An Assessment of DFT Methods for Structure Prediction of Metal–Nucleic Acid Interactions

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Excess metals in our food, drinking water and air have detrimental effects on our health and environment. Current methods used to detect harmful metals are quite expensive and not feasible for onsite measurements. Hence, metal detection methods that are simple to use, mobile and cost-effective are necessary. As a result, the design of biosensors is an expanding field of research and recently nucleic acid bioreceptors have been of growing interest. DNA has several properties that are advantageous for metal detection, including metal binding specificity, structural stability, folding properties, a wide variety of modification sites and cost-effective synthesis. However, challenges arise in designing effective biosensors as there are gaps in our understanding of how a broad spectrum of metals bind to DNA. Using computational chemistry, detailed structural and energetic information can be obtained regarding metal coordination to nucleic acids, which can then be used to rationally design improved biosensors for a greater portion of the periodic table. In order to study nucleic acid–metal interactions, accurate computational methods must be identified. In the present work, 53 metal complexes, including those involving transition and post-transition metals, were extracted from the Cambridge Structural Database (CSD) and the Protein Data Bank (PDB) to serve as representative metal–nucleic acid interactions. Each complex was optimized with 15 different DFT functionals and compared to the crystal structure geometric references. As a result, computational methods that can accurately describe the structural information of metal–nucleic acid interactions were identified, which can subsequently be used to study broader aptamer–metal interactions.