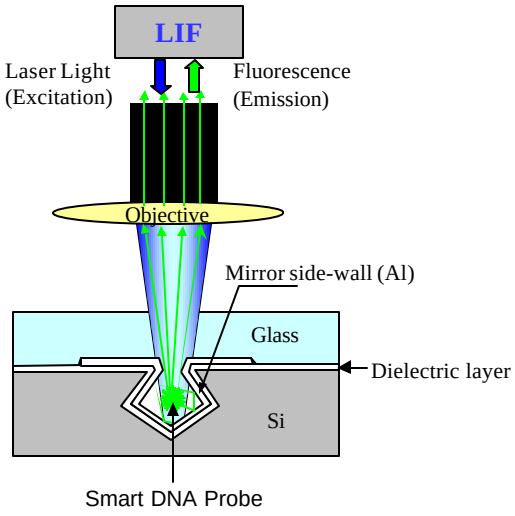
Current Research:

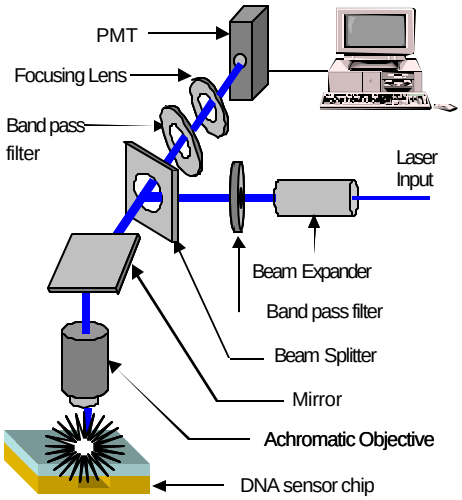
Tza-Huei Wang

A Zepto Mole Micro DNA Sensor

DNA/RNA analysis plays an extremely important and fundamental role in the rapid development of molecular diagnostics, genetics, and drug discovery. One of the fastest growing areas in DNA/RNA analysis is the development of DNA-based biosensors. A variety of biosensors, both optical and electrochemical, have been developed for gene sequence analysis and biological pathogen detection based on the DNA hybridization technique. In DNA hybridization, the target gene sequence is identified by a DNA probe that can form a double-stranded hybrid with its complementary nucleic acid with high efficiency and extremely specificity.

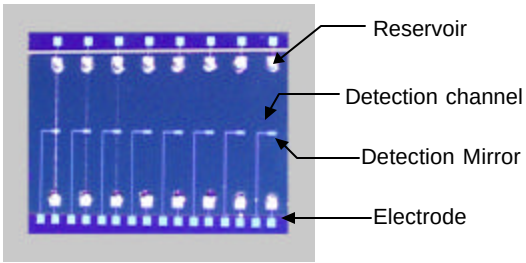


Schematics of LIF based DNA detection

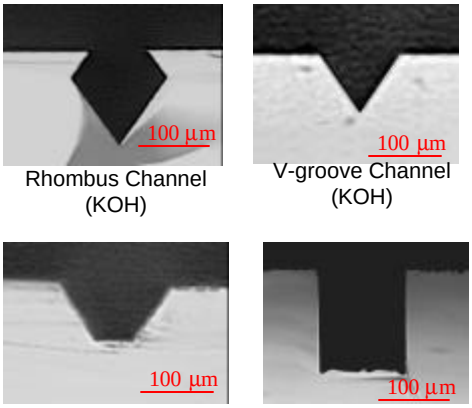


Setup of a Laser Induced Fluorescence System

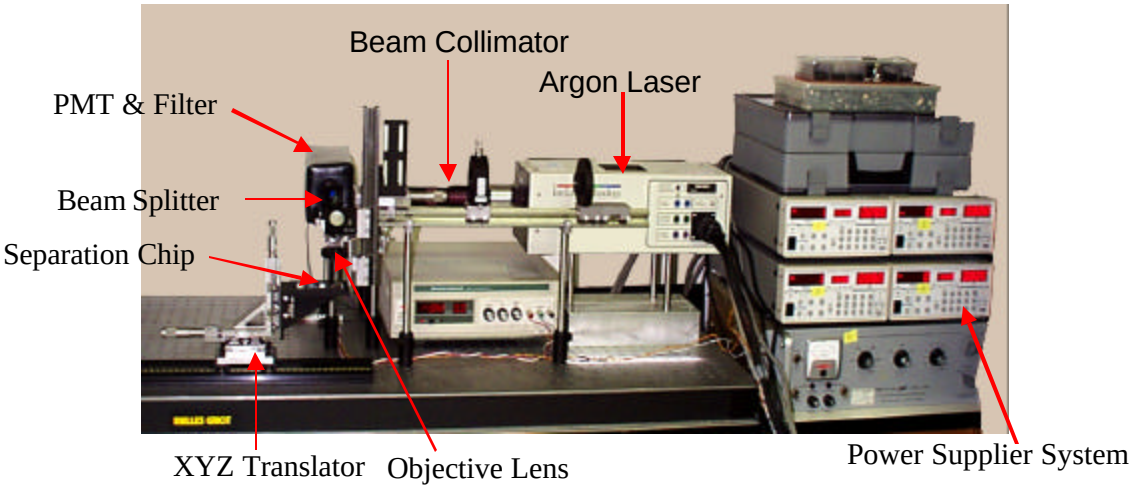
Microchannels with different crosssection geometries were fabricated and their sensitivity of DNA detection were compared to determine the optimum design. Metals with high reflectance like Al and Au were deposited and patterned to form mirror-like sidewalls on the detection region of the channels to enhance the surface reflectance and increase the fluorescence signal level. With this special design, the photon collection efficiency has been greatly improved that enhanced sensitivity. As a result, sensitivity of zepto(10^{-21}) mole DNA molecules was achieved.



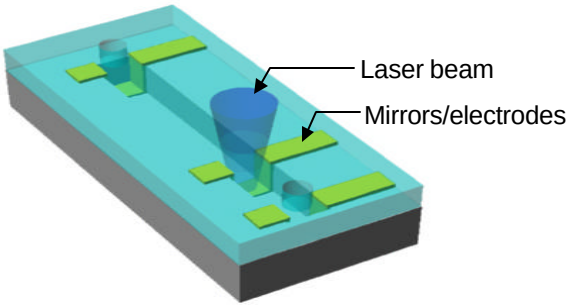
Zepto Mole DNA Sensor Array



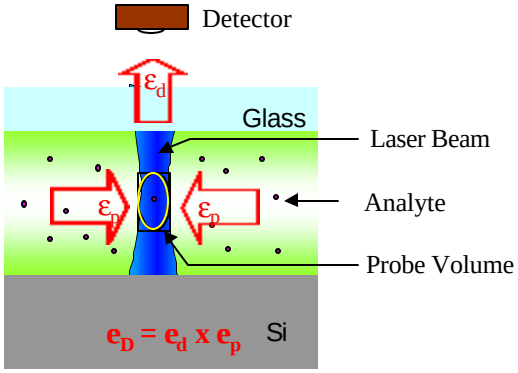
Crosssections of Microchannels



Setup of a Laser Induced Fluorescence Detection System



Overall Detection Efficiency



ε_D : Overall detection efficiency

ε_d : Detection efficiency of optics

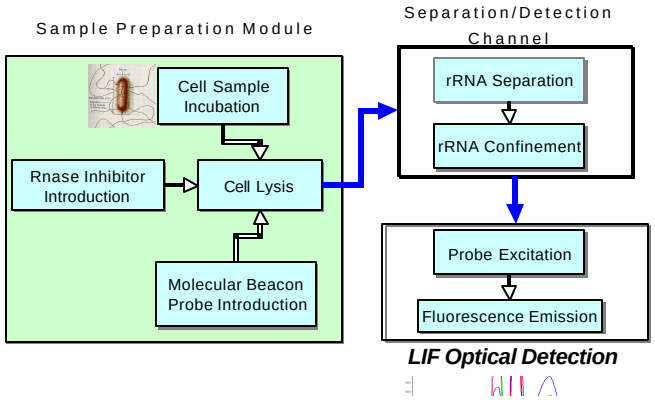
ε_p : Probing efficiency

Conceptual Schematics of Overall Detection Efficiency

Integrated Micro Biological Detection System

A miniaturized sample preparation module assembled using microfluidic devices, a heater, and a reactor is reported in this paper. With the modified protocol of the DNA hybridization technique, the module can finish sample preparation within 20 minutes. The module was connected with a micromachined separation/ detection channel which was integrated with multiple electrodes to perform purification and molecule confinement. The separation/detection channel was then coupled to a Laser Induced Fluorescence (LIF) system for detection. Since molecules were confined in the narrow detection region in the channel, the detection volume was reduced to as low as 30 nl.

Book Size Integrated Detection Svstem



Design of Integrated DNA Detection System

The DNA hybridization technique is one of the methods offering identification of biological agents with high specificity. For typical DNA hybridization techniques, the processes used to accomplish the identification are comprised of probe immobilization, DNA or RNA hybridization with both primary and secondary probes, and washing of non-specific bonding. The non-perfect surface modification for immobilization and incomplete washing are the main sources of noise and hence determine the ultimate sensitivity. Furthermore, these two cumbersome steps add complexities to the lab-on-chip design.

To reduce the immobilization and washing steps, a molecular beacon based RNA-DNA hybridization technique was implemented in the biological detection system. The smart probes are oligonuclotide probes that become fluorescent upon hybridization with target DNA/RNA molecules. Biological detection based on smart probes does not need labeled analyte or intercalation reagents, and is direct, highly selective, and sensitive .