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Quantifying the molecular mechanism for highly stereo-selective DNA threading intercalation ALI ALMAQWASHI, Northeastern University, JOHANNA ANDERSSON, Uppsala University, PER LINCOLN, Chalmers University of Technology, IOULIA ROUZINA, University of Minnesota, FREDRIK WESTERLUND, Chalmers University of Technology, MARK C. WILLIAMS, Northeastern University — DNA threading intercalators, such as binuclear ruthenium complexes, are regarded as potential DNA-targeted therapeutic drugs because of slow kinetics and high affinity. Recent bulk studies reported that poly(dAdT) threading intercalation by the binuclear ruthenium complex $[\mu\text{-dppzip(phen)}_4\text{Ru}_2]^{4+}$(Piz) is highly stereo-selective. The largest fractional binding was achieved for Δ,Λ-Piz, with the Δ (right handed) configuration at the intercalating dipyridophenazine (dppz) subunit and the Λ (left handed) configuration at the distal imidazophenanthroline (ip) subunit. To quantify this highly stereo-selective molecular mechanism, we used optical tweezers to probe single λ-DNA molecules elongation due to the threading intercalation by each of Δ,Δ-Piz and Δ,Λ-Piz. While maintaining a DNA stretching force of 30 pN and a ligand concentration of 5 nM, the elongation was traced until reaching equilibrium. Then it was traced back to the free DNA extension by rinsing out the bound ligands. We found that the equilibrium elongation for Δ,Λ-Piz is 30% larger, and the affinity is 50% higher relative to Δ,Δ-Piz. Further force-dependent study will quantitatively determine the differences in the zero-force binding site size, affinity and the DNA structural dynamics for association and dissociation.

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