金屬-半導體-金屬光電檢測器應用於整合式生物晶片

學生：林志杰　　指導教授：柯富祥 博士

國 立 交 通 大 學

奈米科技研究所

碩士論文

摘要

近年來關於生物檢測器被廣泛研究其應用於蛋白質或是 DNA 分析之可行性。建立一個微型晶片元件並具備直接而且快速偵測鍵結於蛋白質上的小分子，將對於研究和審查新藥物方面提供非常重大的貢獻。

關於DNA晶片的研究通常是利用螢光標定所要偵測的生物分子，共焦式螢光掃描器具有非常高的靈敏度以及準確度。但是螢光檢測分析的步驟相當繁雜瑣碎，而且檢測成本相當高。 這些因素造成了DNA

晶片無法成為一個普及的分析工具。 然而藉由電子訊號分析測來偵測蛋白質雜交可以降低偵測器本身製造成本以及可以做成更微型化的檢測器，但是建立一個微流道系統仍然具有相當高的挑戰性。在此篇研究中，我提出一個新的初步平台，藉由利用金屬-半導體-金屬光檢測器偵測藉由鍵結於 streptavidin 上面的辣根酵素催化而放出之冷光。 此方式可以用來建立一個可自動化而且拋棄式的檢測晶片，並且因為相當便宜所以可以普及化應用。

研究中利用電子束微影來定義檢測器中的主要偵測區域圖案，並藉由標準半導體製程步驟來完成此元件。而且另外針對此檢測器特殊設計了一個塑膠反應槽來完成初步的生物檢測器晶片平台，並可以應用在冷光系統偵測。我們利用此系統來偵測 streptavidin 蛋白質分子,並且作出檢量線， 在 0.1 毫升反應槽中，此元件的最小偵測極限是 4.9 毫微克的 streptavidin。 此外，我們也展示了利用此元件來偵測金奈米粒子之可行性。

以上兩個偵測方法應用到的原理及機制是不同的， 在冷光偵測應用上我們利用光檢測器吸收反應所放出的冷光來決定 streptavidin 分子的多寡。 而金奈米微粒之偵測，應用金奈米粒子會吸收波長在 520 奈米左右的入射光。因為 streptavidin 和 biotin 還有金奈米粒子都可以跟很多生物分子產生鍵結，我們可以藉由此方

式來偵測這些相似之生物分子,例如蛋白質與DNA 等等，利用此新的晶片方法,我們提出的新穎平台將可以在未來偵測許多其他種類之生物分子。

An On-chip Metal-Semiconductor-Metal Photodetector as a Biosensor

Student: Chie-Chieh Lin **Advisor: Fu-Hsiang Ko**

Institute of Nanotechnology

National Chiao Tung University

Abstract

Recently, the biosensor has been received widely attraction for the application in protein and DNA analysis. Development of miniaturized devices that enable rapid and direct analysis of the specific binding of small molecules to proteins could be of substantial importance to the discovery and screening for new drug molecules.

The determination principle of DNA chips is usually based on fluorescence labeling of hybridised target molecules. Combined with the use of confocal fluorescence scanners, this approach shows very high performances in terms of accuracy and sensitivity. However, fluorescence readers remain costly and cumbersome. This prevents the use of DNA chips as a biomolecular testing tool. Electrical monitoring of hybridization is one way to reduce the cost and size of the reader. However, the multiplexing of electric detection-based systems in a

miniaturised form remains challenging. Here, we present a system based on the use of a low cost metal-semiconductor-metal photodetector (MSM-PD) as a solid support for streptavidin-HRP assisted biosensor, in together with the enzyme-catalysed chemiluminescence effect. Combining electric interface and high analytical performances, this opto-electronic biosensor is one attractive solution for bio-molecules detection and analysis in disposable, fully automatised, and total analysis systems developed for biomolecular testing.

Active region of MSM-PD was defined by electron beam lithography and fabricated using standard semiconductor process. Combining reaction chamber made of PDMS, we have demonstrated the MSM-PD as an on-chip biosensor for luminescence detection applications. We obtain the calibration curve and the minimal detection limit (MDL) is 4.9ng in 100uL PDMS reaction chamber. We have also demonstrated the capability of gold nanoparticles detection by the new biosensors.

The above two applications are based on different mechanisms. In luminescence application, the mechanism is based on the absorbance of luminescent emission light. In regard to gold nanoparticles detection, the mechanism is based on the absorbance of gold nanoparticles at 520nm wavelength. Biotin, streptavidin and gold nanoparticles, as we know, can bind with various kinds of bio-molecules, thus we can detect these molecules, like protein, DNA etc. The new platform of MSM-PD chips can be extended to other types of molecular detection in the future.