INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	Abhishek Kumar
Roll Number	:	156106033
Programme of Study	:	Ph.D.

Thesis Title: Monovalent (K^+/Na^+) and Divalent (Mg^{2+}/Ca^{2+}) metal ion selectivity in Group II intron and Cas1 protein

Name of Thesis Supervisor(s)	:	Dr. Priyadarshi Satpati
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SHORT ABSTRACT

Metal ions play crucial roles in biological processes (e.g., catalytic activity, structural stability, transportation, homeostasis, muscle contraction, etc.). Thus, metal-ion selectivity is essential for the function and stability of the biomolecules. This dissertation explores the use of combined classical molecular dynamics (MD) and ab initio quantum chemical calculations to estimate the energetics of metal ion selectivity (K^+ vs. Na^+, Mg^{2+} vs. Ca^{2+}) in group II intron and cas1 protein. Considering X-ray structures of metal-ion bound biomacromolecule (group II intron and cas1 protein) as a template, the strength of selectivity ($\Delta\Delta G$= Free energy difference between cognate vs. near-cognate metal binding to the active site of the biomolecule) was estimated using MD free energy simulations employing appropriate thermodynamic cycles. Classical force-fields are limited by the fact that it does not include electronic polarizability explicitly. Instead of using computationally expensive polarizable force-field, quantum chemical ab initio calculations were performed on the reduced model of the metal ion binding pocket to incorporate the polarization effect. The adopted methodology (combining classical MD and quantum chemical calculation) is not only computationally cheap but also successful in establishing a direct link between the estimated energetics and the 3D structures of cognate and near-cognate metal complexes.