

Parameter Development for Modified Nucleosides in tRNA

Abraham Ustoyev, Maria C. Nagan*

Chemistry Department, Adelphi University, Garden City, New York

In addition to the standard nitrogenous bases found in RNA, there are naturally occurring modified bases. Although modified bases are found in most RNAs, they are most prevalent in cytosolic tRNA. These modified bases are important for a variety of factors involving RNA structure and function, including their role in anticodon-codon recognition. Previous studies involving molecular dynamics (MD) simulations of these modified bases do not reflect experimental data involving sugar pucker and syn/anti distributions. The current force field parameters consider the base, sugar, and phosphate separately. In this study, new AMBER-compatible force field parameters will be developed for twelve modified bases that will consider the whole nucleoside in order to successfully reflect experimental behavior. Of the twelve modified nucleosides, the current one being studied is pseudouridine, an isomer of the nucleoside uridine. HIV-1 Reverse Transcription Primer tRNA (Lys3) carries pseudouridine at position 39, in which its crystal structure was obtained from the protein data bank (PDB) and manipulated in order to make the modified nucleoside an AMBER-compatible file. Currently, the antechamber program from AMBER is being used to generate the file containing the necessary information for the entire nucleoside in order to run simulations on it. In the long term, development of these parameters will be extendable to other modified bases and will lead to more accurate MD simulations in order to successfully study problems involving RNA processes.

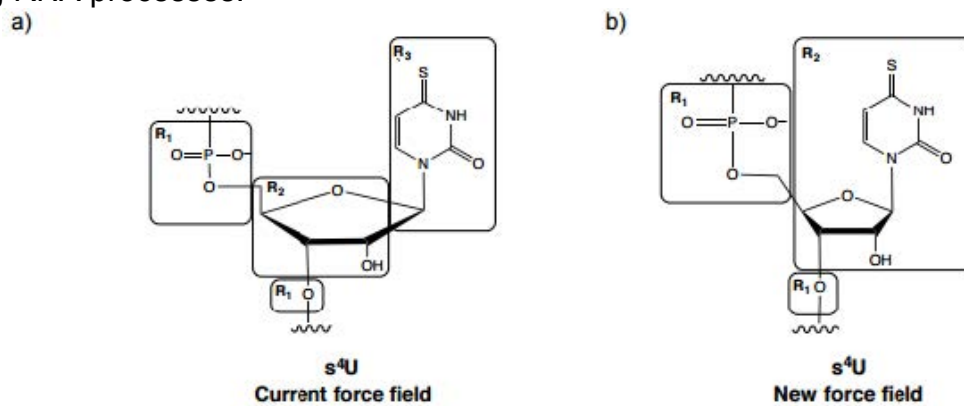


Figure 1. The current force field (a) considers the phosphate (R₁), sugar (R₂) and base (R₃) separately. The new force field (b) will consider the base and sugar (R₂) as one unit and the phosphate (R₁) separately.