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Initial DNA interactions of the binuclear threading intercalator Λ,Λ-[μ-bidppz(bipy)4Ru2]$^{4+}$: An NMR study with [d(CGCGAATTCGCG)]$_2$

Lisha Wu
Chalmers University of Technology, Sweden

Structural understanding of the process of intercalation may greatly gain from a characterisation of the initial interactions between binuclear Ru^{II} compounds and DNA. We report a structural NMR study on the binuclear Ru^{II} intercalator Λ,Λ-B (Λ,Λ-[μ-bidppz(bipy)4Ru2]$^{4+}$; bidppz=11,11'-bis(dipyrido[3,2-a:2',3'-c]phenazinyl, bipy=2,2'-bipyridine) mixed with the palindromic DNA [d(CGCGAATTCGCG)]$_2$. Threading of Λ,Λ-B depends on the presence and length of AT stretches in the DNA. Therefore, the latter was selected to promote initial binding, but due to the short stretch of AT base pairs, final intercalation is prevented. Structural calculations provide a model for the interaction: Λ,Λ-B is trapped in a well-defined surface-bound state consisting of an eccentric minor-groove binding. Most of the interaction enthalpy originates from electrostatic and van der Waals contacts, whereas intermolecular hydrogen bonds may help to define a unique position of Λ,Λ-B. Molecular dynamics simulations show that this minor-groove binding mode is stable on a nanosecond scale. To the best of our knowledge, this is the first structural study by NMR spectroscopy on a binuclear Ru compound bound to DNA. In the calculated structure, one of the positively charged Ru^{2+} moieties is near the central AATT region; this is favourable in view of potential intercalation as observed by optical methods for DNA with longer AT stretches. Circular dichroism (CD) spectroscopy suggests that a similar binding geometry is formed in mixtures of Λ,Λ-B with natural calf thymus DNA. The present minor-groove binding mode is proposed to represent the initial surface interactions of binuclear Ru^{II} compounds prior to intercalation into AT-rich DNA.

Biography

Lisha Wu has completed her Licentiate degree at the age of 28 years from Chalmers University and Technology and currently approaching doctoral degree in October 2013. She finished her Master's degree in Chemical Engineering from 2009. Main research focuses on DNA and protein-ligand binding, and new medicine designs in NMR and optical methods.

lisha@chalmers.se