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# Ellipsometry-Based Biosensor for Label-Free Detection of Biomolecular Interactions in Microarray Format

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Microarrays of biological molecules are useful tools for discovery and functionality characterization in fundamental and applied research of genomics, proteomics, glycomics, and cytomics. They provide a high-throughput platform that enables parallel studies of hundreds to tens of thousands of distinct biomolecular reactions. Usually, the characterization of binding reactions between surface-immobilized targets and solution-phase analytes involves fluorescence-based detection methods. However, labeling analytes inevitably changes innate properties of the molecules and, in turn, modifies analyte-target interactions often in an uncharacterized manner. As a result, label-free microarray detection is desirable. In this study, optical microscopes based on the oblique-incidence reflectivity difference (OI-RD) technique are developed and used to detect biomolecular interactions in microarray format. OI-RD, a most sensitive form of optical elliposometry, measures the difference in reflectivity change (both magnitude and phase) between two polarized components of an optical beam. Such a difference is related to the thickness and dielectric constant of surface-immobilized biomolecules. Here, we report the use of such microscopes to study novel protein-protein, oligosaccharide-protein, and small molecule-protein interactions. These experimental results demonstrate that the OI-RD microscopes can serve as powerful tools in biosensing, high-throughput screening, and other applications in biophysics, biochemistry, and biomedical engineering.

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