Aminoacyl-tRNA Synthetases Dynamics: A Comparison between Coarse-grained and All-atom Simulations

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Aminocyl-tRNA synthetases are a group of multi-domain enzymes responsible for catalyzing the covalent attachment of an amino acid to its corresponding tRNA forming an aminoacyl-tRNA. A characteristic of these enzymes is the large-scale conformational changes they undergo during catalysis. Recent studies in our lab[1-3] show that coarse-grained as well as atomistic simulations can provide reliable results in predicting global dynamics encompassing larger domains. However, these studies also pose serious questions about their abilities in predicting substrate-induced local changes. In order to evaluate the effectiveness of coarse-grained approaches in studying dynamics of large protein systems like aminoacyl-tRNA synthetases, we performed a systematic study to compare the performances of coarse-grained vs. all-atom simulations. Two types of coarse-grained analyses were performed: normal mode calculations and molecular dynamics simulations, each using one-bead per residue elastic network model. For all-atom simulations, regular molecular dynamics was performed using CHARMM forcefield. Herein, we will present the comparative results of this study on three aminoacyl-tRNA synthetases: *Escherichia coli* methionyl-tRNA synthetase, *Thermus thermophilus* leucyl-tRNA synthetase, and *Enterococcus faecium* prolyl-tRNA synthetase.

References

(1) Weimer, K. M.; Shane, B. L.; Brunetto, M.; Bhattacharyya, S.; Hati, S. *J. Biol. Chem.* **2009**, *284*, 10088.

(2) Sanford, B.; Cao, B.; Johnson, J. M.; Zimmerman, K.; Strom, A. M.; Mueller, R. M.; Bhattacharyya, S.; Musier-Forsyth, K.; Hati, S. *Biochemistry* **2012**, *51*, 2146.

(3) Johnson, J. M.; Sanford, B. L.; Strom, A. M.; Tadayon, S. N.; Lehman, B. P.; Zirbes, A. M.; Bhattacharyya, S.; Musier-Forsyth, K.; Hati, S. *Biochemistry* **2013**, *52*, 4399.