An electrical probe of protein–DNA interactions on DNA-modified surfaces

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DNA charge transport chemistry is found to provide a sensitive method for probing protein-dependent changes in DNA structure and enzymatic reactions. Here we describe the development of an electrochemical assay of protein binding to DNA-modified electrodes based upon the detection of associated perturbations in DNA base stacking. Gold electrode surfaces that were modified with loosely packed DNA duplexes, covalently crosslinked to a redox-active intercalator and containing the binding site of the test protein, were constructed. Charge transport through DNA as a function of protein binding was then assayed. Substantial attenuation in current is seen in the presence of the base-flipping enzymes *Hha*I methylase and uracil DNA glycosylase, as well as with TATA-binding protein. When restriction endonuclease *Pvu*II (R.*Pvu*II) binds to its methylated target, little base-stacking perturbation occurs and little diminution in current flow is observed. Importantly, the kinetics of restriction by R.*Pvu*II of its nonmethylated target is also easily monitored electrochemically. This approach should be generally applicable to assaying protein–DNA interactions and reactions on surfaces.