . . \mathrm{O} 4$ '(C6) | 3.34 | 136.84 | 2.50 | 3.35 | 132.10 | 6.36 |
| (C6) $\mathrm{C} 1{ }^{\prime}-\mathrm{H} . . . \mathrm{O} 4{ }^{\prime}(\mathrm{C} 2)$ | 3.28 | 142.69 | 54.44 | 3.26 | 137.69 | 64.15 |
| ( $\mathrm{C}^{+} 12$ ) $\mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4^{\prime}\left(\mathrm{C}^{+} 18\right)$ | 3.29 | 140.66 | 62.18 | 3.25 | 132.88 | 57.59 |
| ( $\left.\mathrm{C}^{+} 18\right) \mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4^{\prime}\left(\mathrm{C}^{+} 12\right)$ | 3.37 | 131.88 | 2.31 | 3.33 | 130.74 | 3.39 |
| ( $\mathrm{C}^{+} 13$ ) $\mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4^{\prime}\left(\mathrm{C}^{+} 17\right)$ | 3.32 | 129.03 | 19.63 | 3.30 | 130.81 | 1.48 |
| ( $\mathrm{C}^{+} 17$ ) $\mathrm{C} 1^{\prime}-\mathrm{H} . . . \mathrm{O} 4$ '( $\mathrm{C}^{+} 13$ ) | 3.27 | 138.40 | 61.20 | 3.30 | 150.97 | 61.18 |

Table S12: Average value along with standard deviation of the base pair step parameters as found in MD simulation of $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ and $5^{\prime} \mathrm{E}_{\mathrm{CGG}}$ form structure ( ${ }^{\prime}$ ' denotes base pair and ' $\because$ ’ denotes base pairs stack).

| System | Base pair step | Shift <br> (A) | Slide <br> (A) | Rise <br> (A) | Tilt $\left(^{\circ}\right)$ | Roll $\left(^{\circ}\right)$ | Twist ( ${ }^{\circ}$ ) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $\begin{gathered} 5^{\prime} \mathrm{E}_{\mathrm{GCC}} \text {-form } \\ \text { structure } \\ \left(5^{\prime} \mathrm{E}\right. \\ \text { topology } \end{gathered}$ | $\begin{gathered} \mathrm{CC} / \mathrm{C}^{+} \mathrm{C}^{+} \\ (1: 13:: 2: 14) \end{gathered}$ | $\begin{gathered} 0.33 \\ {[0.44]} \end{gathered}$ | $\begin{gathered} 0.16 \\ {[0.42]} \end{gathered}$ | $\begin{gathered} 6.19 \\ {[0.23]} \end{gathered}$ | $\begin{gathered} 1.33 \\ {[3.11]} \end{gathered}$ | $\begin{gathered} -1.01 \\ {[4.18]} \end{gathered}$ | $\begin{aligned} & 18.13 \\ & {[4.02]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{CC} / \mathrm{C}^{+} \mathrm{C}^{+} \\ (2: 14:: 3: 15) \end{gathered}$ | $\begin{gathered} 0.50 \\ {[0.47]} \end{gathered}$ | $\begin{gathered} 0.20 \\ {[0.45]} \end{gathered}$ | $\begin{gathered} 6.34 \\ {[0.24]} \end{gathered}$ | $\begin{gathered} 1.04 \\ {[3.93]} \end{gathered}$ | $\begin{gathered} -1.64 \\ {[3.56]} \end{gathered}$ | $\begin{aligned} & 16.61 \\ & {[4.98]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CC} \\ (7: 19:: 8: 20) \end{gathered}$ | $\begin{gathered} -0.57 \\ {[0.43]} \end{gathered}$ | $\begin{gathered} -0.84 \\ {[0.39]} \end{gathered}$ | $\begin{gathered} 6.04 \\ {[0.20]} \end{gathered}$ | $\begin{gathered} 3.04 \\ 2.77] \end{gathered}$ | $\begin{gathered} -2.28 \\ {[4.39]} \end{gathered}$ | $\begin{aligned} & 17.28 \\ & {[3.24]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CC} \\ (8: 20:: 9: 21) \end{gathered}$ | $\begin{gathered} -0.34 \\ {[0.47]} \end{gathered}$ | $\begin{gathered} -0.25 \\ {[0.44]} \end{gathered}$ | $\begin{gathered} 6.31 \\ {[0.24]} \end{gathered}$ | $\begin{gathered} 0.14 \\ {[3.71]} \end{gathered}$ | $\begin{gathered} -1.26 \\ {[3.81]} \end{gathered}$ | $\begin{gathered} 17.90 \\ {[4.31]} \end{gathered}$ |
| $5^{\prime} \mathrm{E}_{\mathrm{CGG}}$-form structure (5'E topology) | $\begin{gathered} \mathrm{CC} / \mathrm{C}^{+} \mathrm{C}^{+} \\ (1: 13:: 2: 14) \end{gathered}$ | $\begin{gathered} 0.26 \\ {[0.41]} \end{gathered}$ | $\begin{gathered} 0.03 \\ {[0.40]} \end{gathered}$ | $\begin{gathered} 6.13 \\ {[0.21]} \end{gathered}$ | $\begin{gathered} 0.64 \\ {[3.14]} \end{gathered}$ | $\begin{gathered} -0.93 \\ {[3.82]} \end{gathered}$ | $\begin{aligned} & 19.63 \\ & {[3.79]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{CC} / \mathrm{C}^{+} \mathrm{C}^{+} \\ (2: 14:: 3: 15) \end{gathered}$ | $\begin{gathered} 0.28 \\ {[0.43]} \end{gathered}$ | $\begin{gathered} 0.16 \\ {[0.36]} \end{gathered}$ | $\begin{gathered} 6.39 \\ {[0.24]} \end{gathered}$ | $\begin{gathered} -0.06 \\ {[3.58]} \end{gathered}$ | $\begin{gathered} 0.17 \\ {[3.51]} \end{gathered}$ | $\begin{aligned} & 19.10 \\ & {[3.92]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CC} \\ (7: 19:: 8: 20) \end{gathered}$ | $\begin{gathered} -0.23 \\ {[0.40]} \end{gathered}$ | $\begin{gathered} -0.27 \\ {[0.37]} \end{gathered}$ | $\begin{gathered} 6.13 \\ {[0.21]} \end{gathered}$ | $\begin{gathered} 2.80 \\ {[2.93]} \end{gathered}$ | $\begin{gathered} -3.38 \\ {[4.04]} \end{gathered}$ | $\begin{aligned} & 14.98 \\ & {[3.01]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CC} \\ (8: 20:: 9: 21) \end{gathered}$ | $\begin{gathered} -0.26 \\ {[0.44]} \end{gathered}$ | $\begin{gathered} -0.04 \\ {[0.35]} \end{gathered}$ | $\begin{gathered} 6.19 \\ {[0.21]} \end{gathered}$ | $\begin{gathered} -0.45 \\ {[3.14]} \end{gathered}$ | $\begin{gathered} -0.26 \\ {[3.56]} \end{gathered}$ | $\begin{gathered} 18.73 \\ {[3.49]} \end{gathered}$ |

Table S13: Average value along with standard deviation of stacking interval and twist between consecutive stacked base pair within i-motif core as found in MD simulation of $5{ }^{\prime} \mathrm{E}_{\mathrm{GCC}}$ and $5{ }^{\prime} \mathrm{E}_{\mathrm{CGG}}{ }^{-}$ form structure ( $\because$ ' denotes base pair and ' $\because: ’$ denotes base pairs stack).

| System | Base pair step | Stacking interval (Å) | Twist between consecutive stacked base pair $\left({ }^{\circ}\right)$ |
| :---: | :---: | :---: | :---: |
| $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$-form structure (5'E topology) | $\begin{gathered} \mathrm{CC}^{+} / \mathrm{CC}^{+} \\ (1: 13:: 9: 21) \end{gathered}$ | $\begin{gathered} 3.44 \\ {[0.24]} \end{gathered}$ | $\begin{aligned} & 113.80 \\ & {[3.94]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{CC}^{+} / \mathrm{CC}^{+} \\ (21: 9:: 14: 2) \end{gathered}$ | $\begin{gathered} 2.74 \\ {[0.22]} \end{gathered}$ | $\begin{aligned} & 84.25 \\ & {[3.06]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{CC}^{+} / \mathrm{CC}^{+} \\ (2: 14:: 8: 20) \end{gathered}$ | $\begin{gathered} 3.56 \\ {[0.23]} \end{gathered}$ | $\begin{aligned} & 113.64 \\ & {[5.09]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{CC}^{+} / \mathrm{CC}^{+} \\ (20: 8:: 15: 3) \end{gathered}$ | $\begin{gathered} 2.77 \\ {[0.23]} \end{gathered}$ | $\begin{aligned} & 82.98 \\ & {[3.74]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{CC}^{+} / \mathrm{CC}^{+} \\ (3: 15:: 7: 19) \end{gathered}$ | $\begin{gathered} 3.24 \\ {[0.26]} \end{gathered}$ | $\begin{aligned} & 114.16 \\ & {[4.42]} \end{aligned}$ |
| $5^{\prime} \mathrm{E}_{\mathrm{CGG}}$-form structure ( $5^{\prime}$ E topology) | $\begin{gathered} \mathrm{CC}^{+} / \mathrm{CC}^{+} \\ (1: 13:: 9: 21) \end{gathered}$ | $\begin{gathered} 3.40 \\ {[0.24]} \end{gathered}$ | $\begin{aligned} & 114.10 \\ & {[4.44]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{CC}^{+} / \mathrm{CC}^{+} \\ (21: 9:: 14: 2) \end{gathered}$ | $\begin{gathered} 2.72 \\ {[0.24]} \end{gathered}$ | $\begin{aligned} & 85.48 \\ & {[2.95]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{CC}^{+} / \mathrm{CC}^{+} \\ (2: 14:: 8: 20) \end{gathered}$ | $\begin{gathered} 3.45 \\ {[0.24]} \end{gathered}$ | $\begin{aligned} & 113.23 \\ & {[4.21]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{CC}^{+} / \mathrm{CC}^{+} \\ (20: 8:: 15: 3) \end{gathered}$ | $\begin{gathered} 2.93 \\ {[0.24]} \end{gathered}$ | $\begin{aligned} & 85.88 \\ & {[2.89]} \end{aligned}$ |
|  | $\begin{gathered} \mathrm{CC}^{+} / \mathrm{CC}^{+} \\ (3: 15:: 7: 19) \end{gathered}$ | $\begin{gathered} 3.18 \\ {[0.25]} \end{gathered}$ | $\begin{aligned} & 108.98 \\ & {[3.39]} \end{aligned}$ |

Table S14: Average value along with standard deviation of the backbone dihedral angles for the bases as found in MD simulation of $5{ }^{\prime} \mathrm{E}_{\mathrm{GCC}}$-form structure.

| Nucleotide | $\alpha\left({ }^{\circ}\right)$ | $\beta\left({ }^{\circ}\right)$ | $\gamma\left({ }^{\circ}\right)$ | $\delta\left({ }^{\circ}\right)$ | $\varepsilon\left(^{\circ}\right.$ ) | $\zeta\left({ }^{\circ}\right)$ | $\chi\left({ }^{\circ}\right)$ | Phase ( ${ }^{\circ}$ ) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| C1 | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{gathered} 66.0 \\ {[26.2]} \end{gathered}$ | $\begin{aligned} & 95.53 \\ & {[25.1]} \end{aligned}$ | $\begin{aligned} & 213.31 \\ & {[23.9]} \end{aligned}$ | $\begin{gathered} 279.34 \\ {[11.1]} \end{gathered}$ | $\begin{gathered} -133.15 \\ {[14.0]} \end{gathered}$ | $\begin{gathered} 70.10 \\ {[49.1]} \end{gathered}$ |
| C2 | $\begin{gathered} 288.98 \\ {[22.5]} \end{gathered}$ | $\begin{gathered} 189.75 \\ {[9.8]} \end{gathered}$ | $\begin{aligned} & 80.98 \\ & {[18.3]} \end{aligned}$ | $\begin{gathered} 90.15 \\ {[17.2]} \end{gathered}$ | $\begin{aligned} & 193.67 \\ & {[14.9]} \end{aligned}$ | $\begin{gathered} 279.83 \\ {[9.7]} \end{gathered}$ | $\begin{gathered} -124.17 \\ {[10.8]} \end{gathered}$ | $\begin{aligned} & 57.91 \\ & {[38.3]} \end{aligned}$ |
| C3 | $\begin{gathered} 281.07 \\ {[38.1]} \end{gathered}$ | $\begin{aligned} & 173.10 \\ & {[23.8]} \end{aligned}$ | $\begin{gathered} 89.2 \\ {[36.0]} \end{gathered}$ | $\begin{aligned} & 112.06 \\ & {[26.4]} \end{aligned}$ | $\begin{gathered} 231.27 \\ {[19.0]} \end{gathered}$ | $\begin{gathered} 289.54 \\ {[11.3]} \end{gathered}$ | $\begin{gathered} -116.30 \\ {[11.8]} \end{gathered}$ | $\begin{aligned} & 106.49 \\ & {[43.3]} \end{aligned}$ |
| G4 | $\begin{gathered} 143.68 \\ {[834.2]} \end{gathered}$ | $\begin{aligned} & 180.69 \\ & {[16.8]} \end{aligned}$ | $\begin{aligned} & 63.52 \\ & {[32.6]} \end{aligned}$ | $\begin{gathered} 147.14 \\ {[9.3]} \end{gathered}$ | $\begin{aligned} & 188.56 \\ & {[15.9]} \end{aligned}$ | $\begin{gathered} 262.69 \\ {[17.5]} \end{gathered}$ | $\begin{gathered} -129.41 \\ {[20.6]} \end{gathered}$ | $\begin{aligned} & 167.20 \\ & {[15.3]} \end{aligned}$ |
| C5 | $\begin{gathered} 288.31 \\ {[10.8]} \end{gathered}$ | $\begin{aligned} & 188.98 \\ & {[14.8]} \end{aligned}$ | $\begin{aligned} & 50.48 \\ & {[11.6]} \end{aligned}$ | $\begin{gathered} 139.51 \\ {[8.6]} \end{gathered}$ | $\begin{gathered} 250.08 \\ {[18.7]} \end{gathered}$ | $\begin{gathered} 278.24 \\ {[12.1]} \end{gathered}$ | $\begin{gathered} -130.11 \\ {[17.6]} \end{gathered}$ | $\begin{aligned} & 155.67 \\ & {[15.7]} \end{aligned}$ |
| C6 | $\begin{gathered} 216.32 \\ {[38.7]} \end{gathered}$ | $\begin{aligned} & 168.62 \\ & {[21.4]} \end{aligned}$ | $\begin{aligned} & 56.26 \\ & {[12.6]} \end{aligned}$ | $\begin{gathered} 145.97 \\ {[7.9]} \end{gathered}$ | $\begin{gathered} 210.65 \\ {[16.1]} \end{gathered}$ | $\begin{gathered} 283.23 \\ {[10.0]} \end{gathered}$ | $\begin{gathered} -128.23 \\ {[15.7]} \end{gathered}$ | $\begin{aligned} & 164.96 \\ & {[13.8]} \end{aligned}$ |
| $\mathrm{C}^{+} 7$ | $\begin{gathered} 288.74 \\ {[9.8]} \end{gathered}$ | $\begin{aligned} & 171.30 \\ & {[10.2]} \end{aligned}$ | $\begin{gathered} 60.05 \\ {[7.6]} \end{gathered}$ | $\begin{aligned} & 85.13 \\ & {[9.0]} \end{aligned}$ | $\begin{aligned} & 192.09 \\ & {[11.3]} \end{aligned}$ | $\begin{gathered} 273.02 \\ {[10.8]} \end{gathered}$ | $\begin{gathered} -143.12 \\ {[9.3]} \end{gathered}$ | $\begin{aligned} & 37.97 \\ & {[46.0]} \end{aligned}$ |
| $\mathrm{C}^{+} 8$ | $\begin{aligned} & 300.43 \\ & {[10.6]} \end{aligned}$ | $\begin{aligned} & 183.55 \\ & {[10.6]} \end{aligned}$ | $\begin{aligned} & 71.27 \\ & {[9.5]} \end{aligned}$ | $\begin{aligned} & 118.10 \\ & {[26.6]} \end{aligned}$ | $\begin{aligned} & 193.88 \\ & {[11.6]} \end{aligned}$ | $\begin{gathered} 268.44 \\ {[17.6]} \end{gathered}$ | $\begin{gathered} -120.63 \\ {[13.9]} \end{gathered}$ | $\begin{aligned} & 110.45 \\ & {[41.7]} \end{aligned}$ |
| $\mathrm{C}^{+} 9$ | $\begin{gathered} 292.20 \\ {[24.2]} \end{gathered}$ | $\begin{aligned} & 178.62 \\ & {[16.1]} \end{aligned}$ | $\begin{aligned} & 78.54 \\ & {[31.7]} \end{aligned}$ | $\begin{aligned} & 130.48 \\ & {[16.8]} \end{aligned}$ | $\begin{gathered} 250.35 \\ {[34.7]} \end{gathered}$ | $\begin{gathered} 218.67 \\ {[31.7]} \end{gathered}$ | $\begin{gathered} -106.51 \\ {[14.5]} \end{gathered}$ | $\begin{aligned} & 138.43 \\ & {[24.6]} \end{aligned}$ |
| G10 | $\begin{gathered} 287.22 \\ {[12.1]} \end{gathered}$ | $\begin{aligned} & 154.81 \\ & {[24.3]} \end{aligned}$ | $\begin{gathered} 57.63 \\ {[10.7]} \end{gathered}$ | $\begin{gathered} 145.55 \\ {[7.7]} \end{gathered}$ | $\begin{aligned} & 183.18 \\ & {[11.9]} \end{aligned}$ | $\begin{gathered} 273.02 \\ {[9.6]} \end{gathered}$ | $\begin{gathered} -103.73 \\ {[11.6]} \end{gathered}$ | $\begin{aligned} & 167.30 \\ & {[15.3]} \end{aligned}$ |
| C11 | $\begin{gathered} 291.04 \\ {[13.6]} \end{gathered}$ | $\begin{aligned} & 168.71 \\ & {[11.2]} \end{aligned}$ | $\begin{gathered} 64.30 \\ {[9.3]} \end{gathered}$ | $\begin{aligned} & 139.36 \\ & {[13.8]} \end{aligned}$ | $\begin{gathered} 276.44 \\ {[20.9]} \end{gathered}$ | $\begin{gathered} 73.73 \\ {[14.7]} \end{gathered}$ | $\begin{gathered} -126.13 \\ {[21.7]} \end{gathered}$ | $\begin{aligned} & 148.58 \\ & {[18.2]} \end{aligned}$ |
| C12 | $\begin{gathered} 72.08 \\ {[11.8]} \end{gathered}$ | $\begin{aligned} & 190.97 \\ & {[15.5]} \end{aligned}$ | $\begin{gathered} 298.22 \\ {[8.9]} \end{gathered}$ | $\begin{gathered} 151.95 \\ {[8.8]} \end{gathered}$ | $\begin{gathered} 233.14 \\ {[32.0]} \end{gathered}$ | $\begin{aligned} & 139.13 \\ & {[24.2]} \end{aligned}$ | $\begin{gathered} -147.31 \\ {[16.9]} \end{gathered}$ | $\begin{aligned} & 172.33 \\ & {[17.0]} \end{aligned}$ |
| $\mathrm{C}^{+} 13$ | $\begin{gathered} 272.31 \\ {[22.9]} \end{gathered}$ | $\begin{aligned} & 144.42 \\ & {[24.5]} \end{aligned}$ | $\begin{aligned} & 55.23 \\ & {[9.4]} \end{aligned}$ | $\begin{aligned} & 86.20 \\ & {[7.9]} \end{aligned}$ | $\begin{gathered} 195.25 \\ {[9.6]} \end{gathered}$ | $\begin{gathered} 273.39 \\ {[8.9]} \end{gathered}$ | $\begin{gathered} -136.18 \\ {[8.1]} \end{gathered}$ | $\begin{gathered} 42.89 \\ {[41.0]} \end{gathered}$ |
| $\mathrm{C}^{+} 14$ | $\begin{aligned} & 299.26 \\ & {[13.1]} \end{aligned}$ | $\begin{aligned} & 178.87 \\ & {[10.0]} \end{aligned}$ | $\begin{aligned} & 74.20 \\ & {[12.6]} \end{aligned}$ | $\begin{aligned} & 123.69 \\ & {[26.3]} \end{aligned}$ | $\begin{aligned} & 197.67 \\ & {[13.8]} \end{aligned}$ | $\begin{gathered} 270.65 \\ {[14.7]} \end{gathered}$ | $\begin{gathered} -115.23 \\ {[12.8]} \end{gathered}$ | $\begin{aligned} & 131.54 \\ & {[43.4]} \end{aligned}$ |
| $\mathrm{C}^{+} 15$ | $\begin{gathered} 279.17 \\ {[28.8]} \end{gathered}$ | $\begin{aligned} & 185.59 \\ & {[21.0]} \end{aligned}$ | $\begin{gathered} 70.98 \\ {[31.7]} \end{gathered}$ | $\begin{aligned} & 119.46 \\ & {[19.8]} \end{aligned}$ | $\begin{gathered} 242.43 \\ {[30.2]} \end{gathered}$ | $\begin{gathered} 258.86 \\ {[29.8]} \end{gathered}$ | $\begin{gathered} -99.55 \\ {[8.3]} \end{gathered}$ | $\begin{aligned} & 122.05 \\ & {[45.8]} \end{aligned}$ |
| G16 | $\begin{gathered} 270.60 \\ {[34.4]} \end{gathered}$ | $\begin{aligned} & 184.04 \\ & {[16.5]} \end{aligned}$ | $\begin{aligned} & 108.45 \\ & {[49.1]} \end{aligned}$ | $\begin{aligned} & 147.65 \\ & {[14.2]} \end{aligned}$ | $\begin{gathered} 208.20 \\ {[14.0]} \end{gathered}$ | $\begin{gathered} 275.48 \\ {[15.2]} \end{gathered}$ | $\begin{aligned} & 148.29 \\ & {[15.6]} \end{aligned}$ | $\begin{aligned} & 170.22 \\ & {[27.6]} \end{aligned}$ |
| C17 | $\begin{gathered} 206.75 \\ {[25.0]} \end{gathered}$ | $\begin{aligned} & 169.13 \\ & {[16.2]} \end{aligned}$ | $\begin{aligned} & 59.24 \\ & {[13.3]} \end{aligned}$ | $\begin{gathered} 149.73 \\ {[6.9]} \end{gathered}$ | $\begin{gathered} 229.73 \\ {[18.3]} \end{gathered}$ | $\begin{gathered} 291.35 \\ {[10.6]} \end{gathered}$ | $\begin{gathered} -146.95 \\ {[21.3]} \end{gathered}$ | $\begin{gathered} 170.94 \\ {[14.11]} \end{gathered}$ |
| C18 | $\begin{gathered} 288.89 \\ {[14.1]} \end{gathered}$ | $\begin{aligned} & 169.66 \\ & {[12.1]} \end{aligned}$ | $\begin{gathered} 69.09 \\ {[21.9]} \end{gathered}$ | $\begin{gathered} 145.76 \\ {[8.3]} \end{gathered}$ | $\begin{gathered} 225.13 \\ {[20.2]} \end{gathered}$ | $\begin{aligned} & 177.02 \\ & {[14.9]} \end{aligned}$ | $\begin{gathered} -127.79 \\ {[14.8]} \end{gathered}$ | $\begin{aligned} & 162.24 \\ & {[14.7]} \end{aligned}$ |
| C19 | $\begin{gathered} 201.42 \\ {[24.1]} \end{gathered}$ | $\begin{aligned} & 188.35 \\ & {[14.0]} \end{aligned}$ | $\begin{aligned} & 63.22 \\ & {[13.2]} \end{aligned}$ | $\begin{gathered} 95.56 \\ {[7.3]} \end{gathered}$ | $\begin{gathered} 201.39 \\ {[9.8]} \end{gathered}$ | $\begin{gathered} 279.21 \\ {[7.9]} \end{gathered}$ | $\begin{gathered} -112.15 \\ {[8.8]} \end{gathered}$ | $\begin{gathered} 0.03 \\ {[20.2]} \end{gathered}$ |
| C20 | $\begin{gathered} 294.94 \\ {[10.5]} \end{gathered}$ | $\begin{gathered} 174.20 \\ {[8.8]} \end{gathered}$ | $\begin{aligned} & 67.09 \\ & {[9.4]} \end{aligned}$ | $\begin{aligned} & 85.50 \\ & {[7.0]} \end{aligned}$ | $\begin{gathered} 190.84 \\ {[8.8]} \end{gathered}$ | $\begin{gathered} 279.05 \\ {[8.1]} \end{gathered}$ | $\begin{gathered} -126.80 \\ {[7.9} \end{gathered}$ | $\begin{aligned} & 24.11 \\ & {[14.2]} \end{aligned}$ |
| C21 | $\begin{gathered} 294.91 \\ {[21.8]} \end{gathered}$ | $\begin{gathered} 178.49 \\ {[8.6]} \end{gathered}$ | $\begin{gathered} 70.02 \\ {[15.3]} \end{gathered}$ | $\begin{gathered} 80.73 \\ {[7.9]} \end{gathered}$ | $\begin{aligned} & 188.42 \\ & {[14.5]} \end{aligned}$ | $\begin{gathered} 278.05 \\ {[10.9]} \end{gathered}$ | $\begin{gathered} -124.87 \\ {[8.7]} \end{gathered}$ | $\begin{aligned} & 33.13 \\ & {[17.3]} \end{aligned}$ |
| G22 | $\begin{gathered} 297.2 \\ {[12.7]} \end{gathered}$ | $\begin{aligned} & 193.79 \\ & {[11.0]} \end{aligned}$ | $\begin{aligned} & 63.88 \\ & {[15.9]} \end{aligned}$ | $\begin{aligned} & 132.07 \\ & {[19.8]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{gathered} -110.18 \\ {[20.8]} \end{gathered}$ | $\begin{aligned} & 111.31 \\ & {[45.4]} \end{aligned}$ |

Table S15: Average value along with standard deviation of the backbone dihedral angles for the bases as found in MD simulation of $5{ }^{\prime} \mathrm{E}_{\mathrm{CGG}}$-form structure.

| Nucleotide | $\alpha\left({ }^{\circ}\right)$ | $\beta\left({ }^{\circ}\right)$ | $\gamma\left({ }^{\circ}\right)$ | $\delta\left({ }^{\circ}\right)$ | $\varepsilon\left(^{\circ}\right)$ | $\zeta\left({ }^{\circ}\right)$ | $\chi\left({ }^{\circ}\right)$ | Phase ( ${ }^{\circ}$ ) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| C1 | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 64.26 \\ & {[18.5]} \end{aligned}$ | $\begin{aligned} & 82.62 \\ & {[12.9]} \end{aligned}$ | $\begin{aligned} & 197.20 \\ & {[14.7]} \end{aligned}$ | $\begin{gathered} 275.79 \\ {[9.2]} \end{gathered}$ | $\begin{gathered} -128.75 \\ {[9.6]} \end{gathered}$ | $\begin{aligned} & 39.71 \\ & {[28.6]} \end{aligned}$ |
| C2 | $\begin{gathered} 294.77 \\ {[21.8]} \end{gathered}$ | $\begin{aligned} & 174.78 \\ & {[15.8]} \end{aligned}$ | $\begin{gathered} 69.60 \\ {[20.0]} \end{gathered}$ | $\begin{gathered} 85.12 \\ {[9.0]} \end{gathered}$ | $\begin{gathered} 191.20 \\ {[9.5]} \end{gathered}$ | $\begin{gathered} 280.59 \\ {[8.3]} \end{gathered}$ | $\begin{gathered} -126.83 \\ {[8.6]} \end{gathered}$ | $\begin{aligned} & 33.74 \\ & {[23.8]} \end{aligned}$ |
| C3 | $\begin{gathered} 297.42 \\ {[18.2]} \end{gathered}$ | $\begin{gathered} 178.68 \\ {[8.9]} \end{gathered}$ | $\begin{aligned} & 68.88 \\ & {[13.8]} \end{aligned}$ | $\begin{aligned} & 82.91 \\ & {[11.7]} \end{aligned}$ | $\begin{gathered} 210.73 \\ {[22.8]} \end{gathered}$ | $\begin{gathered} 285.69 \\ {[11.1]} \end{gathered}$ | $\begin{gathered} -121.63 \\ {[10.0]} \end{gathered}$ | $\begin{aligned} & 45.47 \\ & {[21.7]} \end{aligned}$ |
| C4 | $\begin{gathered} 232.01 \\ {[41.5]} \end{gathered}$ | $\begin{gathered} 253.94 \\ {[46.1]} \end{gathered}$ | $\begin{gathered} 298.37 \\ {[10.9]} \end{gathered}$ | $\begin{aligned} & 150.75 \\ & {[10.7]} \end{aligned}$ | $\begin{gathered} 190.10 \\ {[8.1]} \end{gathered}$ | $\begin{gathered} 280.14 \\ {[8.3]} \end{gathered}$ | $\begin{gathered} -110.09 \\ {[13.9]} \end{gathered}$ | $\begin{aligned} & 166.21 \\ & {[15.9]} \end{aligned}$ |
| G5 | $\begin{gathered} 288.90 \\ {[8.8]} \end{gathered}$ | $\begin{gathered} 168.11 \\ {[8.0]} \end{gathered}$ | $\begin{gathered} 56.84 \\ {[8.1]} \end{gathered}$ | $\begin{gathered} 141.40 \\ {[7.5]} \end{gathered}$ | $\begin{aligned} & 270.94 \\ & {[10.9]} \end{aligned}$ | $\begin{gathered} 283.46 \\ {[13.8]} \end{gathered}$ | $\begin{gathered} -88.16 \\ {[11.3]} \end{gathered}$ | $\begin{aligned} & 152.07 \\ & {[11.6]} \end{aligned}$ |
| G6 | $\begin{gathered} 238.02 \\ {[47.0]} \end{gathered}$ | $\begin{aligned} & 179.07 \\ & {[12.5]} \end{aligned}$ | $\begin{aligned} & 53.36 \\ & {[11.9]} \end{aligned}$ | $\begin{gathered} 147.29 \\ {[9.3]} \end{gathered}$ | $\begin{gathered} 203.55 \\ {[13.9]} \end{gathered}$ | $\begin{gathered} 283.80 \\ {[9.9]} \end{gathered}$ | $\begin{gathered} -119.82 \\ {[36.4]} \end{gathered}$ | $\begin{aligned} & 164.22 \\ & {[17.1]} \end{aligned}$ |
| $\mathrm{C}^{+} 7$ | $\begin{gathered} 290.34 \\ {[11.2]} \end{gathered}$ | $\begin{aligned} & 174.15 \\ & {[10.3]} \end{aligned}$ | $\begin{aligned} & 63.41 \\ & {[10.1]} \end{aligned}$ | $\begin{aligned} & 83.28 \\ & {[7.9]} \end{aligned}$ | $\begin{gathered} 189.59 \\ {[11.2]} \end{gathered}$ | $\begin{gathered} 271.10 \\ {[10.9]} \end{gathered}$ | $\begin{gathered} -132.81 \\ {[10.5]} \end{gathered}$ | $\begin{aligned} & 28.53 \\ & {[16.1]} \end{aligned}$ |
| $\mathrm{C}^{+} 8$ | $\begin{gathered} 298.52 \\ {[9.8]} \end{gathered}$ | $\begin{aligned} & 177.46 \\ & {[10.1]} \end{aligned}$ | $\begin{aligned} & 68.95 \\ & {[8.5]} \end{aligned}$ | $\begin{aligned} & 98.42 \\ & {[19.5]} \end{aligned}$ | $\begin{gathered} 187.94 \\ {[9.8]} \end{gathered}$ | $\begin{gathered} 273.21 \\ {[12.1]} \end{gathered}$ | $\begin{gathered} -124.53 \\ {[11.0]} \end{gathered}$ | $\begin{gathered} 19.53 \\ {[14.3]} \end{gathered}$ |
| $\mathrm{C}^{+} 9$ | $\begin{gathered} 297.76 \\ {[16.3]} \end{gathered}$ | $\begin{gathered} 180.69 \\ {[9.4]} \end{gathered}$ | $\begin{gathered} 72.79 \\ {[15.5]} \end{gathered}$ | $\begin{aligned} & 116.60 \\ & {[25.4]} \end{aligned}$ | $\begin{gathered} 202.01 \\ {[22.0]} \end{gathered}$ | $\begin{gathered} 258.30 \\ {[29.7]} \end{gathered}$ | $\begin{gathered} -113.96 \\ {[12.7]} \end{gathered}$ | $\begin{aligned} & 96.93 \\ & {[21.7]} \end{aligned}$ |
| C10 | $\begin{gathered} 282.59 \\ {[30.2]} \end{gathered}$ | $\begin{aligned} & 137.65 \\ & {[41.7]} \end{aligned}$ | $\begin{gathered} 79.48 \\ {[39.8]} \end{gathered}$ | $\begin{aligned} & 143.80 \\ & {[11.6]} \end{aligned}$ | $\begin{gathered} 210.43 \\ {[32.8]} \end{gathered}$ | $\begin{gathered} 259.22 \\ {[32.7]} \end{gathered}$ | $\begin{gathered} -113.55 \\ {[15.2]} \end{gathered}$ | $\begin{aligned} & 158.37 \\ & {[19.9]} \end{aligned}$ |
| G11 | $\begin{gathered} 291.82 \\ {[13.0]} \end{gathered}$ | $\begin{aligned} & 163.03 \\ & {[16.7]} \end{aligned}$ | $\begin{gathered} 55.72 \\ {[9.7]} \end{gathered}$ | $\begin{gathered} 143.0 \\ {[11.9]} \end{gathered}$ | $\begin{gathered} 251.41 \\ {[29.3]} \end{gathered}$ | $\begin{aligned} & 138.10 \\ & {[38.1]} \end{aligned}$ | $\begin{aligned} & 112.17 \\ & {[34.6]} \end{aligned}$ | $\begin{aligned} & 157.99 \\ & {[19.5]} \end{aligned}$ |
| G12 | $\begin{array}{r} 281.47 \\ {[11.2]} \end{array}$ | $\begin{gathered} 70.77 \\ {[22.9]} \end{gathered}$ | $\begin{aligned} & 186.41 \\ & {[34.6]} \end{aligned}$ | $\begin{aligned} & 144.81 \\ & {[11.0]} \end{aligned}$ | $\begin{gathered} 221.09 \\ {[29.7]} \end{gathered}$ | $\begin{aligned} & 155.29 \\ & {[14.8]} \end{aligned}$ | $\begin{gathered} -118.75 \\ {[29.7]} \end{gathered}$ | $\begin{aligned} & 159.39 \\ & {[20.0]} \end{aligned}$ |
| $\mathrm{C}^{+} 13$ | $\begin{gathered} 285.71 \\ {[14.1]} \end{gathered}$ | $\begin{aligned} & 173.13 \\ & {[13.4]} \end{aligned}$ | $\begin{aligned} & 59.02 \\ & {[9.1]} \end{aligned}$ | $\begin{aligned} & 102.27 \\ & {[22.2]} \end{aligned}$ | $\begin{gathered} 203.54 \\ {[26.3]} \end{gathered}$ | $\begin{gathered} 274.87 \\ {[13.3]} \end{gathered}$ | $\begin{gathered} -131.33 \\ {[12.6]} \end{gathered}$ | $\begin{aligned} & 67.79 \\ & {[34.0]} \end{aligned}$ |
| $\mathrm{C}^{+} 14$ | $\begin{gathered} 294.22 \\ {[18.3]} \end{gathered}$ | $\begin{aligned} & 188.67 \\ & {[10.5]} \end{aligned}$ | $\begin{gathered} 78.17 \\ {[19.4]} \end{gathered}$ | $\begin{aligned} & 132.75 \\ & {[16.4]} \end{aligned}$ | $\begin{aligned} & 199.11 \\ & {[14.6]} \end{aligned}$ | $\begin{gathered} 260.67 \\ {[21.1]} \end{gathered}$ | $\begin{gathered} -108.37 \\ {[15.6]} \end{gathered}$ | $\begin{aligned} & 141.30 \\ & {[31.5]} \end{aligned}$ |
| $\mathrm{C}^{+} 15$ | $\begin{aligned} & 287.32 \\ & {[15.7]} \end{aligned}$ | $\begin{aligned} & 185.91 \\ & {[15.2]} \end{aligned}$ | $\begin{gathered} 66.33 \\ {[18.8]} \end{gathered}$ | $\begin{aligned} & 124.36 \\ & {[14.9]} \end{aligned}$ | $\begin{gathered} 249.00 \\ {[24.1]} \end{gathered}$ | $\begin{gathered} 267.61 \\ {[20.2]} \end{gathered}$ | $\begin{aligned} & -92.26 \\ & {[12.9]} \end{aligned}$ | $\begin{aligned} & 128.33 \\ & {[16.8]} \end{aligned}$ |
| C16 | $\begin{aligned} & 107.07 \\ & {[46.3]} \end{aligned}$ | $\begin{aligned} & 179.38 \\ & {[18.1]} \end{aligned}$ | $\begin{aligned} & 57.29 \\ & {[10.7]} \end{aligned}$ | $\begin{gathered} 145.56 \\ {[9.3]} \end{gathered}$ | $\begin{gathered} 220.74 \\ {[24.4]} \end{gathered}$ | $\begin{gathered} 283.61 \\ {[10.8]} \end{gathered}$ | $\begin{gathered} -137.74 \\ {[21.5]} \end{gathered}$ | $\begin{aligned} & 157.64 \\ & {[12.4]} \end{aligned}$ |
| G17 | $\begin{gathered} 264.64 \\ {[32.9]} \end{gathered}$ | $\begin{gathered} 242.09 \\ {[48.3]} \end{gathered}$ | $\begin{gathered} 299.86 \\ {[8.1]} \end{gathered}$ | $\begin{aligned} & 139.77 \\ & {[13.0]} \end{aligned}$ | $\begin{aligned} & 186.76 \\ & {[10.9]} \end{aligned}$ | $\begin{gathered} 276.50 \\ {[8.9]} \end{gathered}$ | $\begin{aligned} & 67.24 \\ & {[16.0]} \end{aligned}$ | $\begin{aligned} & 150.44 \\ & {[16.0]} \end{aligned}$ |
| G18 | $\begin{gathered} 290.93 \\ {[8.8]} \end{gathered}$ | $\begin{gathered} 172.54 \\ {[8.8]} \end{gathered}$ | $\begin{aligned} & 55.91 \\ & {[8.3]} \end{aligned}$ | $\begin{aligned} & 131.73 \\ & {[11.0]} \end{aligned}$ | $\begin{gathered} 246.64 \\ {[13.8]} \end{gathered}$ | $\begin{gathered} 289.63 \\ {[9.5]} \end{gathered}$ | $\begin{gathered} -95.42 \\ {[13.5]} \end{gathered}$ | $\begin{aligned} & 142.04 \\ & {[20.1]} \end{aligned}$ |
| C19 | $\begin{gathered} 263.23 \\ {[19.2]} \end{gathered}$ | $\begin{aligned} & 166.03 \\ & {[14.1]} \end{aligned}$ | $\begin{aligned} & 53.66 \\ & {[11.4]} \end{aligned}$ | $\begin{aligned} & 87.94 \\ & {[8.0]} \end{aligned}$ | $\begin{aligned} & 195.76 \\ & {[11.1]} \end{aligned}$ | $\begin{gathered} 275.22 \\ {[8.2]} \end{gathered}$ | $\begin{gathered} -114.10 \\ {[10.1]} \end{gathered}$ | $\begin{gathered} 17.66 \\ {[19.4]} \end{gathered}$ |
| C20 | $\begin{gathered} 295.52 \\ {[9.7]} \end{gathered}$ | $\begin{gathered} 175.18 \\ {[9.0]} \end{gathered}$ | $\begin{gathered} 64.87 \\ {[8.2]} \end{gathered}$ | $\begin{aligned} & 85.83 \\ & {[7.5]} \end{aligned}$ | $\begin{gathered} 189.82 \\ {[8.6]} \end{gathered}$ | $\begin{gathered} 276.57 \\ {[7.9]} \end{gathered}$ | $\begin{gathered} -126.42 \\ {[8.2]} \end{gathered}$ | $\begin{aligned} & 23.75 \\ & {[16.0]} \end{aligned}$ |
| C21 | $\begin{gathered} 296.91 \\ {[15.7]} \end{gathered}$ | $\begin{gathered} 176.10 \\ {[8.5]} \end{gathered}$ | $\begin{gathered} 70.35 \\ {[14.4]} \end{gathered}$ | $\begin{aligned} & 83.18 \\ & {[7.5]} \end{aligned}$ | $\begin{aligned} & 189.92 \\ & {[16.5]} \end{aligned}$ | $\begin{gathered} 277.60 \\ {[9.8]} \end{gathered}$ | $\begin{gathered} -127.70 \\ {[8.1]} \end{gathered}$ | $\begin{aligned} & 29.91 \\ & {[16.6]} \end{aligned}$ |
| C22 | $\begin{gathered} 293.59 \\ {[22.8]} \end{gathered}$ | $\begin{aligned} & 171.46 \\ & {[33.0]} \end{aligned}$ | $\begin{aligned} & 75.90 \\ & {[30.1]} \end{aligned}$ | $\begin{aligned} & 116.38 \\ & {[30.3]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{aligned} & 0.00 \\ & {[0.0]} \end{aligned}$ | $\begin{gathered} -127.74 \\ {[12.6]} \end{gathered}$ | $\begin{aligned} & 100.08 \\ & {[31.34]} \end{aligned}$ |

Table S16: Average hydrogen bonding geometry and occupancy (considering $\mathrm{C}-\mathrm{O}$ distance $\leq 3.4$ $\AA$ and C-H...O angle > $120^{\circ}$ ) of possible C-H...O mediated hydrogen bond between sugar moieties of the antiparallel strands along the narrow grooves of $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ and $5^{\prime} \mathrm{E}_{\mathrm{CGG}}$ i-motif DNA.

| C-H...O mediated hydrogen bond between sugar moiety | $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ |  |  | $5^{\prime} \mathrm{E}_{\text {CGG }}$ |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Distance between C and O (Å) | C-H...O angle $\left({ }^{\circ}\right)$ | Occupancy <br> (\%) | Distance between C and O (A) | C-H...O angle $\left({ }^{\circ}\right)$ | Occupancy <br> (\%) |
| (C1) C1'-H...O4' (G22/C22) | 3.30 | 134.89 | 42.86 | 3.28 | 133.52 | 49.45 |
| (G22/C22) C1'-H...O4' (C1) | 3.31 | 134.94 | 7.84 | 3.28 | 132.90 | 26.22 |
| (C2) C1'-H...O4' (C21) | 3.27 | 135.21 | 69.27 | 3.26 | 131.88 | 70.43 |
| (C21) C1'-H...O4' (C2) | 3.28 | 132.49 | 61.74 | 3.26 | 131.41 | 71.02 |
| (C3) C1'-H...O4' (C20) | 3.34 | 132.96 | 38.49 | 3.29 | 129.49 | 53.03 |
| (C20) C1'-H...O4' (C3) | 3.28 | 134.18 | 69.72 | 3.24 | 130.10 | 66.84 |
| ( $\mathrm{C}^{+} 8$ ) C1'-H...O4' ( $\mathrm{C}^{+} 15$ ) | 3.31 | 133.96 | 47.55 | 3.27 | 133.85 | 59.24 |
| ( $\mathrm{C}^{+} 15$ ) $\mathrm{C} 1{ }^{\prime}-\mathrm{H} . . . \mathrm{O} 4{ }^{\prime}\left(\mathrm{C}^{+} 8\right)$ | 3.32 | 130.59 | 21.71 | 3.34 | 129.66 | 9.94 |
| ( $\mathrm{C}^{+} 9$ ) C1'-H...O4' ( $\mathrm{C}^{+} 14$ ) | 3.30 | 133.26 | 33.34 | 3.28 | 131.32 | 45.10 |
| ( $\mathrm{C}^{+} 14$ ) C1'-H...O4' ( $\left.\mathrm{C}^{+} 9\right)$ | 3.28 | 133.31 | 55.57 | 3.31 | 133.28 | 36.16 |
| (G10/C10) C1'-H...O4' (C' 13 ) | 3.39 | 129.73 | 7.21 | 3.34 | 130.08 | 10.10 |
| (C'13) C1'-H...O4' (G10/C10) | 3.26 | 132.86 | 39.52 | 3.24 | 139.96 | 66.63 |

## Figures:

Fig. S1: Variation of RMSD with respect to the initial energy minimized structure in case of studied i-motif systems: (a) 3'E-form structure with hemi-protonated cytosines and normal cytosines at 300 K , (b) 3 'E-form structure with hemi-protonated cytosines at elevated temperatures, (c) $5^{\prime} \mathrm{E}$ form structure with hemi-protonated cytosines and normal cytosines at 300 K , (d) $5^{\prime} \mathrm{E}$-form structure with hemi-protonated cytosines at elevated temperatures, (e) $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ and $5^{\prime} \mathrm{E}_{\mathrm{CGG}}$-form structure with hemi-protonated cytosines at 300 K and (f) $5^{\prime}$ E-form structure with hemi-protonated cytosines and normal cytosine at 300 K with TIP3P water model.


Fig. S2: Representative backbone refined conformations of model (a)-(h) $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structures having different rotational orientation of intercalated base pair about its base pair helix axis and (i)-(p) tetranucleotide structures of two intercalated $\mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CC}$ dinuceotides with different helical rotations around their base pair helix axis.


Fig. S3: Root mean square fluctuation (RMSF) of the nucleotides in (a) 3'E and (b) 5'E-form imotif structure under acidic pH with hemi-protonated cytosines.


Fig. S4: Distribution of distance between the N3 atoms of paired bases in equilibrated MD trajectory of $3^{\prime} \mathrm{E}$ (a) and $5^{\prime} \mathrm{E}$-form (b) i-motif structure with hemi-protonated cytosines, and distance matrix for the nucleobases in equilibrated conformation of $3^{\prime} \mathrm{E}$ (c) and $5^{\prime} \mathrm{E}$-form (d) i-motif structure with hemi-protonated cytosines.


Fig. S5: Variation of distance between the N3 atoms of paired bases along the MD simulated trajectory of $3^{\prime} \mathrm{E}$ (a)-(b) and $5^{\prime} \mathrm{E}$-form (c)-(d) structure in deprotonated state with normal cytosines.




Fig. S6: Average conformation of (a) $3^{\prime} \mathrm{E}$ and (b) $5^{\prime} \mathrm{E}$-form structure, and distance matrix for the nucleobases in equilibrated conformation of (c) $3^{\prime} \mathrm{E}$ and (d) $5^{\prime} \mathrm{E}$-form structure under neutral pH with deprotonated cytosines.


Fig. S7: Variation of distance between the N3 atoms of paired bases along the MD simulated trajectory of $3^{\prime} \mathrm{E}$ (a) and $5^{\prime} \mathrm{E}$-form (b) structure in deprotonated state with normal cytosine considering larger simulation box, and considering TIP3P water model in case of $5^{\prime}$ ' E -form structure (c).


Fig. S8: $1^{\text {st }}$ and $2^{\text {nd }}$ normal mode of motions in the equilibrated MD trajectory of (a)-(b) $3^{\prime} \mathrm{E}$ and (c)(d) 5'E-form structure under neutral pH with deprotonated cytosines.


Fig. S9: Average structure of i-motif core in the equilibrated MD trajectory of (a) $3^{\prime} \mathrm{E}$ and (b) $5^{\prime} \mathrm{E}-$ form topology under acidic pH with hemi-protonted cytosines.


Fig. S10: Average values along with standard deviations of narrow grooves and wide grooves backbone phosphate-phosphate distances in (a)-(b) 3'E and (c)-(d) 5'E-form i-motif structure under acidic pH with hemi-protonted cytosines.


Fig. S11: Variation of energy of the sugar-phosphate backbone refined conformation of model (a) $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide structure with helical rotations $(\theta)$ of the intercalated base pair around their base pair helix axis, and (b) tetranucleotide conformations of two intercalated $\mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CC}$ dinuceotides with helical rotations $(\theta)$ around their base pair helix axis.


Fig. S12: Radial distributions of the oxygen (O) atom of solvent water molecule around backbone phosphate group of bases $\left(g\left(r_{P-O}\right)\right)$ within i-motif core with hemi-protonated cytosines under acidic pH for (a) $3^{\prime} \mathrm{E}$ and (b) $5^{\prime} \mathrm{E}$-form structure, and in deprotonated state of cytosines under neutral pH for (c) $3^{\prime} \mathrm{E}$ and (d) $5^{\prime} \mathrm{E}$-form structure.


Fig. S13: Radial distributions of the oxygen (O) atoms of solvent water molecule around N4 atom of cytosines $(g(r))$ within i-motif core in hemi-protonated and deprotonated state of cytosines for (a) $3^{\prime} \mathrm{E}$ and (b) 5'E-form structure considering $\mathrm{SPC} / \mathrm{E}$ water model, and (c) 5'E-form structure considering TIP3P water model.




Fig. S14: Radial distributions of the oxygen (O) atoms of solvent water molecule around N 4 atom of cytosines $\left(g\left(r_{N 4-O}\right)\right)$ within i-motif core at elevated temperatures with hemi-protonated cytosines under acidic pH for (a) $3^{\prime} \mathrm{E}$ and (b) 5'E-form i-motif structure.


Fig. S15: (a) DFT optimized geometry of six water molecules in wider grooves first solvation cell considering MD average model conformation of $\mathrm{C}^{+} \mathrm{C}^{+} \mathrm{C}^{+} / \mathrm{CCC}$ trinucleotide within the i-motif core and fixing all the non-hydrogen atoms of the bases. (b) DFT optimized structure of a water molecule along with cytosine base.


Fig. S16: First normal mode of motions at different temperature in the equilibrated MD trajectory of (a)-(c) $3^{\prime} \mathrm{E}$ and (d)-(f) $5^{\prime} \mathrm{E}$-form i-motif structure under acidic pH with hemi-protonated cytosines.


Fig. S17: Root mean square fluctuation (RMSF) of the nucleotides at different temperature in (a) $3^{\prime} \mathrm{E}$ and (b) $5^{\prime} \mathrm{E}$-form i-motif structure with hemi-protonated cytosines under acidic pH .


Fig. S18: At different temperature distribution of wide grooves width in (a) $3^{\prime} E$ and (b) $5{ }^{\prime} E$-form structure, narrow grooves width in (c) $3^{\prime} \mathrm{E}$ and (d) $5^{\prime} \mathrm{E}$-form structure, and hydrogen bonding distance and angle between sugar oxygen O 4 ' of one strand and C 1 ' on the anti-parallel strand across the narrow grooves in (e) $3^{\prime} \mathrm{E}$ and (f) $5^{\prime} \mathrm{E}$-form structure, as derived from the equilibrated MD trajectory of i-motif DNA under acidic pH with hemi-protonated cytosines.


Fig. S19: Temperature dependent grid water density distribution ( $\rho_{\text {wat }}$ ) around the i-motif core in (a)-(c) $3^{\prime} \mathrm{E}$ and (d)-(f) 5 'E-form structure under acidic pH having probability of water molecules stay in that grid points greater than 0.5 . Grid points are represented with a sphere of color tints wheat.


Fig. S20: (a) At different temperature distribution of number of water molecules forming hydrogen bonds with the N 4 atom of cytosines in the wide grooves of $5^{\prime}$ 'E-form i-motif DNA in equilibrated trajectory under acidic pH . (b) Distribution of hydrogen bonded life time at different temperature for the hydrogen bonded water molecules in the wide grooves of $5^{\prime} \mathrm{E}$-form structure with hemiprotonated cytosines.


Fig. S21: In case of $5{ }^{\prime} \mathrm{E}_{\mathrm{CGG}}$ (a)-(b) and $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ (c)-(d) form structure first two normal modes of motions in the equilibrated trajectory. Distribution of (e) narrow grooves width and (f) hydrogen bonding distance and angle between sugar oxygen O 4 ' of one strand and $\mathrm{C1}$ ' on the anti-parallel strand across the narrow minor grooves in $5^{\prime} \mathrm{E}$ (TAA), $5^{\prime} \mathrm{E}_{\mathrm{CGG}}$ (CGG) and $5^{\prime} \mathrm{E}_{\mathrm{GCC}}$ (GCC) form structure, as derived from the equilibrated MD trajectory of i-motif DNA under acidic pH with hemi-protonted cytosines.


