BIOMOLECULAR ANALYSIS VIA MOLECULAR DAM, PLASMONIC NANOGAPS, NANOFLUIDIC FLUORESCENCE MICROSCOPY (NFM) AND ATTENUATED TOTAL REFLECTION INFRARED (ATR-IR) SPECTROSCOPY[#]

Chia-Fu Chou*
Institute of Physics, Academia Sinica, 128, Sec. 2, Academia Road, Taipei 11529, Taiwan

[#]Work performed in collaboration with the groups of Nathan Swami (University of Virginia, Charlottesville, VA 22904, USA), Andreas Erbe (Max-Planck-Institut für Eisenforschung GmbH, 40237 Düsseldorf, Germany), and Thierry Leichle (LAAS-CNRS, F-31077 Toulouse, France)

* Email: cfchou@phys.sinica.edu.tw; Tel.: +886-2-27896761

In recent years, we have developed several versatile analysis platforms for the manipulation and sensing of biomolecules, particularly for low-copy number molecule detection. In the first scenario, sub-30 nm insulating nanoconstriction, serving as *molecular dam* operating under the balance of negative dielectrophoresis (DEP), electrophoresis, and electroosmosis, enables protein enrichment of 10^5-fold in 20 seconds [1], which can then be coupled with graphene-modified electrodes for sensitive electrochemical detection of peptides, cancer biomarkers, and cortisol [2-4] (Fig. 1). In the second scenario, an array of electrode nanogaps with sub-10 nm gap size function as templates for AC DEP-based molecular trapping, plasmonic hot spots for surface-enhanced Raman spectroscopy as well as electronic measurements, and fluorescence imaging (Fig. 2), demonstrated with R-phycoerythrin [5] and Alzheimer's disease candidate biomarkers A-beta 40 and 42 peptides. In the third scenario, we implemented nanoslit as a cost-effective nanofluidic-based immunosensor for low-noise real-time kinetic measurement of fluorescently labeled protein binding (Fig. 3), with a limit of detection down to 1 pM, regardless of the analyte size [6]. Further, a 10 nm deep sub-nanoliter fluidic nanochannels is developed on germanium crystal for attenuated total reflection infrared (ATR-IR) spectroscopy for ultralow volume (~650 pL) molecular characterization [7] (Fig. 4). Our platforms open up simple ways for low-concentration or low-volume sample analysis.

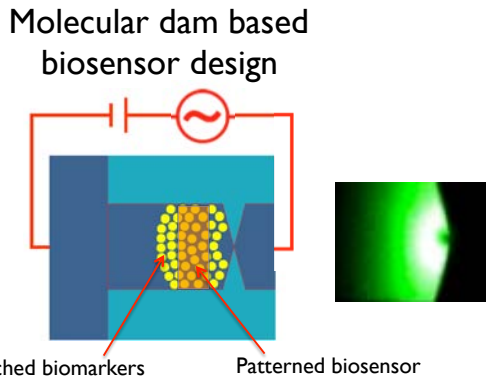

Fig. 1. The concept of nanoscale molecular dam and its coupling with a biosensor for enhanced sensing [1-4].

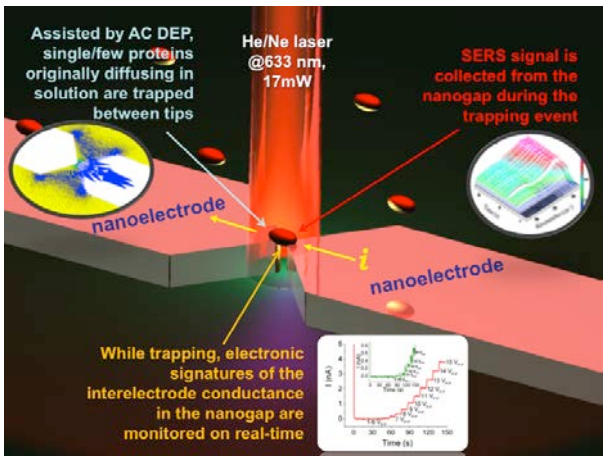

Fig. 2. The concept of a multifunctional, electrode nanogap-based molecular analyzer enabled by dielectrophoretic trapping [5].

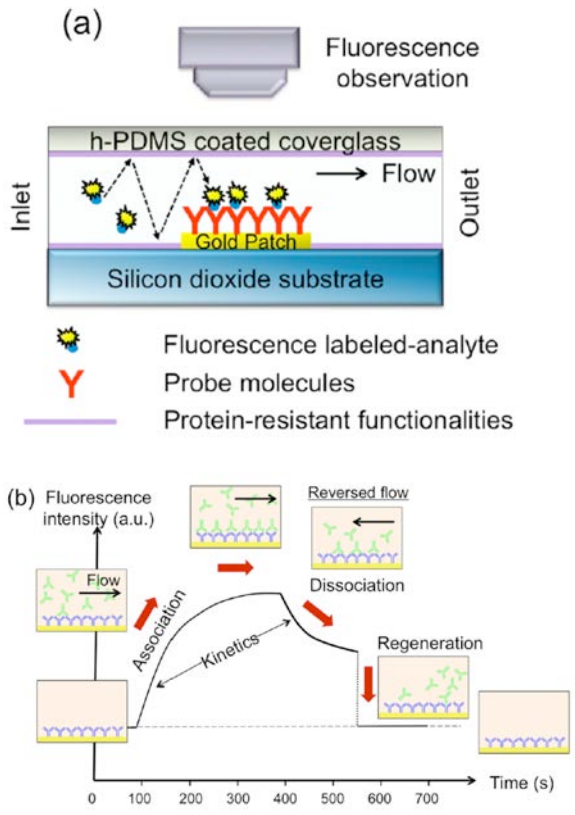

Fig. 3. (a) Schematic representation of biofunctional nanoslit used in protein kinetic study. Receptor probe molecules are immobilized on the gold sensor surface located at the bottom of the nanochannel. Fluorescent target molecules are introduced by means of pressure-driven flow. The kinetic reaction of protein-ligand binding is monitored in real-time using fluorescence microscopy. (b) Typical sensorgram of kinetic analysis performed in nanofluidic device. The dissociation phase is simply induced by reversing the fluid flow in order to replace the analyte solution by the buffer solution [6].

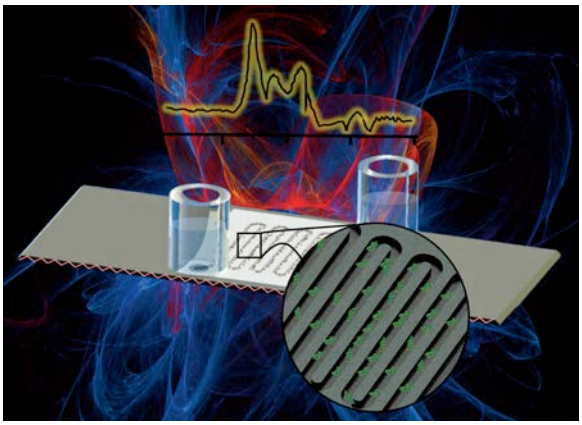

Fig. 4 Nanofluidic channels (10 nm depth) have been fabricated on a germanium internal reflection element. These hermetically bonded channels have been demonstrated to detect ~100 fmol of human serum albumin by infrared absorption spectroscopy [7].

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