# Defining the Structure of a Protein–Spherical Nucleic Acid Conjugate and Its Counterionic Cloud

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Protein–spherical nucleic acid conjugates (Pro-SNAs) are an emerging class of bioconjugates that have properties defined by their protein cores and dense shell of oligonucleotides. Here, we determine the counterion radial distribution profile surrounding Pro-SNAs dispersed in RbCl with 1 nm resolution through *in situ* anomalous small-angle X-ray scattering (ASAXS) and classical density functional theory (DFT). SAXS analysis also reveals the radial extension of the DNA and the linker used to covalently attach the DNA to the protein surface. At the experimental salt concentration of 50 mM RbCl, $Rb^+$ cations compensate ~90% of the negative charge due to the DNA and linker. Above 75 mM, DFT calculations predict overcompensation of the DNA charge by $Rb^+$. This study suggests a method for exploring Pro-SNA structure and function in different environments through predictions of ionic cloud densities as a function of salt concentration, DNA grafting density, and length. Overall, our study demonstrates that solution X-ray scattering combined with DFT can discern counterionic distribution and submolecular features of highly charged, complex nanoparticle constructs such as Pro-SNAs and related nucleic acid conjugate materials.

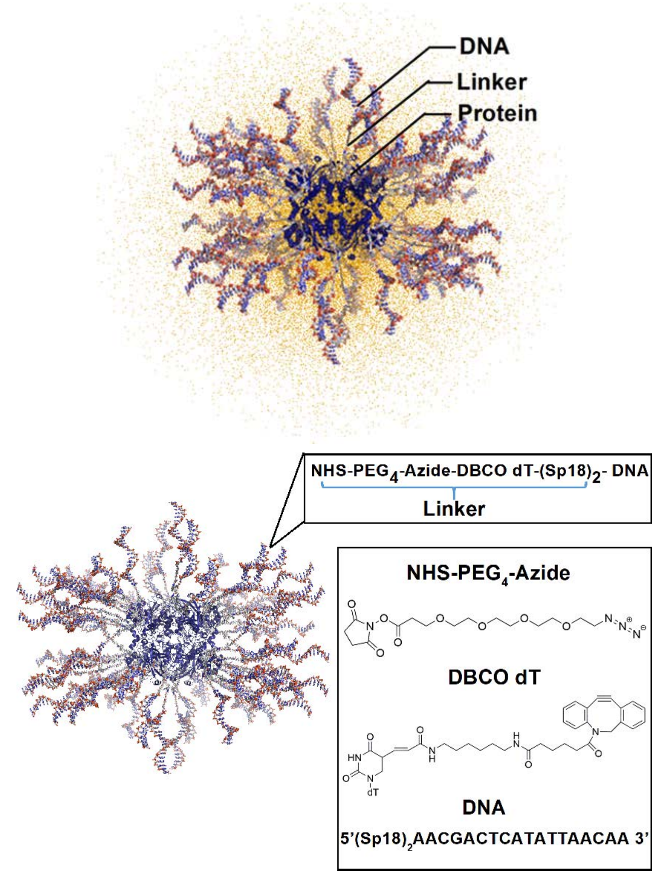


*Figure: Schematic illustration of Cg catalase functionalized with 18 base long ss-DNA strands.*

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