Supporting information for:

All-atom MD Simulation of DNA Condensation Using Ab-initio Derived Force Field Parameters of Cobalt(III)-Hexammine

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1. Zhang & Mu's $CoHex^{3+}$ model does not induce DNA condensation with CHARMM36.

Simulations of four DNA oligomers have been carried out in presence of $CoHex^{3+}$ to investigate the experimentally known condensing effect of $CoHex^{3+}$ on double helical DNA. The DNA oligonucleotides was described by the CHARMM36 force field[1] with $CoHex^{3+}$ ions by the parameters from the earlier work.[2] Two separate simulations with different box sizes as well as different starting configurations were performed, one for 830 ns and the other for 300 ns. The first system containing four 40-bp DNA double helices with 110 added $CoHex^{3+}$, 72 Na^+, 110 K^+, 150 Cl^- ions and 112,300 TIP3P water molecules was simulated in a cubic box of $15\times15\times15$ nm^3. Double helical DNA 40-mers had the following sequences:

5'-GGATTAATGGAACGTAGCATATTCTTCAAGTTGTCACGCC-3'

5'-GGCAAAACCTGATGCACACTGTAACATGAGATCCCGCGCC-3'

5'-CCTCGGCTTATAGAGGGCCAGCTCGTATCGACGGACCGGG-3'

5'-CCGCTAGTACCCCACCAATTTAGGCGAAAGGAGTCTGCGG-3'

The second, 300 ns long simulation, was performed in a cubic box of $16.4\times16.4\times16.4$ nm^3 with four 36-bp DNA double helices. These oligo-DNA molecules were derived from the first

simulation by removing two base pairs from each end of aforementioned sequences. To keep the same ionic condition with the first simulation, 140 $CoHex^{3+}$, 95 Na^{+}, 140 K^{+}, 375 Cl^{-} were add to the system along with 147,000 TIP3P water molecules.

Both simulations with this $CoHex^{3+}$ model showed only a weak attraction of DNA but did not demonstrate ability of DNA oligomers to aggregate. As shown in Figure S1 and Figure S2, DNA double helix did not exhibit close contact up to 830 ns. Comparing to our other simulations of DNA oligomers with spermidine (not shown here), it is not in agreement with well-established experimental results showing higher condensing potential of $CoHex^{3+}$ (see e.g. ref [3-4]).

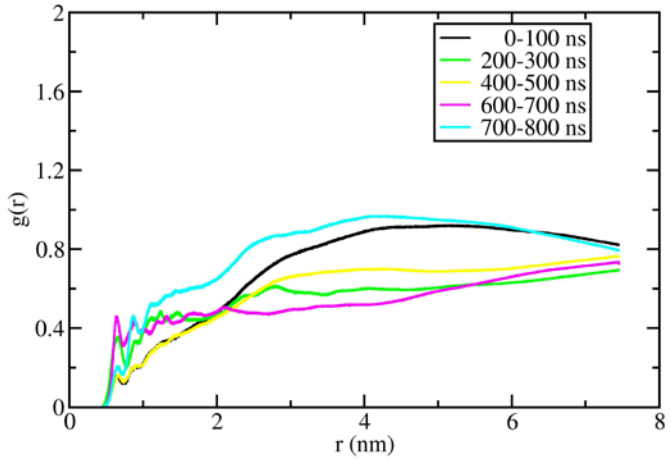

Figure S1 Inter-DNA phosphate-phosphate radial distribution function calculated based on the 830ns trajectory. Each curve is calculated from a 100 ns window, as indicated by the legend.

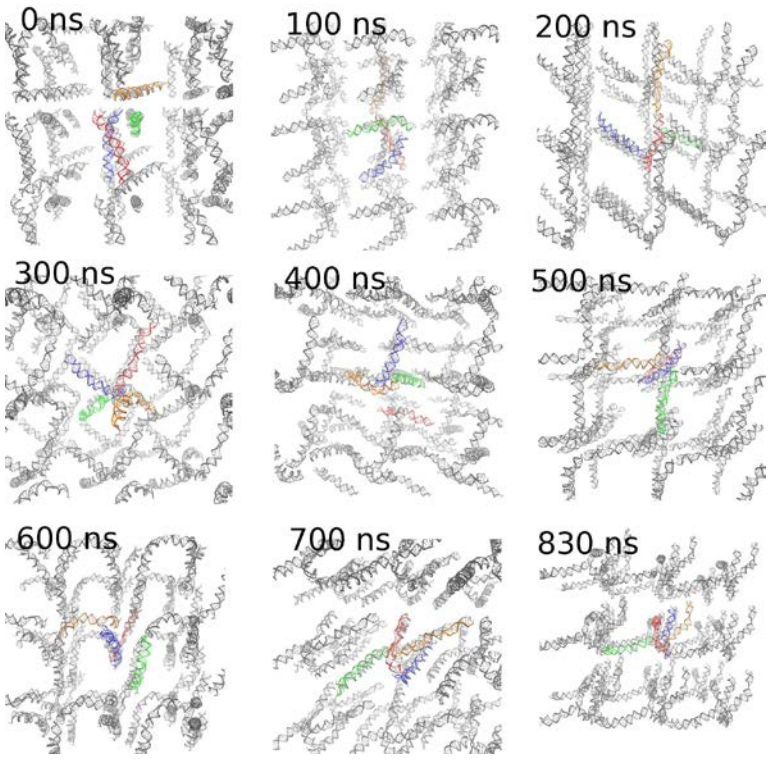

Figure S2: Snapshots from the 830 ns simulation with DNA oligomers and $CoHex^{3+}$. Four DNA oligomers are colored differently. Periodic images are colored gray. No attraction was displayed through the whole trajectory.

References

1. Hart, K.; Foloppe, N.; Baker, C. M.; Denning, E. J.; Nilsson, L.; MacKerell, A. D., Jr., Optimization of the CHARMM additive force field for DNA: Improved treatment of the BI/BII conformational equilibrium. *J.Chem.Theory Comput.* **2012,** *8* (1), 348-362.

2. Zhang, T.; Mu, Y., Initial binding of ions to the interhelical loops of divalent ion transporter CorA: replica exchange molecular dynamics simulation study. *PLoS One* **2012,** *7* (8), e43872.

3. Matulis, D.; Rouzina, I.; Bloomfield, V. A., Thermodynamics of DNA binding and condensation: isothermal titration calorimetry and electrostatic mechanism. *J.Mol.Biol.* **2000,** *296*, 1053-1063.

4. Korolev, N.; Berezhnoy, N. V.; Eom, K. D.; Tam, J. P.; Nordenskiöld, L., A universal description for the experimental behavior of salt-(in)dependent oligocation-induced DNA condensation. *Nucleic Acids Res.* **2012,** *40* (6), 2808-2821.