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Electrical Manipulation of DNA on Metal Surfaces

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Summary
We review recent work on the active manipulation of DNA on metal substrates by electric fields. This includes the controlled positioning, alignment, or release of DNA on or into dedicated locations and the control of hybridization. In this context, we discuss techniques for immobilizing DNA on metal surfaces and methods of characterizing such hybrid systems. In particular, we focus on electrically induced, conformational changes of monolayers of short oligonucleotides on gold substrates. Such switchable layers allow for molecular dynamics studies at interfaces and have demonstrated large potential in label-free biosensing applications.

Key Words: Biomolecular films; biosensors; conformational changes; DNA-based sensing; molecular dynamics; nano-electromechanical system (NEMS); oligonucleotides; self-assembled monolayers; surface functionalization; switchable layer.

1. INTRODUCTION
Functional biomolecular layers on surfaces have been gaining significant importance as a result of their widespread relevance in surface and physical sciences, molecular biology, and nanobiotechnology. They find diverse applications in the field of biosensors, biomedical diagnostics, functionalized Lab-on-Chip devices, and catalysis of reactions on surfaces.

From a more fundamental point of interest, biomolecular layers have been considered a particular species of organic monolayers that serve as model systems for biophysical studies, molecular dynamics, and fundamental biomedical research involving, for example, the study of regulatory and signaling pathways. Biomolecular layers of most current interest involve protein microarrays as a major tool in proteome research (1), antibody arrays, or even whole-cell arrays, among others.
A particular focus has been put on monolayers of DNA, often in the form of short oligonucleotides that are being tethered to solid substrates. The most widespread applications are fluorescence-based DNA microarrays, commonly termed “DNA chips” in the form of microarrays on activated glass surfaces. These arrays have been extensively used for gene-expression analysis and have found widespread applications in the field of human health such as disease prognosis and drug discovery (2–6). In contrast, biosensors based on DNA (7) find more applications in the field of diagnostics or general bioanalytical applications such as screening, e.g., the detection of single-nucleotide polymorphisms (SNPs). They mostly target the judgment of certain disease susceptibilities, or, more generally, make genetic tests feasible. The underlying common architecture of DNA-based sensors is probe strands that are immobilized on a solid surface. Those strands then act as a molecular recognition element for a complementary strand, for proteins or other small molecules. As an important feature of the operation principle, the solid substrate and/or DNA takes part in transducing the recognition event into, for instance, an electrical read-out signal.

In addition to the functionality inherent to the DNA molecules themselves—by virtue of their sequence—any additional active control over their immobilization, steric orientation, hybridization, or molecular recognition properties on the surface is highly advantageous. Such controlled manipulation facilitates applications in diverse fields like the molecular alignment in microelectronics, drug delivery by controlled release, biosensing, or DNA computing. This review will address several of these issues, thereby mostly focusing on the electrical manipulation of layers of short oligonucleotides on gold surfaces, based on the direct interaction of the charged DNA with external electric fields. The largely reported work on DNA immobilized on surfaces other than metal, such as semiconductors, remains beyond the scope of this chapter and will not be described.

Following this short introduction, techniques for immobilizing DNA oligonucleotides on metal surfaces are addressed, concentrating on specific (covalent) chemical bonds to the substrate. Subsequently, methods of characterizing such monolayers are reviewed. The main part of this chapter then focuses on the active manipulation of DNA on metal substrates by electric fields, including, in particular, the reported work on layers of short oligonucleotides. Finally, such manipulation in the context of DNA-based sensing and time-resolved studies of the DNA dynamics are discussed.

2. METAL SURFACE MODIFICATION WITH DNA

2.1. Structure of DNA

The DNA molecule is a linear, oligomer-like chain of nucleotides that are each composed of a ribose sugar, a phosphate group, and an attached nitrogenous heterocyclic base. For details of the structure, the reader is