MOLECULAR DYNAMICS SIMULATIONS OF *ESCHERICHIA COLI* TRNA^{PHE}

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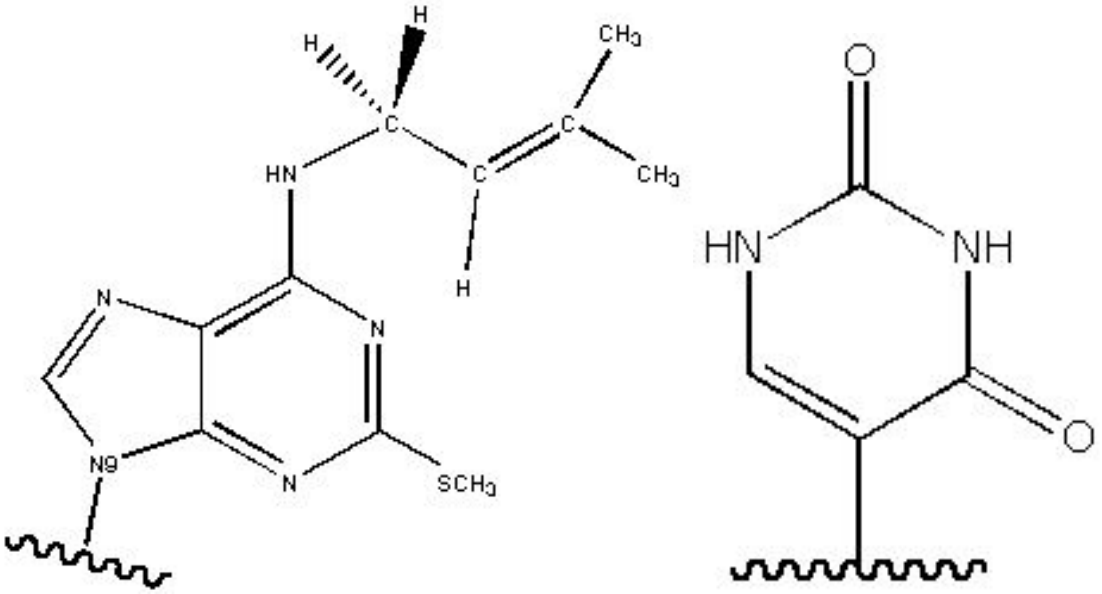
Modifications of the four primary nitrogenous bases are quite common in ribonucleic acid (RNA). Nonstandard nucleic acid bases occur in all organisms. Many people are interested in determining the role of these modifications in transfer RNA (tRNA) structure and function. *Escherichia coli* tRNA^{Phe} requires two modified bases, 2-thiomethyl-N6-dimethylallyl adenosine (ms^2i^6A) and pseudouridine for accurate translation of the genetic code. The preliminary nuclear magnetic spectroscopy (NMR) structure of the fully modified and unmodified *E. coli* tRNA^{Phe} anticodon stem loop has been solved (Cabello-Villegas *J. Mol. Biol.* **2002,** *319.* 1015-1034). The purpose of this project is to observe how *E. coli* tRNA^{Phe} behaves in solution with and without its modified bases. To better characterize the structure and how modified bases affect the function of tRNA^{Phe}, molecular dynamics simulations of six different anticodon stem loops with different combinations of modified bases in *E. coli* tRNA^{Phe} have been conducted in explict solvent, employing the Parm98 force field and AMBER 8.0. An additional two systems containing cobalt(III)hexamine have also been started to model outer-sphere binding that occurs with magnesium. Charges of the modified bases ms^2i^6A and pseudouridine have been derived. Analysis of production runs 10.0 ns each will be presented. Convergence of simulations and preliminary analysis of tRNA structural parameters are evaluated. These studies will provide a better understanding of how nucleic acid base modifications affect tRNA structure and therefore accurate translation.



2-thiomethyl-N6-dimethylallyl adenosine **Pseudouridine**