

Invited Paper (Oral, Sensors and Biosensors)

A Case for Synthetic DNA Mimics in Electrochemical Diagnostics

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One of the more common bioanalytical needs in genomics is determination of sequence concentrations in mixtures of nucleic acids. A common method for identifying sequence concentrations is through hybridization with complementary strands on a solid support, which allows localization and parallel monitoring of a large number of arrayed hybridization reactions. Conventional platforms geared to this type of analysis, such as DNA microarrays, must contend with limitations stemming from the very high charge density and crowding effects associated with immobilized DNA films. Morpholino oligonucleotides, which also hybridize with nucleic acids following conventional Watson-Crick pairing rules, provide a synthetic, nonionic alternative that brings a number of advantages stemming from their uncharged nature. These advantages include altered dependencies on experimental conditions that allow, for example, tuning selectivity of interactions in favor of the desired morpholino-DNA binding. Morpholinos also open up prospects for sensitive label-free detection based on charge effects, and for effective electric-field control over the hybridization reaction. A Poisson-Boltzmann model explains how molecular organization at the surface translates to the functionality of morpholino films in diagnostics. The non-optical, electrochemical nature of detection is expected to facilitate adaptation to CMOS technology, although morpholino diagnostics are equally adaptable to traditional fluorescence based assays.