

Effect of Metal Ion Incorporation on the Properties of Peptide Nucleic Acid Duplexes

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Peptide nucleic acid (PNA), a DNA synthetic analog, assembles into helical duplexes as a consequence of Watson-Crick hydrogen bonds formed between nucleobases but has an achiral pseudo-peptide backbone, in contrast to DNA which has a phosphodiester backbone. Placing ligand-modified monomers in complementary positions in PNA oligomers makes possible metal ion incorporation within the PNA duplex (Figure 1).

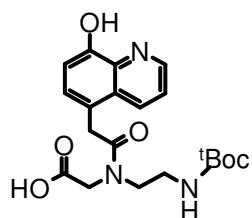


Figure 2: 8-hydroxyquinoline-modified PNA monomer (**Q**).

We have synthesized an 8-hydroxyquinoline-modified PNA monomer (**Q**, Figure 2) and have included it in PNA oligomers with different degrees of complementarity. Thermal denaturation experiments demonstrated high-affinity binding of Cu^{2+} to **Q**-modified PNA duplexes. UV spectrophotometric titrations and EPR spectroscopy indicated the formation within the PNA duplex of a CuQ_2 complex with square-planar geometry (Figure 3). The high changes in absorbance at 260 nm observed in the melting curves of

metal-containing PNA duplexes indicate strong π - π interactions between the bases brought in close proximity by the metal-ligand moiety, which promote mismatch tolerance. CD spectroscopy has showed that an L-lysine attached to the ligand-modified PNA duplexes exerts a chiral induction effect only in the presence of Cu^{2+} , further supporting a significant relationship between metal binding and π - π interactions within the duplex.

This biomimetic strategy for metal ion incorporation in PNA can be used to create duplexes containing one or multiple metal ions at predefined positions, bridged by a combination of hydrogen and coordinative bonds. These supramolecules have potential applications in molecular electronics, which we are presently evaluating.

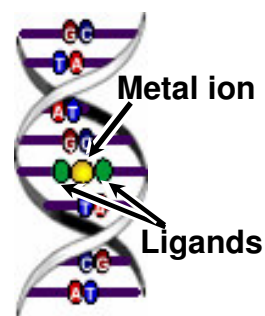


Figure 1: PNA duplex containing **Q** ligands bound to Cu^{2+} .

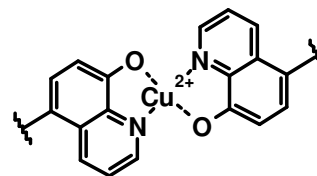


Figure 3: CuQ_2 moiety at center of PNA duplex.