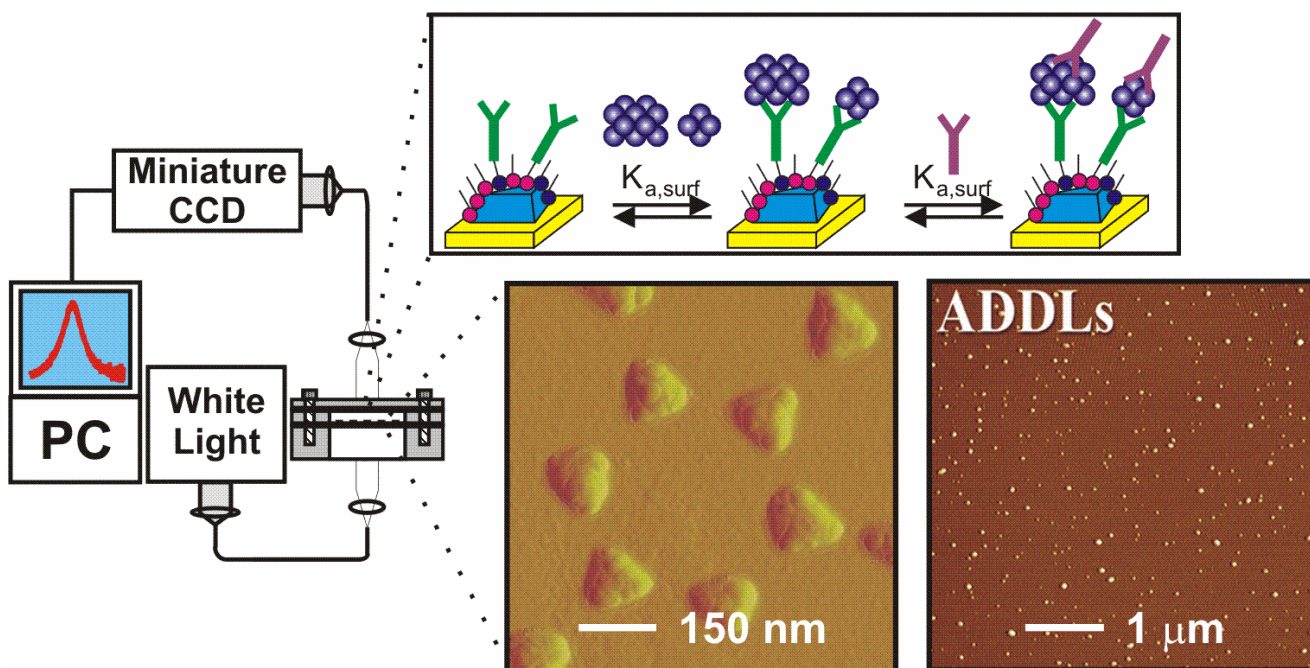


## 4.2 CURRENT CONNECTIONS BETWEEN DISCOVERIES AND THEIR USE IN SERVICE TO SOCIETY

### 4.2.1 DETECTION OF A BIOMARKER FOR ALZHEIMER'S DISEASE FROM SYNTHETIC AND CLINICAL SAMPLES USING A NANOSCALE OPTICAL BIOSENSOR

A. J. Haes, L. Chang, W. L. Klein, R. P. Van Duyne, "Detection of a Biomarker for Alzheimer's Disease from Synthetic and Clinical Samples Using a Nanoscale Optical Biosensor," *J. Amer. Chem. Soc.*, **2005**, *127*, 2264-2271.

In this work, a nanoscale optical biosensor based on the localized surface plasmon resonance (LSPR) of silver nanoparticles was used to study the interactions between antigens, amyloid- $\beta$  derived diffusible ligands (ADDLs), and specific anti-ADDL antibodies. Using a sandwich assay format, the LSPR nanosensor provided quantitative binding information for both antigen and second antibody detection that permits the determination of ADDL concentration. This unique capability offers the possibility of analyzing the aggregation mechanisms of this putative Alzheimer's disease pathogen at physiologically relevant monomer concentrations. Monitoring the LSPR-induced shifts from both ADDLs and a second polyclonal anti-ADDL antibody as a function of ADDL concentration reveals two ADDL epitopes that have binding constants to the specific anti-ADDL antibodies of  $7.3 \times 10^{12} \text{ M}^{-1}$  and  $9.5 \times 10^8 \text{ M}^{-1}$ . Furthermore, this study demonstrated, for the first time, that the LSPR nanosensor was successful at analyzing human brain extract and cerebrospinal fluid samples. Examination of these results from both Alzheimer's disease and control patients reveals that the LSPR nanosensor provides new information relevant to the understanding and possible diagnosis of Alzheimer's disease. This exciting advance is one of the first examples in which nanotechnology has been applied to clinical materials for biomolecular diagnostics.



Schematic representation of LSPR immunoassay for an Alzheimer's disease biomarker. The usefulness of LSPR nanosensor technology for the screening of human samples for disease diagnosis has been demonstrated for the first time. These results suggest that a more general approach to the understanding of diseases and drug-target interactions may be at hand.