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Label-free optical detection of biochemical reactions in microarray format J. P. LANDRY, X. D. ZHU, Department of Physics, University of California at Davis, J. P. GREGG, Department of Pathology, University of California, Davis School of Medicine — We have developed an oblique-incidence optical reflectivity difference (OI-RD) scanning microscope for detecting biochemical reactions involving unlabeled macromolecules such as DNA, protein, or lipid membranes in microarray format. This optical microscope detects changes in density, thickness, and conformation of macromolecules as a result of the reactions of probe molecules with target molecules immobilized on a solid surface such as a chemically functionalized glass microscope slide. Of particular interest to our current investigation are microarrays of small ligands and macromolecules that are targeted for protein binding. Our OI-RD microscope is particularly desirable for such microarray-based proteomic investigations as it offers the capability to detect activities of protein molecules without the influence of extrinsic "tag" molecules attached to the protein (such as organic fluorophore molecules) and other undesirable effects such as photobleaching. We have used our OI-RD scanning microscope in a series of proof-of-principle studies of oligonucleotide hybridization and antibody-antigen capture reactions *without labeling*.

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