Structural Properties of Small Single-Stranded Circular Nucleic Acids

Parth Chaturvedi, Lela Vuković*

Department of Chemistry and Biochemistry, University of Texas at El Paso, El Paso, TX 79968

*Authors to whom all correspondence should be addressed: lvukovic@utep.edu

Electronic Supporting Information (ESI)
Patch to create a covalent bond between 3’ and 5’ ends of nucleic acids:

PRES LKRI   0.0   ! Patch to join to nucleic acid segments (eg for IMAGES)
            ! eg: patch sega 10 segb 1
            ! sega should have std 3’ (gene sega ... last none)
            ! segb should have std 5’ (gene segb ... first none)
            ! USE AUTOgen ANGL DIHE after this patch,
            ! but before water-generation
BOND 1O3’  2P
IC  1O3’  2P  2O5’  2C5’  1.6001  101.45  -39.25  119.00  1.4401
IC  1O3’  2O5’ *2P  2O1P  1.6001  101.45  -115.82  109.74  1.4802
IC  1O3’  2O5’ *2P  2O2P  1.6001  101.45  115.90  109.80  1.4801
IC  1C4’  1C3’  1O3’  2P  1.5284  111.92  159.13  119.05  1.6001
IC  1C3’  1O3’  2P  2O5’  1.4212  119.05  -98.86  101.45  1.599

Table S1. Summary of simulation parameters used in MDFF simulations for different oligonucleotides.

<table>
<thead>
<tr>
<th></th>
<th>(GT)₃ &amp; (GU)₃</th>
<th>(GT)₄ &amp; (GU)₄</th>
<th>(GT)₆ &amp; (GU)₆</th>
<th>(GT)₈ &amp; (GU)₈</th>
<th>(GT)₂₄</th>
<th>(GU)₂₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (n) of dummy atoms</td>
<td>18</td>
<td>24</td>
<td>36</td>
<td>75</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>used to generate circular</td>
<td>n/3</td>
<td>n/3</td>
<td>n/3</td>
<td>n/5</td>
<td>n/5</td>
<td>n/5</td>
</tr>
<tr>
<td>potential</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radius (r) of circular</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>potential for MDFF (Å)</td>
<td>n/3</td>
<td>n/3</td>
<td>n/3</td>
<td>n/5</td>
<td>n/5</td>
<td>n/5</td>
</tr>
<tr>
<td>$g_{scale}(\xi)$, scaling</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>factor for MDFF potential</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docking by colores (Situs)</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Force constant (kcal/molÅ²)</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Figure S1. Radial distribution functions (RDFs) of phosphorous atoms of circNAs calculated over 1 µs in MD simulations. RDFs are computed with a 10 ns time step. (GU), circRNAs have P-atoms that are more likely to be closer to each other than P-atoms of (GT), circDNAs, for all circRNAs examined.

Figure S2. Sodium ions (yellow) within 4 Å of (GT), circDNAs, as observed after 1 µs of MD simulations. The scale bars in panels (a-d) are 1 Å in length, and in panel (e) is 10 Å in length. Only the backbones of circDNAs are shown (atom color scheme: C-grey, O-red, P-orange).
Figure S3. Sodium ions (yellow) within 4 Å of (GU)$_n$ circRNAs, as observed after 1 μs of MD simulation. The scale bars in panels (a-d) are 1 Å in length, and in panel (e) is 10 Å in length. Only the backbones of circRNAs are shown (atom color scheme: C-grey, O-red, P-orange).

Figure S4. Conformations of circular (GT)$_8$ circDNA and (GU)$_8$ circRNAs at 1 μs showing base stacking as observed in MD simulations. The scale bars in panels are 1 Å in length.
Figure S5. Contact areas between nucleotide bases and aqueous solvent for circRNAs calculated over 1 µs in MD simulations. The areas are computed with a 10 ns time step. (GT)$_n$ circDNA bases are more water-exposed than (GU)$_n$ circRNA bases in circular nucleic acids.

Figure S6. Distribution of number of contacts between four (GT)$_6$ circDNA (left) and four (GU)$_6$ circRNAs (right) molecules, as observed in 1 µs simulations.
Figure S7. Contacts between pairs of circDNA-(GT)$_6$ molecules, as observed in 1 µs simulations of four circDNA-(GT)$_6$ molecules (at 7.9 mM concentration).
Figure S8. Contacts between pairs of circRNA-(GU)$_6$ molecules, as observed in 1 µs simulations of four circRNA-(GU)$_6$ molecules (at 7.9 mM concentration).

Figure S9. Number of contacts between four (GT)$_6$ circDNAs or four (GU)$_6$ circRNAs (at 7.9 mM concentration, left), and between three (GT)$_6$ circDNAs or three (GU)$_6$ circRNAs (at 5.9 mM concentration, right).
Figure S10. Distribution of phosphate angles for all P-atom triplets in the last 500 ns of trajectories of all circular DNA (blue) and RNA (red) molecules examined in Figure 2.

Figure S11. Distribution of phosphate angles for all P-atom triplets in the last 500 ns of trajectories of four circular (GT)$_6$ DNA (blue) and four circular (GU)$_6$ RNA (red) molecules, examined in simulations of multiple circular molecules (shown in Figure 5).