

## **535h Binding of Target DNA with Overhanging Bases to DNA Probes in Lipid Bilayers and Micelles**

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Applications such as gene expression analysis, RNA extraction, and genomic sensing rely on the use of surface-anchored probes to selectively bind DNA or RNA. These probes hybridize to a particular sequence, between 10 and 100 base pairs in length, on the target DNA. Depending on its source and the processing conditions used to obtain it, target DNA often has overhanging stretches of DNA that do not hybridize with the surface-bound probe. The presence of these overhangs, particularly on the proximal side of the probe, can destabilize the probe-target interaction, leading to poor binding kinetics and lower binding constants. Here we demonstrate that the “soft” surfaces provided by surfactant microstructures, including lipid bilayers and surfactant micelles, can accommodate the overhangs. In many cases, the overhangs even stabilize the probe-target interaction by favorable interactions between the exposed DNA nucleobases and the nonpolar interior of lipid bilayers and micelles.

Two different systems have been interrogated, both containing probes of peptide nucleic acid (an uncharged, synthetic DNA mimic) attached to mono- and di-alkyl groups to form PNA amphiphiles (PNAA). PNAA liposomes were constructed by co-extrusion of phospholipids with a small fraction of PNAA. Using a combination of capillary electrophoresis and Forster resonance energy transfer (FRET), we demonstrate that 40- and 60-mer DNA oligomers bind PNAA probes on the liposome surface, even when 15-20 bp overhangs face the lipid bilayer. Similar results were obtained using mono- and di-alkyl PNAA probes solubilized in SDS or Triton X-100 micelles. FRET and CE data will be presented for a wide range of ionic strength conditions and lengths of DNA. The results will be discussed within a thermodynamic model accounting for electrostatic, hydrophobic, and hydrogen bonding interactions. This work argues for the use of the soft, mobile interface presented by surfactant microstructures for DNA sensing applications. Importantly, lipid bilayers and micelles sequester proteins, lipid, and other adventitious material into their nonpolar interiors, without surface fouling that can lead to probe deactivation.