COMMUNICATIONS IN COMPUTATIONAL PHYSICS
Vol. **3**, No. 5, pp. 1051-1070

Commun. Comput. Phys.
May 2008

The Role of Anionic Protein Residues on the Salt Dependence of the Binding of Aminoacyl-tRNA Synthetases to tRNA: A Poisson-Boltzmann Analysis

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Received 26 October 2007; Accepted (in revised version) 18 December 2007

Available online 25 January 2008

Abstract. Long-range electrostatic interactions in proteins/peptides associating to nucleic acids are reflected in the salt-dependence of the binding process. According to the oligocationic binding model, which is based on counterion condensation theory, only the cationic residues of peptides/proteins near the binding interface are assumed to affect the salt dependence in the association of peptides and proteins to nucleic acids. This model has been used to interpret and predict the binding of oligocationic chains - such as oligoarginines/lysines - to nucleic acids, and does an excellent job in these kinds of systems. This simple relationship, which is used to compare or count the number of ionic interactions in protein-nucleic acid complexes, does not hold when acidic residues, *i.e.* glutamate and aspartate, are incorporated in the protein matrix. Here, we report a combined molecular mechanics (by means of energy-minimization of the structure under the influence of an empirical energy function) and Poisson-Boltzmann (PB) study on the salt-dependence in binding to tRNA of two important enzymes that are involved in the seminal step of peptide formation in the ribosome: Glutamine synthetase (GluRS) and Glutaminyl synthetase (GlnRS) bound to their cognate tRNA. These two proteins are anionic and contain a significant number of acidic residues distributed over the entire protein. Some of these residues are located in the binding interface to tRNA. We computed the salt-dependence in association, SK_{pred}, of these enzyme-tRNA complexes using both the linear and nonlinear solution to the Poisson-Boltzmann Equation (PBE). Our findings demonstrate that the SK_{pred} obtained with the nonlinear PBE is in good agreement with the experimental SK_{obs}, while use of the linear PBE resulted in the SK_{pred} being anomalous. We conclude that electrostatic interactions between the binding partners in these systems are less favorable by means of charge-charge repulsion between negatively charged protein residues and phosphate-oxygens in the tRNA backbone but also play a significant role in the association process

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