Summer 2021

Varied Behavior of Dinucleotides on Ice

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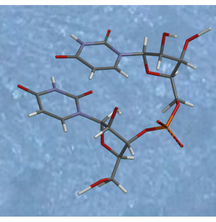

Introduction

RNA world theory posits RNA as the precursor to both DNA and proteins, and consequently all life on earth, but it is debated how exactly this occurred. Many hypotheses posit that RNA formed first in aqueous water, but RNA degrades very quickly in aqueous solutions at room temperature. In this study, we focus on the chemistry of RNA on ice. Not only does ice protect the RNA from hydrolysis, it may also serve as a catalyst for various reactions between separate RNA strands. Past studies have confirmed that the orientation of the RNA strand on the ice lattice is important in this regard. Thus we will be investigating the orientation of the phosphodiester group for the CC, CG, and GG dinucleotides to elucidate their behaviors while in an ice slab environment.

Background

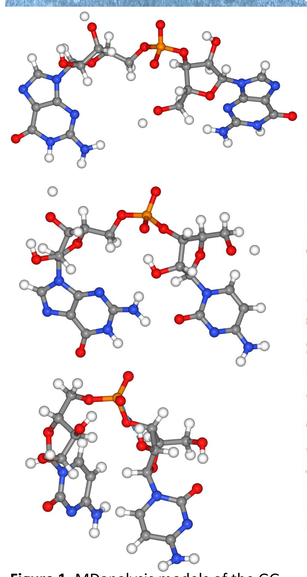

Figure 1. MDanalysis models of the GG dinucleotide (top) CG dinucleotide (middle) and CC dinucleotide (bottom). Color coding is: P (orange), O (red), H (white), N (blue) and C (gray).

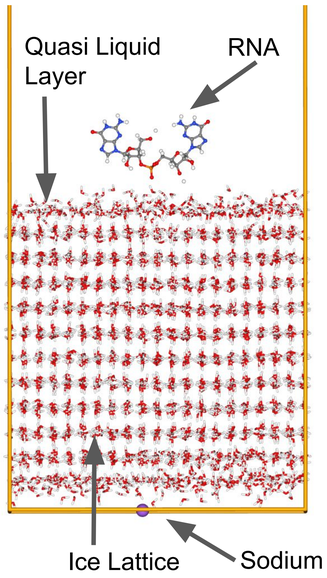

Figure 2. Labeled MDanalysis model of a GG dinucleotide, ice slab, and sodium counterion at the start of a trajectory

Methods

1. A model of an RNA strand was constructed using modeling software such as SPARTAN or Macro Molecule Builder.

2. Then the Molecular Dynamics (MD) software GROMACS performed physics calculations to create a trajectory.

3. The end product was analyzed with the python plugin MDAnalysis which converted all the data generated by GROMACS into visualizations such as 3D models and graphs.

Objectives

- Develop proficiency with the computing software GROMACS, MDanalysis, SPARTAN, and MMB
- Develop methods for modeling custom RNA systems and simple organic molecules
- Assess behavior of various RNA nucleotides on an ice lattice and quasi-liquid layer (QLL)

Results

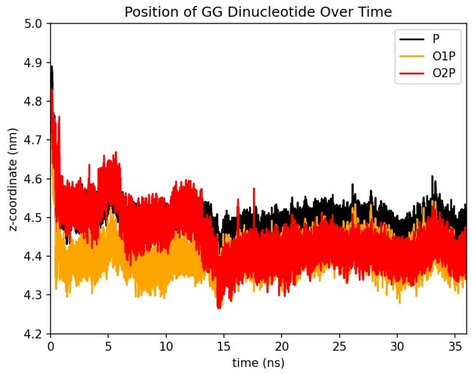

Figure 3. MDanalysis rendering of the z-position of the atoms constituting the phosphodiester group on the GG dinucleotide.

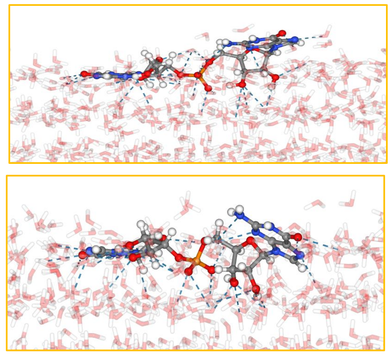

Figure 4. Snapshots taken from the GG dinucleotide trajectory at 12 ns (top) and 35 ns (bottom). Color coding is: P (orange), O (red), H (white), N (blue) and C (gray).

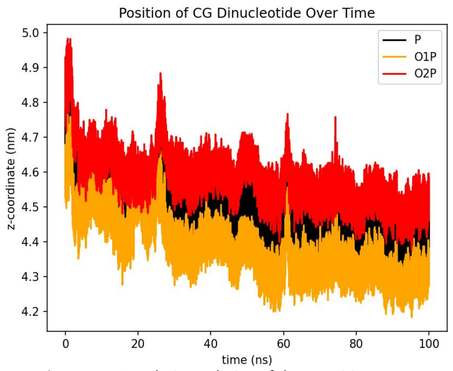

Figure 5. MDanalysis rendering of the z-position of the atoms constituting the phosphodiester group on the CG dinucleotide.

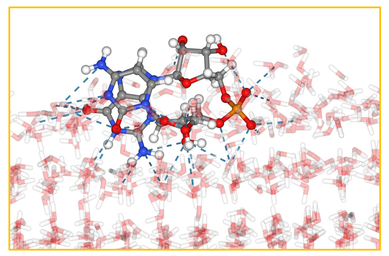

Figure 6. A snapshot taken from the last frames of the CG dinucleotide trajectory.

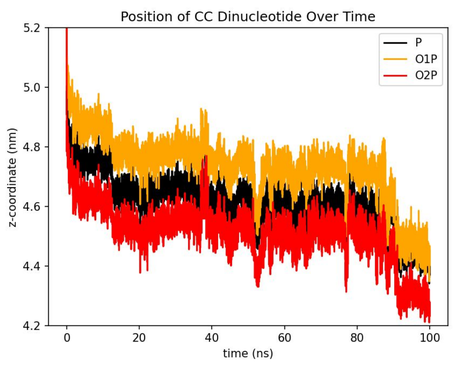

Figure 7. MDanalysis rendering of the z-position of the atoms constituting the phosphodiester group on the CC dinucleotide.

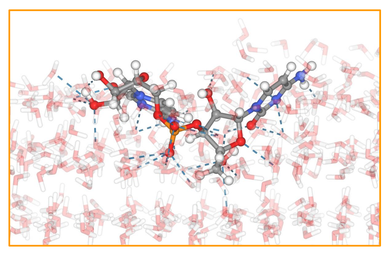

Figure 8. A snapshot taken from the last frames of the CC dinucleotide trajectory.

The phosphodiester groups of the CC and CG dinucleotides were positioned so that one oxygen was sitting horizontally on top of the ice and the other was imbedded into it. The Phosphodiester group of the GG dinucleotide had the same orientation as the other dinucleotides at the beginning of the trajectory, but settled into a different position where both oxygens were at approximately the same depth in the ice.

Conclusions

1. Within a few dozen nanoseconds the phosphate group anchors itself into the second bilayer of the ice on the surface
2. The bases and ribose sugars play a secondary (but significant) role in governing its orientation

Future Plans

Future projects will continue to focus on the behavior and orientation of various RNA molecules. In particular it would be worthwhile to observer the hydrogen bonding behavior of the bases and phosphodiester groups while they are immersed in the QLL. In addition, future projects will increase the size and complexity of the simulated molecules to incorporate investigations into the behavior of double stranded RNA, RNA hairpin structures, and RNA ribozymes on ice.

References

Attwater, J.; Wochner, A.; Holliger, P., In-ice evolution of RNA polymerase ribozyme activity. Nat. Chem. 2013, 5, 1011.

Gromacs 2021 Reference Manual, https://manual.gromacs.org/documentation/current/reference-manual/index.html (Consulted August 6, 2021)

"Solvation and Stabilization of Single Strand RNA at the Air/Ice Interface Support a Primordial RNA World on Ice," Ivan Gladich, Margaret L. Berrens, Penny M. Rowe, Rodolfo G. Pereyra, and Steven Neshyba The Journal of Physical Chemistry C 2020 124 (34), 18587-18594 DOI: 10.1021/acs.jpcc.0c04273

Acknowledgments

University of Puget Sound
National Science Foundation - NSF CHE-1807898
Ivan Gladich
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