出國報告（出國類別：參加國際會議）

參加第35屆IEEE生物醫學工程國際研討會會議報告

35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society

服務機關：國立中正大學生命科學系
姓名職稱：周正中 助理教授
派赴國家：日本
出國期間：民國 102 年 7 月 4 至 7 日
報告日期：民國 102 年 8 月 27 日

摘要

IEEE 學會生物醫學工程國際研討會是國際上規模宏大且極具影響力的會議，今年在日本大阪國際會議中心舉行，匯集了來自世界各地的專家學者家與會，有超過 2500 篇的論文投稿，可說是工程在生物醫學研究領域每年一次極為重要的社群聚會。個人於會議中發表壁報論文壹篇「New tools for rapid diagnosis of avian influenza and human pandemic influenza」（全新禽流感及新型流感快速檢驗試劑之開發），這個論文內容主要是結合生物資訊、分子診斷技術以及光電生物感測器，發展出一套快速、靈敏、即時且準確的可攜式螢光奈米檢測系統，可以在短時間之內確認禽流感及新型流感的感染。這篇跨領域的論文獲得許多學者的認同並給于一些寶貴的意見，這就是參加國際會議的最大的好處，可以即時與國際相關領域的學者直接交流，以隨時調整自已的研究方向和步調。

目次

一、目的

近年來由於全球商業和旅遊交流頻繁，新興感染性疾病如SARS、禽流感H5N1、以及H1N1和H7N9新型流感等很容易迅速擴散而對全球公共衛生帶來極大的威脅。其中，開發合適有效的快速診斷試劑，對疫情的即時監控與降低疾病的傳播極為重要。IEEE學會每年都會舉辦生物醫學工程國際研討會，會議中的診斷試劑與生醫感測器主題，每年皆會發表最新的技術與知識。因此藉由參加這個會議，對目前各先進國家診斷試劑的最新研發狀況與趨勢有所瞭解；並發表本實驗室有關流感快速檢驗試劑開發的最新研究成果，期望與國際相關領域的學者專家進行交流，甚至建立國際的合作模式，達到積極參與國際學術交流的目的。

二、行程與工作紀要

日　期	工作記要
六月三十日（日）	啟程（台北→東京）
七月　三日（三）	資料準備（東京→大阪）
七月　四日（四）	出席研討會
七月　五日（五）	出席研討會
七月　六日（六）	出席研討會
七月　七日（日）	出席研討會
七月　八日（一）	返程抵台

三、會議重點摘要

IEEE 學會生物醫學工程國際研討會是國際上規模宏大且極具影響力的會議，今年在日本大阪國際會議中心舉行，匯集了來自世界各地的專家學者家與會，有超過 2500 篇的論文投稿，可說是工程在生物醫學研究領域每年一次極為重要的社群聚會。由於生物醫學工程相關研究範疇包羅萬象，因此會中一共區分

12 個主題進行廣泛的探討:

1. Signal Processing（訊號處理）
2. Biomedical Imaging & Image Processing（生醫影像與影像處理）
3. Bioinstrumentation: Sensors, Micro, Nano and Wearable Technologies（生醫儀器：感測器、微奈米和穿戴技術）
4. Bioinformatics, Computational Biology; Systems Biology, Modeling Methodologies（生物資訊與計算生物學；系統生物學、模型建立方法）
5. Cardiovascular & Respiratory Systems Engineering（心血管與呼吸系統工程）
6. Neural Engineering, Neuromuscular Systems & Rehabilitation Engineering（神經工程、神經肌肉系統和復健工程）
7. Molecular and Cellular Biomechanics, Tissue Engineering, Biomaterials （分子和細胞生物力學、組織工程，生物材料）
8. Bio-Robotics, Surgical Planning and Biomechanics（倣生機器人、手術規劃以及生物力學）
9. Therapeutic & Diagnostic Systems, Devices and Technologies, Clinical Engineering（疾病治療和診斷系統、器具與技術，臨床工程）
10. Healthcare Information Systems, Telemedicine（健康照護資訊系統與遠距醫療）
11. Biomedical Engineering Education and Society（生物醫學工程教育和社群）
12. Healthcare Technologies in Major Disasters（重大災害之健康照護科技）

本次會議為期總共四天,每天從早上 8:00 到下午 6:00 皆是進行各項主題的深入探討，可謂議程緊湊。七月四日清晨前往大阪國際會議中心，完成報到手續並領取會議相關資料，隨即開始規劃聆聽演講的題目與時刻表，以及參觀各類生醫檢測廠商儀器設備和技術的展示。中午有大會主席的歡迎演說，並邀請哈佛大學的 John

Halamka（約翰‧哈拉姆卡）教授進行關鍵演講（keynote speaker）。哈拉姆卡教授正協助美國歐巴馬總統進行醫療電子雲的建置，第一步是完成各級醫療院所病人健康資訊與病歷資料的電子化，接著探討如何在保護個人隱私的前提下，對這些巨量數據進行分析，並對各國類似計畫的發展情況進行比較性的深入探討，令我受益良多。下午分別聆聽研討會及與海報展示部分的學者交流，晚上 19:30 出席大會所舉辦的歡迎晚宴。

在整個會議的議程中，其中第三（生醫儀器：感測器，微奈米與穿戴技術）和第四項（生物資訊、計算生物學與系統生物學）主題，與我先前主持一項有關禽流感快速診斷的國科會計畫內容相關，主要是結合生物資訊、分子診斷技術以及光電生物感測器技術的跨領域研究，因此成為我此次會議主要參與、觀摩和學習的對象。這個研究主題總共超過 80 篇口頭論文發表和壁報論文展示，涵蓋微奈米檢測器具的發展和製作、各種感測技術的研究與發展、與疾病診斷等多個領域，短時間內可以認識到最新國際研究動態，對於我未來的研究有很大助益。附件一的列表是我四天中在會場聆聽的演講題目與摘要以供參考。大部分的演講雖然所描述的技術都是已發展多年的成熟方法如即時 DNA 聚合酶鏈鎖反應（Real-time polymerase chain reaction）、免疫測定法（immunoassay）以及生物晶片（biochip）等，但更著重在如何將這些技術微小化到可攜式的檢測產品，並將其轉化為商業產品，期間的製程、法規以及市場機制所遭遇到的困難是難以想像，著實讓我上了寶貴的一課。例如，就有學者利用奈米碳管塗佈在試紙上作成微流體可拋棄式的檢測試紙；或使用互補式金屬氧化物半導體（complementary metal oxide semi- conductor, CMOS）製程制作微流體可拋棄式的檢測晶片。除此之外，也有數個學者利用抗體抗原結合時電阻的改變作為檢測的依據，這種非標記性（label-free）的方法可大幅減少檢測硬體的需求，有助於可攜式的檢測技術的開發。

上述微小化可攜式的檢測觀念，與另一個紐澤西理工學院的 Dhawan 教授的關鍵專題演講相互輝映。Dhawan 教授強調定點照護檢驗（Point-of-Care Testing）

的重要性。所謂定點照護檢驗最主要的特色是簡便、快速，不論是醫院、診所、公共衛生機構、甚至是個人的健康監測都可使用。這些非傳統性的定點照護檢驗方式由於具有即時檢測和現場隔離的優勢，對於傳統和新興感染性疾病如HIV/AIDS、流感、肺結核與瘧疾等的防疫效率及總體成本節省上扮演一個重要的角色。然而要達到定點照護檢驗的目標，開發可攜式的檢測試劑或儀器就成為極端重要的一個環節。

除此之外，還有幾個非常不錯的學術和商業演講帶給我很大的啟發。其中之一是使用 DNA 版本抗體的適體（aptamer）取代傳統單株抗體，再結合奈米金或奈米螢光粒子技術，發展出檢測毒品和毒物重金數屬的快速呈色試紙。適體是核酸分子可依序列不同而形成許多穩定的結構，並且如同抗體可專一地與特定標的分子結合。與抗體相較，適體具有許多優點，包括可以化學合成製造、具有很好的組織穿透性、低致免疫性等。由於我目前也正利用適體技術從事一些新的研究，這個演講使我獲益良多。另一個是美國一家生技公司使用 PDZ 蛋白質功能區塊（protein domain）來偵測流感病毒。由於流感病毒的 NS1 蛋白(nonstructural protein 1)會與人類細胞的 PDZ 蛋白質功能區塊結合，而且不同亞型的流感病毒的 NS1 蛋白會與不同 PDZ 蛋白質功能區塊結合，可藉此發展出流感病毒診斷試劑。該公司宣稱該診斷試劑已送交 WHO 測試，也已向 FDA 申請上市。由於 PDZ 蛋白質功能區塊也參與許多癌症的致病機轉，該公司也據此開發胰臟癌診斷試劑和治療藥物。這個演講內容是我第一次聽到，觀念帶給我無比的震撼。

個人於會議中發表壁報論文壹篇「New tools for rapid diagnosis of avian influenza and human pandemic influenza」（全新禽流感及新型流感快速檢驗試劑之開發，全文摘要如附件二所示），這個論文主題原本被安排為口頭報告，但由於尚處於專利申請過程中，無法揭露詳盡內容，只藉著壁報說明一些原則性的觀念。主要是結合生物資訊、分子診斷技術以及光電生物感測器，發展出一套快速、靈敏、即時且準確的可攜式螢光奈米檢測系統，可以在短時間之內確認禽流感及新型流感的感染。這篇論文整個概念是利用恆溫 RNA 擴增反應（nucleic acid

sequence-based amplification，NASBA）簡化檢測流程，再結合螢光共振轉換技術（fluorescence resonance energy transfer，FRET）無須分離純化即可於檢體內即時檢測目標存在與否。我們已經發展出新的短序列編碼比對演算法，設計出可以鑑別所有 A 和 B 型流感病毒保守不變的檢測探針以及 A 型流感 H5 和 N1 專一性探針。為了進一步縮小檢測系統至可攜式大小，我們使用 UV light emitting diode（LED）取代傳統笨重的燈泡光源以及拋棄式光學穿透電極玻璃作為檢測平台。檢測原理是將檢體置於表層塗佈導電物質 ITO (Indium Tin Oxide)的光學玻璃上，藉由控制電壓可精確地控制檢體反應溫度。由於這個系統具有光學電極導電性及光學穿透的特性，可同時將 NASBA 反應所須的溫控與 FRET 即時光學偵測整合於同一架構內，將大幅縮小檢測系統的體積，非常適合開發可攜式現場防疫檢測系統。此外我們的實驗數據證實，FRET 探針量子點(quantum dot)和螢光 Alexa660 與其互補的 H5 序列結合確能產生 FRET 效應，顯示可使用不同大小的 QD，藉由單一 UV LED 光源分別激發出不同的 FRET 反射波長以同時進行多目標(multiplex)檢測。所以從檢體處理、RNA 放大以及 FRET 即時偵測皆無須人工介入，真正達到開發出適用於地區診所和原野調查的可攜式現場即時暨多目標檢測儀器。這篇跨領域的論文獲得許多學者的認同並給于一些寶貴的意見，這就是參加國際會議的最大的好處，可以即時與國際相關領域的學者直接交流，以隨時調整自已的研究方向和步調。

四、心得

參加這次生物醫學工程國際研討會，最大的收穫是瞭解國際上有關生醫檢測研究的最新趨勢，那就是微小化可攜式的檢測觀念與定點照護檢驗的重要性。由於它們具有即時檢測和現場隔離的優勢，對於近幾年來發生在國內以及臨近區域的新興感染性疾病如 SARS、禽流感 H5N1、以及 H1N1 和 H7N9 新型流感等防疫效率特別重要。

此外，這是本人第一次參加這類規模宏大的國際研討會。可以想見，舉辦如此大型的國際會議，必須投入相當大量的人力與物力，但從中所學習到的組織與協調的寶貴經驗卻是無價的。此外，各種主題的論文投稿必須徵召世界各地相關領域的專家參與審稿和後續論文的歸類與演講安排，無疑是生物醫學工程社群的一次總動員；若台灣日後能夠爭取到這類會議的主辦權，對於國內相關研究學者和學生應是一次與國際接軌的難得學習機會。另一方面，參與國際性研討會除了增加個人與研究同行交流的機會，更可以藉由許多的學術演講、討論以及壁報論文的展示瞭解各領域的發展現況。雖然每個作者的報告大約只有 15 到 20 分鐘，不足以讓人對其研究有徹底的了解，但是卻可以讓人對當今國際上研究的趨勢、方法、進度、狀況都有基本的認識，這對我們的未來研究的探索有極大的幫助；而各個相關主題的分類更可以使相同領域的學者們針對彼此不同的概念、想法做分享，以瞭解到自己的不足以及一些研究點新想法。

五、建議

未來政府投入經費開發新興感染性疾病的檢測試劑或儀器，建議可主動邀請學術專家與生技業者，就微小化可攜式的檢測概念徵求計畫，以達成即時監測與現場隔離，有效降低疾病傳播為計畫目標。

六、攜回資料

1. The 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 書面會議議程與內容一本
2. 會議論文光碟一片

七、附件一（聆聽演講標題與摘要）

IEEE Engineering in Medicine and Biology Society

My Program for EMBC'13

Compiled on August 26, 2013

Day	Time	Paper Title or Activity	Authors	Session	Room
Thursday, July 4, 2013	08:00-08:15	**A CMOS Enhanced Solid-State Nanopore Based Single Molecule Detection Platform** ThA08.1	Chinhsuan Chen, Sukru Yemenicioglu, Ashfaque Uddin, Ellie Corgliano, Luke Theogarajan	Bioelectric Sensors and Systems I – ThA08	1005 (10F)
		Abstract– Solid-state nanopores have emerged as a single molecule label-free electronic detection platform. Existing transimpedance stages used to measure ionic current nanopores suffer from dynamic range limitations resulting from steadystate baseline currents. We propose a digitally-assisted baseline cancellation CMOS platform that circumvents this issue. Since baseline cancellation is a form of auto-zeroing, the 1/f noise of the system is also reduced. Our proposed design can tolerate a steady state baseline current of 10A and has a usable bandwidth of 750kHz. Quantitative DNA translocation experiments on 5kbp DNA was performed using a 5nm silicon nitride pore using both the CMOS platform and a commercial system. Comparison of event-count histograms show that the CMOS platform clearly outperforms the commercial system, allowing for unambiguous interpretation of the data.			
	08:15-08:30	**Development of a Paper-Based Carbon Nanotube Sensing Microfluidic Device for Biological Detection** ThA08.2	Shih-I Yang, Kin Fong Lei, Shiao-Wen Tsai, Hsiao-Ting Hsu	Bioelectric Sensors and Systems I – ThA08	1005 (10F)
		Abstract– Carbon nanotube (CNT) has been utilized for the biological detection due to its extremely sensitive to biological molecules. A paper-based CNT sensing microfluidic device has been developed for the demonstration of the detection of biotin-avidin binding. We have developed a fabrication method that allows controlled deposition of CNTs with well-defined dimensions to form sensors on paper. Then, polydimethyl siloxane (PDMS) was used to pattern the hydrophilic boundary on paper to form the reaction sites. The proposed fabrication method is based on vacuum filtration process with a metal mask covering on a filter paper for the definition of the dimension of sensor. The length, width, and thickness of the CNT-based sensors are readily controlled by the metal mask and the weight of the CNT powder used during the filtration process, respectively. Homogeneous deposition of CNTs with well-defined dimensions can be achieved. The CNT-based sensor on paper has been demonstrated on the detection of the protein-protein binding. Biotin was first immobilized on the CNT's sidewall and avidin suspended solution was applied to the site. The result of the protein-protein binding was measured by the resistance change of the sensor, which is a label-free detection method. It showed the CNT is sensitive to the biological molecules and the proposed paper-based CNT sensing device is a possible candidate for point-of-care biosensors. Thus, electrical bio-assays on paper-based microfluidics can be realized to develop low cost, sensitive, and specific diagnostic devices.			
	08:30-08:45	**A Novel Bioelectronic Glucose Sensor to Process Distinct Electrical Activities of Pancreatic Beta-Cells** ThA08.3	Quang Vinh Nguyen, Anton Juan-Jorge Caro, Matthieu Raoux, Adam Quotb, Jean-Baptiste Floderer, Yannick Bornat, Sylvie Renaud, Jochen Lang	Bioelectric Sensors and Systems I – ThA08	1005 (10F)
		Abstract– Glucose sensors have improved and facilitated therapy for type 1 diabetes. However, they are still not capable to sense all physiological signals and to act in a closed-loop. Pancreatic beta-cells have been shaped during evolution as biological sensors and offer the advantage to integrate all physiological signals in addition to glucose. Moreover, biosensors based on these cells may also serve for non-invasive and continuous long-term characterization of beta-cells, drug research, tissue engineering and pre-transplantation quality control. beta-cells alter their electrical activity upon exposure to glucose and physiological hormones and we have used these properties to design a biosensor. To this end signals were recorded extracellularly from islet cells kept on multi-electrode arrays. Slow and rapid oscillations were observed, both modulated by glucose. Especially slow oscillations are very robust and have an excellent signal/noise ratio. Signal processing functions were designed to separate the two activities to extract and analyze relevant parameters. These parameters correlate very well with either increasing or decreasing glucose concentrations. An electronic device is under construction, based on an embedded FPGA capable of processing multiple channels in parallel. In the future, such a device shall be used as a portable real-time biosensor regulating insulin delivery from a pump.			
	08:30-08:45	**Semi-Disposable Chips for CMOS-Based Biosensors** ThA20.3	Yuksel Temiz, Carlotta Guiducci	Electronic DNA Detection (2) – ThA20	806 (8F)
		Abstract– Integrating biosensing functions and microfluidics on top of CMOS electronics has enabled a new generation of lab-on-a-chip systems that have addressing, sensing, and data elaboration functions on the same device. Such integration promises to overcome the limitations of existing optical techniques and enable new possibilities for low-cost, low-power and portable devices, particularly for DNA detection, genome research, point-of-care diagnostics, and neural activity sensing. Although CMOS integration is favorable for such biosensing applications, it brings additional challenges and limitations, such as: (i) the materials used in the CMOS fabrication are not always suitable for bio-measurements due to the issues of bio-compatibility and stability in electrolyte solution; (ii)			

		the packaging leads to additional cost and reliability problems, as the wire bonds have to be protected, and leak-free microfluidic channels and reservoirs have to be implemented; (iii) the disposability of the assay-substrate is a key parameter for the commercialization and the widespread use of the biosensor. In this context, the present study proposes a disposable biosensing layer that can be aligned and temporarily attached to the electronics through flexible interconnections and can be replaced after each measurement to eliminate the cleaning steps and cross-contamination of samples. This idea promises three key benefits: (i) high-density microelectrode array thanks to vertical interconnections; (ii) high-performance operation thanks to circuits in close proximity; (iii) low-cost and configurable biochips by fully decoupling the fabrication of the sensor and the electronics. This paper also presents fully CMOS-compatible TSV fabrication and 3D integration platforms to realize electronics with higher performance and functionality.			
	08:45-09:00	**Enhanced differentiation of rat MSCs into cardiomyocytes with 5-azacytidine/collagen I nano-molecules** ThA14.4	Yi-jhen Wu, Shu-Ying Chen, Shwu Jen Chang, Shyh Ming Kuo	Biological Sensors and Systems for Diagnostics – ThA14	804 (8F)
		Abstract– This study was to investigate the enhancement ability of 5-azacytidine (5-aza) and collagen I nano-molecules treatment to the differentiation of rat mesenchymal stem cells (MSCs) towards a cardiomyocytes in vitro. The results demonstrated that the size of the cells increased significantly and connecting with adjoining cells by forming myotube-like structures. Also, additional treatment of the MSCs with collagen I nano-fibrils significantly increased two transcription factors GATA-4 and Nkx2.5 expressions and three expressions of cardiac genes of troponin I, β-myosin heavy chain and cardiac α-actin compared with MSC groups treated only with 5-aza at early 3 d culturing(all, P<0.01 or better). These results indicate that culturing MSCs with collagen I nano-molecules, which could act as scaffolds or soluble protein ingredients, leads to alterations in gene expression and affects the differentiation fate induced with 5-aza.			
	09:00-09:15	**Non-Invasive Measurement of Cell Viability in 3-Dimensional Cell Culture Construct** ThA08.5	Kin Fong Lei, Min-Hsien Wu, Che-Wei Hsu, Yi-Dao Chen	Bioelectric Sensors and Systems I – ThA08	1005 (10F)
		Abstract– In this work, a non-invasive measurement technique for the quantitative determination of cell viability in a three-dimensional (3D) cell culture construct is proposed. This technique is based on on-site electrical impedance measurement and a microfluidic chip with a 3D culture chamber is fabricated to demonstrate this technique. In vitro 3D cell culture has been interpreted for faithfully representation of the in vivo cellular responses in living tissues. However, monitoring of the cellular responses in 3D cell culture construct is normally time-consuming and labor-intensive. In this study, the microfluidic chip consists of a culture chamber, in which a pair of vertical electrodes at its opposite sidewalls was embedded, and a fluidic channel for drug perfusion. Cancer cells encapsulated in agarose gel were loaded into the culture chamber to perform 3D cell culture under the perfusion of culture medium and anti-cancer drug in different concentrations (6, 12, 18, and 24 ug/ml) for 2 days. Since higher drug concentration led to more cell damage or death, the total impedance magnitude of the culture construct was shown to be reasonably proportional to the cell viability. Moreover, cell proliferation can be also monitored using this technique. The proposed measurement method can determine cell viability without affecting the cellular behaviors during culture. It has a high potential to develop a fast and easy measurement compared with the conventional cellular analysis techniques.			
	09:30-11:00	**Smart Sensing of Tool/Tissue Interaction by Resistive Coupling** ThB07.5	Shunsuke Yoshimoto, Yoshihiro Kuroda, Masataka Imura, Osamu Oshiro, Kosuke Sato	New Sensing Techniques II – ThB07	Event Hall-Area A (3F)
		Abstract– A smart sensing of tool-tissue interaction is required to monitor the surgical task without disturbing the tool manipulation. We proposed a new tactile sensing method that enables us to detect the tool-tissue interaction with a simple hardware by resistive coupling. The system consists of two electrodes, a bridge circuit and a differential amplifier for the robust sensing of the contact resistance between the tool and tissue. In order to evaluate the sensing method, we investigated the relationship between the sensor output and the deformation of a wet sponge sample by retraction task. According to the model fitting of the deformation-output profile, we concluded that the proposed sensor provide enough reproducibility in the simple situation. Furthermore, we confirmed that the developed sensor works with a biological sample.			
	13:30-13:45	**Label-Free Monitoring of Whole Cell Vitality** ThC14.1	Daniel Weiss, Martin Brischwein, Helmut Grothe, Bernhard Wolf, Joachim Wiest	Auto-Bio-Lab (ABL) Technologies – ThC14	804 (8F)
		Abstract– The Intelligent Mobile Lab (IMOLA) delivers metabolic and morphological parameters of living cells in a label-free and real time way. It represents a key technology for the development of new cell-based assays. Electrochemical microsensors are used to measure the extracellular acidification (pH), cellular respiration (pO2), changes in cell number and morphology (electric impedance) in a controlled environment. These parameters are closely linked to the intracellular signaling network of the living cells. They are thus likely to respond sensitively to changes in cellular vitality. A wide spectrum of cell types can be tested with the system, including adherent and suspended cells, continuous cell lines, primary cells or tissue samples. The platform is described in detail and applications in the field's oncology, toxicology and environmental monitoring are shown.			
	13:45-14:00	**Low-Voltage DEP Microsystem for Submicron Particle Manipulation in Artificial Cerebrospinal Fluid** ThC14.2	Amine Miled, Mohamad Sawan	Auto-Bio-Lab (ABL) Technologies – ThC14	804 (8F)
		Abstract– In this paper, we present a new low voltage biochip for micro and nanoparticle separation. The proposed system is designed to detect the concentration of particles after being separated through reconfigurable DEP-based electrode architecture. The described system in this work is focusing on the particle frequency dependent separation. Experimental results in artificial cerebrospinal fluid (ACSF) show that each particle has its own crossover frequency. Thus based on the crossover frequency, particles are attracted to the electrode's surface, while others are pushed away. Five different particles are tested with different diameters in the range of 500 nm to 4 um. All separation process is controlled by a CMOS chip fabricated using 0.18 um technology from TSMC and powered with 3.3 V. Efficient particle separation is observed with low voltage, below 3.3V unlike other techniques in the range of kV. The proposed platform includes an advanced PDMS based assembly technique for fast testing and prototyping in			

		addition to reconfigurable electrode architecture.			
	14:00-14:15	**An Ultra-Low Power (ULP) Bandage-Type ECG Sensor for Efficient Cardiac Disease Management** ThC08.3	Kunsoo Shin, Gunguk Park, Jong Pal Kim, Tak Hyung Lee, Byung-Hoon Ko, Youn Ho Kim	Bioelectric Sensors and Systems II – ThC08	1005 (10F)
		Abstract– This paper proposed an ultra-low power bandage-type ECG sensor (the size: 76x34x3 (mm3) and the power consumption: 1 mW) which allows for a continuous and real-time monitoring of a user's ECG signals over 24h during daily activities. For its compact size and lower power consumption, we designed the analog front-end, the SRP (Samsung Reconfigurable Processor) based DSP of 30uW/MHz, and the ULP wireless RF of 1 nJ/bit. Also, to tackle motion artifacts (MA), a MA monitoring technique based on the HCP (Half-cell Potential) is proposed which resulted in the high correlation between the MA and the HCP, the correlation coefficient of 0.75±0.18. To assess its feasibility and validity as a wearable health monitor, we performed the comparison of two ECG signals recorded form it and a conventional Holter device. As a result, the performance of the former is a little lower as compared with the latter, although showing no statistical significant difference (the quality of the signal: 94.3% vs 99.4%; the accuracy of arrhythmia detection: 93.7% vs 98.7%). With those results, it has been confirmed that it can be used as a wearable health monitor due to its comfortability, its long operation lifetime and the good quality of the measured ECG signal.			
	14:15-14:30	**Optogenetic LED Array for Perturbing Cardiac Electrophysiology** ThC14.4	Oscar Abilez	Auto-Bio-Lab (ABL) Technologies – ThC14	804 (8F)
		Abstract– Optogenetics is the targeted genetic introduction of light-sensitive channels, such as Channelrhodopsin, and pumps, such as Halorhodopsin, into electrically-excitable cells that enables high spatiotemporal electrical stimulation and inhibition by optical actuation. Technologies for inducing optogenetically-based electrical stimulation for investigating in vitro and in vivo neural perturbations have been described. However, modification of existing technologies or creation of new ones has not been described for chronic cardiac applications. Here, an LED array system for optogenetically perturbing cardiac electrophysiology is described. The overall layout of the system consists of an LED holder containing six LED's that deliver pulsed ~470 nm light to pluripotent stem cell-derived cardiomyocytes cultured in a 6-well tissue culture plate. The response of the cardiomyocytes is monitored by microscopy and the system is enclosed within a standard incubator. This system is relatively simple to create and uses mostly off-the-shelf components. The overall function of the system is to deliver chronic light stimulation over days to weeks to differentiating stem cell-derived cardiomyocytes in order to investigate perturbations in their electrophysiology.			
	14:30-14:45	**Preamplifiers for Non-Contact Capacitive Biopotential Measurements** ThC08.5	GuoChen Peng, Zeljko Ignjatovic, Mark Bocko	Bioelectric Sensors and Systems II – ThC08	1005 (10F)
		Abstract– Non-contact biopotential sensing is an attractive measurement strategy for a number of health monitoring applications, primarily the ECG and the EEG. In all such applications a key technical challenge is the design of a low-noise trans-impedance preamplifier for the typically low-capacitance, high source impedance sensing electrodes. In this paper, we compare voltage and charge amplifier designs in terms of their common mode rejection ratio, noise performance, and frequency response. Both amplifier types employ the same operational-transconductance amplifier (OTA), which was fabricated in a 0.35um CMOS process. The results show that a charge amplifier configuration has advantages for small electrode-to-subject coupling capacitance values (less than 10 pF - typical of noncontact electrodes) and that the voltage amplifier configuration has advantages for electrode capacitances above 10 pF.			
	14:45-15:00	**Electrical Stimulation Via a Biocompatible Conductive Polymer Directs Retinal Progenitor Cell Differentiation** ThC14.6	Rajiv Saigal, Elisa Cimetta, Nina Tandon, Jing Zhou, Robert Langer, Michael Young, Gordana Vunjak-Novakovic, Stephen Redenti	Auto-Bio-Lab (ABL) Technologies – ThC14	804 (8F)
		Abstract– The goal of this study was to simulate in vitro the spontaneous electrical wave activity associated with retinal development and investigate if such biometrically designed signals can enhance differentiation of mouse retinal progenitor cells (mRPC). To this end, we cultured cells on an electroconductive transplantable polymer, polypyrrole (PPy) and measured gene expression and morphology of the cells. Custom-made 8-well cell culture chambers were designed to accommodate PPy deposited onto indium tin oxide-coated (ITO) glass slides, with precise control of the PPy film thickness. mRPCs were isolated from post-natal day 1 (P1) green fluorescent protein positive (GFP+) mice, expanded, seeded onto PPY films, allowed to adhere for 24 hours, and then subjected to electrical stimulation (100 μA pulse trains, 5 s in duration, once per minute) for 4 days. Cultured cells and non-stimulated controls were processed for immunostaining and confocal analysis, and for RNA extraction and quantitative PCR. Stimulated cells expressed significantly higher levels of the early photoreceptor marker cone-rod homebox (CRX, the earliest known marker of photoreceptor identity), and protein kinase-C (PKC), and significantly lower levels of the glial fibrillary acidic protein (GFAP). Consistently, stimulated cells developed pronounced neuronal morphologies with significantly longer dendritic processes and larger cell bodies than non-stimulated controls. Taken together, the experimental evidence shows that the application of an electrical stimulation designed based on retinal development can be implemented to direct and enhance retinal differentiation of mRPCs, suggesting a role for biomimetic electrical stimulation in directing progenitor cells toward neural fates.			
	15:00-16:30	**Electromagnetic Levitation Platform for Wireless Study of Insect Flight Neurophysiology** ThD02.6	Alexander Verderber, Michael McKnight, Alper Bozkurt	Biological Sensors – ThD02	Event Hall-Area A (3F)
		Abstract– An electromagnetic levitation platform for use in a light emitting diode (LED) arena based virtual reality environment was developed for wireless recording of neural and neuromuscular signals from the flight related muscle groups in Manduca sexta. The platform incorporates the use of Early Metamorphosis Insertion Technology to implant recording electrodes into the flight muscles of late stage pupal moths. Analysis of the insects' response to changes in the LED arena rotation direction indicate that this setup could be used to perform a variety of flight behavior studies during yaw maneuvers.			
	15:00-16:30	**Concept for E.coli Detection Using Interdigitated Microelectrode Impedance Sensor** ThD02.4	Kalpana Settu, Jen-Tsai Liu, Ching-Jung Chen, Jang-Zern Tsai, Shwu Jen Chang	Biological Sensors – ThD02	Event Hall-Area A

					(3F)
		Abstract– This paper presents the concept to detect Escherichia coli O157:H7 based on electrochemical impedance spectroscopy at interdigitated microelectrode. Interdigitated microelectrode structures was designed and fabricated, with glass as substrate material and gold electrodes. The performance of the sensors was studied by measuring the capacitance in air and impedance spectra in DI water. The feasibility of the fabricated sensor for detecting different concentrations of Escherichia coli in water was demonstrated. Electrochemical impedance spectroscopy (EIS) was employed as the detection technique. The impedance based response significant change for different E.coli concentrations in the frequency range between 1 kHz to 100 kHz.			
	15:00-16:30	**Polycarbazole-Based Organic Photodiodes for Highly Sensitive Chemiluminescent Immunoassays** ThD02.1	Nuno M.M. Pires, Tao Dong	Biological Sensors – ThD02	Event Hall-Area A (3F)
		Abstract– It is reported the development of a polycarbazole-based organic photodetector for chemiluminescent immunoassays. The optical detector comprised a 1:4 blend by weight of poly [N-9`-heptadecanyl-2,7-carbazole-alt-5,5-(4`,7`-di-2-thienyl-2`,1`,3`-benzothiadiazole)] (PCDTBT) and [6,6]-phenyl C71-butyric acid methyl ester (PC70BM). Optimization of the photodetector design was conducted aiming to maximize photosensitivity and reduce the background level. Quantitation of recombinant human thyroid stimulating hormone indicated good linearity and yielded a detection sensitivity of ~3.7 nA nM-1 and a detection limit of 80 pg/ml.			
	16:30-16:45	**Differential Network Biology Reveals a Positive Correlation between a Novel Protein-Protein Interaction and Cancer Cells Migration** ThE09.1	Chia-Hung Liu, Tzu-Chi Chen, Chun-Houh Chen, Cheng-Yan Kao, Chi-Ying F. Huang	Quantitative Biology – ThE09	1006 (10F)
		Abstract– This paper introduces a differential network biology for discovering tumor migration. We applied statistical methods to prioritize PPI candidates and an in situ proximity ligation assay to verify 67 endogenous PPIs among 21 interlinked pathways in two hepatocellular carcinoma (HCC) cells, Huh7 (minimally migratory cells) and Mahlavu (highly migratory cells). Differential network biology analysis was applied to determine the novel interaction, CRKL-FLT1, has a high centrality ranking, and the expression of this interaction is strongly correlated with the migratory ability of HCC and other cancer cell lines. Knockdown of CRKL and FLT1 in HCC cells leads to a decrease in cell migration. This study demonstrated that functional exploration of a disease network with differential network in interlinked pathways via PPIs can be used to discover tumor migration.			
Friday, July 5, 2013	09:30-11:00	**Design of a Dual-Mode Electrochemical Measurement and Analysis System** FrB01.9	Jr-Fu Yang, Chia-Ling Wei, Jian-Fu Wu, Bin-Da Liu	Integrated Sensor Systems II – FrB01	Event Hall-Area A (3F)
		Abstract– A dual-mode electrochemical measurement and analysis system is proposed. This system includes a dual-mode chip, which was designed and fabricated by using TSMC 0.35 μm 3.3V/5 V 2P4M mixed-signal CMOS process. Two electrochemical measurement and analysis methods, chronopotentiometry and voltammetry, can be performed by using the proposed chip and system. The proposed chip and system are verified successfully by performing voltammetry and chronopotentiometry on solutions.			
	09:30-11:00	**A New Radio Propagation Model at 2.4 GHz for Wireless Medical Body Sensors in Outdoor Environment** FrB01.10	Daniel Yang	Integrated Sensor Systems II – FrB01	Event Hall-Area A (3F)
		Abstract– This study investigates the effect of antenna height, receive antenna placement on human body, and distance between transmitter and receiver on the loss of wireless signal power in order to develop a wireless propagation model for wireless body sensors. Although many studies looked at the effect of distance, few studies were found that investigated methodically the effect of antenna height and antenna placement on the human body. Transmit antenna heights of 1, 2, and 3 meters, receive antenna heights of 1 and 1.65 meters, “on-body” and “off-body” placements of receive antenna, and a total of 11 distances ranging from 1 to 45 meters are tested in relation to received power in dBm. Multiple regression is used to analyze the data. Significance of a variable is tested by comparing its p-value with alpha, and model fit is assessed using adjusted R^2 and σ of residuals. It is found that an increase in antenna height would increase power—but only for transmit antenna. The receive antenna height has a surprising, opposite effect in the on-body case and an insignificant effect in the off-body case. To formalize the propagation model, coefficient values from multiple regression are incorporated in an extension of the log-distance model to produce a new empirical model for on-body and off-body cases, and the new empirical model could conceivably be utilized to design more reliable wireless links for medical body sensors.			
	13:30-13:45	**CMOS Capacitive Biosensors for Highly Sensitive Biosensing Applications** FrC14.1	An-Yu Chang, S.C Lu	Electronic DNA Detection, Self-Assembled Biomaterials – FrC14	804 (8F)
		Abstract– Magnetic microbeads are widely used in biotechnology and biomedical research for manipulation and detection of cells and biomolecules. Most lab-on-chip systems capable of performing manipulation and detection require external instruments to perform one of the functions, leading to increased size and cost. This work aims at developing an integrated platform to perform these two functions by implementing electromagnetic microcoils and capacitive biosensors on a CMOS (complementary metal oxide semiconductor) chip. Compared to most magnetic-type sensors, our detection method requires no externally applied magnetic fields and the associated fabrication is less complicated. In our experiment, microbeads coated with streptavidin were driven to the sensors located in the center of microcoils with functionalized anti-streptavidin antibody. Detection of a single microbead was successfully demonstrated using a capacitance-to-frequency readout. The average capacitance changes for the experimental and control groups were -5.3 fF and -0.2 fF, respectively.			
	13:45-14:00	**Detection of RNAP-DNA Complexes Using Solid State Nanopores** FrC14.2	Camille Raillon, Pierre Granjon, Michael Graf, Aleksandra Radenovic	Electronic DNA Detection, Self-Assembled	804 (8F)

				Biomaterials – FrC14	
		Abstract– Transcription is the first step in gene expression where DNA is copied into RNA. It is extensively studied at the bulk level especially the regulation mechanism, which in cancerous cells is impaired. We were interested in studying E. coli RNAP enzyme at the single-molecule level for its functional as well as molecular motor properties. With nanopore sensing we were able to observe RNA polymerase-DNA complexes translocate through nanopores and capable to distinguish between individual complexes and bare RNA polymerase. We were also able to observe orientation of RNA polymerase in the nanopore whether flow or electric field predominates. The complexity of the signals from the protein-DNA complexes experiment motivated the development of level detection software. This software is based on a change detection method called the CUSUM algorithm. Our software was designed to analyze in details current blockages in nanopore signals with very little prior knowledge on the signal. With this work one can separate events according to their number of levels and study those sub-populations separately.			
	14:00-14:15	**Temporal Resolution of Nanopore Sensor Recordings** FrC14.3	Jacob Rosenstein, Kenneth Shepard	Electronic DNA Detection, Self-Assembled Biomaterials – FrC14	804 (8F)
		Abstract– Here we discuss the limits to temporal resolution in nanopore sensor recordings, which arise from considerations of both small-signal frequency response and accumulated noise. Nanopore sensors have strong similarities to patch-clamp ion channel recordings, except that the magnitudes of many physical parameters are substantially different. We will present examples from our recent work developing high-speed nanopore sensing platforms, in which we integrated nanopores with custom low-noise complementary metal-oxide-semiconductor (CMOS) circuitry. Close physical proximity of the sensor and amplifier electronics can reduce parasitic capacitances, improving both the signal-to-noise ratio and the effective temporal resolution of the recordings.			
	14:15-14:30	**Physical Stability of Cholesterol Derivatives Combined with Liposomes and Their in Vitro Behavior** FrC14.4	Bin Yang, Sheng-Yong Geng, Jin-Ye Wang	Electronic DNA Detection, Self-Assembled Biomaterials – FrC14	804 (8F)
		Abstract– The purpose of this study was to investigate the physical stability and drug release of two cholesterol derivatives (4-cholesterocarbonyl-4'-(N,N,N-triethylamine butyloxyl bromide, CTBBA, and 4-cholesterocarbonyl-4'-(N,N'- diethylamino-butyloxy, CDBA), when combined with doxorubicin (DOX)-loaded liposomes in vitro. CTBBA-liposome revealed a positive charge at a pH between 3 and 10, as indicated by the -potential. DOX-encapsulated CTBBA-liposomes possessed better physical stability both in PBS and in fetal bovine serum (FBS) added to PBS.			
	14:30-14:45	**Engineered Virus-Like Nanoparticle Heparin Antagonists** FrC14.5	Andrew Udit	Electronic DNA Detection, Self-Assembled Biomaterials – FrC14	804 (8F)
		Abstract– Virus nanoparticles provide a self-assembling, reproducible multivalent platform that can be chemically and genetically manipulated for the presentation of a wide array of epitopes. Presented herein are engineered bacteriophage Q-beta nanoparticles that function as potent heparin antagonists. Three successful approaches have been used: 1) chemically appending poly-Arg peptides; 2) point mutations to Arg on the virus capsid; 3) incorporation of heparin-binding peptides displayed externally on the virus surface. Each approach generates particles with good heparin antagonist activity with none of the toxic side effects of protamine, the only drug currently FDA-approved for clinical use as a heparin antagonist.			
	14:45-15:00	**Effects of Low Level Light Irradiation on the Migration of Mesenchymal Stem Cells Derived from Rat Bone Marrow** FrC14.6	Wen-Tyng Li	Electronic DNA Detection, Self-Assembled Biomaterials – FrC14	804 (8F)
		Abstract– Low level light irradiation (LLLI) was found to exert positive effects on various cells in vitro. The aim of this study was to investigate the effect of LLLI on the migration of rat bone marrow mesenchymal stem cells (rbMSCs). Light irradiation was applied at the energy density of 4 J/cm2 using red (630 nm) and near infrared (NIR, 850 nm) light emitting diodes (LEDs). Wound healing assay showed both red and NIR light irradiation increased cell mobility. Red and NIR light enhanced transmembrane migration of rbMSCs up to 292.9% and 263.6% accordingly. This agreed with enzymatic activities of MMP-2 and MMP-9 enhanced by irradiation. F-actin accumulation and distribution correlated to increased migration in light-irradiated MSCs. Reactive oxygen species production as well as the expression of pFAK and pNF-κB were elevated after red and NIR LLLI. The study demonstrated that red and NIR LLLI increased rbMSCs migration and identified the phosphorylation of FAK and NF-κB as critical steps for the elevated cell migration upon LLLI.			
	15:00-16:30	**Research of PLGA Microspheres Preparation Based on the Micro-Jetting Technology** FrD07.3	Sun Huaiyuan	Micro and Nano Sensors II – FrD07	Event Hall-Area A (3F)
		Abstract– Micro-jetting is a new method to manufacture microcapsule. According to the principle of micro-jetting technology, applying micro-jetting system to manufacture polylactic acid-glycolic acid copolymer(PLGA) microspheres; with PLGA for shell material on the ball, poly(vinyl alcohol) and twain as surfactant, using single factor analysis method to study the influence of driving voltage, jetting frequency and stirrer speed to the PLGA microspheres mean grain size and size distribution. The inside diameter of glass nozzles used in the experiments were 40μm. The results show that, in the conditions of experimental drug prescription certain, the driving voltage was proportional to the particle size, jet frequency and stirrer speed were inversely proportional. When the driving voltage for			

		60V~100V,the jet frequency for 1000Hz~5000Hz and the stirrer speed for 150~450rpm, the particle size distribution was in an ideal state.			
Saturday, July 6, 2013	08:00-08:15	**Wirelessly Addressable Heater Array for Centrifugal Microfluidics and Escherichia Coli Sterilization** SaA08.1	Xing Chen, LeLe Song, Babak Assadsangabi, Jie Fang, Mohamed Sultan Mohamed Ali, Kenichi Takahata	Microfluidics in Biological Applications I – SaA08	1005 (10F)
		Abstract– Localized temperature control and heater interface remain challenges in centrifugal microfluidics and integrated lab-on-a-chip devices. This paper presents a new wireless heating method that enables selective activation of micropatterned resonant heaters using external radiofrequency (RF) fields and its applications. The wireless heaters in an array are individually activated by modulating the frequency of the external field. Temperature of 93 degree C is achieved in the heater when resonated with a 0.49-W RF output power. The wireless method is demonstrated to be fully effective for heating samples under spinning at high speeds, showing its applicability to centrifugal systems. Selective sterilization of Escherichia coli through the wireless heating is also demonstrated. Healthcare applications with a focus on wound sterilization are discussed along with preliminary experiments, showing promising results.			
	08:15-08:30	**Characteristics of Magnetic Probes for Identifying Sentinel Lymph Nodes** SaA07.2	Tetsu Ookubo, Yusuke Inoue, Dongmin Kim, Hiroyuki Ohsaki, Yusuke Mashiko, Moriaki Kusakabe, Masaki Sekino	Integrated Sensor Systems I – SaA07	1004 (10F)
		Abstract– The identification of the sentinel lymph nodes that cause tumor metastasis is important in breast cancer therapy. The detection of magnetic fluid accumulating in the lymph nodes using a magnetic probe allows surgeons to identify the lymph nodes. In this study, we carried out numerical simulations and experiments to investigate the sensitivity and basic characteristics of a magnetic probe consisting of a permanent magnet and a small magnetic sensor. The measured magnetic flux density arising from the magnetic fluid agreed well with the numerical results. In addition, the results helped realize an appropriate probe configuration for achieving high sensitivity to magnetic fluid. A prototype probe detected magnetic fluid located 30 mm from the probe head.			
	08:30-08:45	**Multi-Level 3D Implementation of Thermo-Pneumatic Pumping on Centrifugal Microfluidic CD Platforms** SaA08.3	Tzer Hwai Gilbert Thio, Fatimah Ibrahim, Wisam Al Faqheri, Norhayati Soin, Maria Kahar Bador Abdul Kahar, Marc Madou	Microfluidics in Biological Applications I – SaA08	1005 (10F)
		Abstract– Thermo-pneumatic (TP) pumping is a method employing the principle of expanding heated air to transfer fluids back towards the CD center on the centrifugal microfluidic CD platform. While the TP features are easy to fabricate as no moving parts are involved, it consumes extra real estate on the CD, and because heating is involved, it introduces unnecessary heating to the fluids on the CD. To overcome these limitations, we introduce a multi-level 3D approach and implement forced convection heating. In a multi-level 3D CD, the TP features are relocated to a separate top level, while the microfluidic process remains on a lower bottom level. This allows for heat shielding of the fluids in the microfluidic process level, and also improve usage of space on the CD. To aid in future implementations of TP pumping on a multi-level 3D CD, studies on the effect of heat source setting, and the effect of positioning the TP feature (it distance from the CD center) on CD surface heating are also presented. In this work, we successfully demonstrate a multi-level 3D approach to implement TP pumping on the microfluidic CD platform.			
	08:45-09:00	**Liquid-Phase Sample Preparation Method for Real-Time Monitoring of Air-Borne Asbestos Fibers by Dual-Mode High-Throughput Microscopy** SaA08.4	Myoung-Ock Cho, Jung Kyung Kim, Hwataik Han, Jeonghoon Lee	Microfluidics in Biological Applications I – SaA08	1005 (10F)
		Abstract– Asbestos that had been used widely as a construction material is first-level carcinogen recognized by the World Health Organization. It can be accumulated in body by inhalation, and causes virulent respiratory diseases such as lung cancer. In our previous study, we developed a high-throughput microscopy (HTM) system that is able to replace the conventional phase contrast microscopy (PCM) through automated counting of fibrous materials and thus significantly reduced time consumption and labor. Also, we attempted selective detection of chrysotile using DksA protein which is extracted from Escherichia coli through a recombinant protein production technique, and developed fluorescent HTM (HTMred) by upgrading the HTM device we developed. We demonstrated that fluorescently-labeled chrysotile asbestos fibers were identified and enumerated automatically among other types of asbestos fibers or non-asbestos particles in a high-throughput manner through a newly modified HTM device for dual-mode reflection and fluorescence imaging. However it has limitations to be applied air-borne sample to fluorescence HTM in current air collecting method due to the difficulty of applying the protein to the dry asbestos. In this study, we developed the technique for making liquid phase asbestos sample using impinger that is used to collect order molecule in the air. It is possible to improve the feasibility of the dual-mode HTM through the liquid-phase sample manufacture process. The new technique we developed for highly sensitive and automated asbestos detection can replace conventional manual method, and it can be applied as a fast and reliable environmental monitoring tool.			
	09:00-09:15	**A Simple Microfluidic Gradient Generator with a Soft-Lithographically Prototyped, High-Aspect-Ratio, ~2 μ M Wide Microchannel** SaA08.5	Tomohisa Ogawa, Nirai Matsunaga, Saori Inomata, Masato Tanaka, Nobuyuki Futai	Microfluidics in Biological Applications I – SaA08	1005 (10F)
		Abstract– We have developed a cast microfluidic chip that contains a thin (~2 μm wide) microchannel that is smoothly connected to thick microfluidics. The thin line features having high aspect ratio for a low-cost photolithography in which an emulsion photomask was used (1:1 ~ 1:3) were fabricated by exposing SU-8 photoresist to diffused 185 nm UV light emitted by a low-cost ozone lamp from the backside of the substrate to ensure sufficient crosslinking of small regions of the SU-8 photoresist. An H-shaped microfluidic configuration was used, in which the thin channel maintained constant diffusion fronts beyond purely static diffusion. We also demonstrated the long-term effects of a gradient of nerve growth factor on axon elongation by primary neurons cultured in the micro channel.			
	09:15-09:30	**Distinct Patterns of Cell Motion Inside a Micro-Channel under Different Osmotic Conditions** SaA08.6	Chia-Hung Dylan Tsai, Makoto Kaneko, Shinya Sakuma, Fumihito Arai	Microfluidics in Biological Applications I –	1005 (10F)

				SaA08	
		Abstract– The effect of osmotic condition on a living cell inside a micro-channel is firstly studied in this work. By utilizing a high-speed camera, we observed distinct patterns of cell motion under different osmotic conditions, which are established by saline with different concentrations of sodium chloride (NaCl). The cells' motions are tracked by a computer, and are shown in the coordinates of location and time (x-t chart) here. The motions of cells under hypotonic condition (NaCl% < 0.9%) are convex curves on the chart while the ones under isotonic and hypertonic conditions (NaCl% ≥ 0.9%) are concave curves. Since saline is widely used in both medical practices and cell-related researches, our results point out two important facts: 1) Cells are sensitive to the percentage of NaCl. One percent difference in overall concentration makes dramatic changes in cell characteristics, such as cell stiffness. 2) The micro-channel method can clearly tell the difference between hypotonic, isotonic and hypertonic conditions according to the pattern of cell motion. Interpretations of the phenomena from different perspectives are also discussed in this paper.			
Sunday, July 7, 2013	08:00-08:15	**Design Considerations for a CMOS Lab-On-Chip Microheater Array to Facilitate the in Vitro Thermal Stimulation of Neurons** SuA07.1	Ferran Reverter, Yan Liu, Pantelis Georgiou, Themistoklis Prodromakis, Timothy Constandinou	Micro and Nano Sensors I – SuA07	1004 (10F)
		Abstract– This paper identifies and addresses key design considerations and trade-offs in the implementation of a high-resolution microheater array for CMOS Lab-on-Chip (LOC) applications. Specifically, this is investigated in the context of facilitating the in vitro thermal stimulation of single neurons. The paper analyses the electro-thermal response (by means of COMSOL simulations) and reliability issues (such as melting and electromigration) of different microheater designs. The analysis shows that a small-area heater is more efficient in terms of power, but it has more reliability problems essentially due to electromigration effects. For the proposed heater designs, the expected lifetime is a few days (in continuous operation) in the worst scenario, which is still generally acceptable for LOC applications.			
	08:15-08:30	**Silicon Nanotweezers with a Microfluidic Cavity for the Real Time Characterization of DNA Damage under Therapeutic Radiation Beams** SuA07.2	Gregoire Perret	Micro and Nano Sensors I – SuA07	1004 (10F)
		Abstract– We report the biomechanical characterization of λ-DNA bundle exposed to a therapeutic radiation beam by silicon Nanotweezers. The micromechanical device endures the harsh environment of radiation beams, and still retains molecular-level detection accuracy. The real-time DNA bundle degradation is observed in terms of biomechanical stiffness and viscosity reduction, both in air and in solution. These results pave the way for both fundamental and clinical studies of DNA degradation mechanisms under ionizing radiation for improved tumor treatment.			
	08:30-08:45	**Nanopore Single-Molecule Dielectrophoretic Detection of Cancer-Derived MicroRNA Biomarkers** SuA07.3	Li-Qun Gu	Micro and Nano Sensors I – SuA07	1004 (10F)
		Abstract– The nanopore-based single-molecule biosensor has been extensively investigated for various biomedical detections. It has demonstrated the potential in gene sequencing and diagnosis-oriented biomarker detection such as microRNAs. In real-time detection, however, samples extracted from bio-fluids contain various non-target nucleic acids components. These components can cause severely influence the target detection accuracy. We have discovered that a polycationic probe can solve this issue. The polycationic peptide domain of the probe can separate the target:probe complex from free nucleic acids, and only lead the complex into the pore, therefore realizing simultaneous enrichment and detection of target microRNAs. This study establishs a universal approach to detecting any short pathogenic nucleic acids fragment in complex samples.			
	08:45-09:00	**Non-Planar and Flexible Chip Technology for Biomedical Applications** SuA07.4	Ching-Yu Liu, Hsiao-Chien Lin, Chih-Chiao Teng, Long-Sheng Fan	Micro and Nano Sensors I – SuA07	1004 (10F)
		Abstract– We report a novel non-planar flexible silicon chip technology by means of patterning thin films of high residual stress on top of shaped thin silicon substrate. High residual stresses of thin films make thin chip deform into designed three-dimensional shapes. In this study, a series of patterned stress films and "petal-like" chips were fabricated and analyzed. Large curvatures can also be formed and maintained by the packaging process bonding the chips to constraining elements such as thin-film polymer ring structures. As a demonstration, a CMOS image-sensing retina chip is made into a contact-lens shape conforming to a human eyeball 12.5mm in radius. This non-planar and flexible chip technology provides a desirable device surface interface to soft or non-planar bio surfaces and opens up possibilities for many biomedical applications.			
	09:00-09:15	**Threshold Levels for Wettability in Nano and Micro-Meter Periodic Structures** SuA07.5	Masaki Yamaguchi, Shinya Sasaki, Yuto Sasaki, Makoto Sasaki, Tsuyoshi Chiba, Nobuyuki Itoh, Tatsuro Nakanishi	Micro and Nano Sensors I – SuA07	1004 (10F)
		Abstract– The purposes of this study are to clarify the relationship between surface wettability and the pitch and size of periodic structures on the surface and to determine the thresholds at which the wettability switches from being hydrophobic to hydrophilic. To this various nano- and micro-meter scale periodic structures were fabricated. By applying a fine periodic structure to the surface, the wettability can be controlled between + 50° (hydrophobic) and -55° (hydrophilic). The pitch of the periodic structure at which the wettability switches from hydrophilic to hydrophobic was found to between 500 and 1,000 nm. Additionally, the height of the periodic structure at which the wettability switches from hydrophobic to hydrophilic was found to between 300 and 700 nm.			
	09:15-09:30	**Softening of the Mouse Zona Pellucida During Oocyte Maturation** SuA07.6	Yoshinobu Murayama, Kenta Yoshida, Takahashi Harutaka, JInji Mizuno, Kazuyuki Akaishi, Hiroaki Inui	Micro and Nano Sensors I – SuA07	1004 (10F)
		Abstract– A change in the elasticity and the resistance to dissolution of the mouse zona pellucida (ZP) was quantitatively evaluated at immature germinal vesicle (GV), mature metaphase II (MII) and fertilized pronuclear (PN) stages. Young's modulus of the ZP was measured using a micro tactile sensor (MTS), a highly sensitive resonator-based sensor for a micro scale elasticity measurement. 0.25% α-chymotrypsin was used for the ZP dissolution assay. The results of measuring the ZP elasticity and the dissolution time clearly showed that the ZP softened during oocyte maturation and the ZP hardened after fertilization. The results indicate that the amount of the zona softening can be a criterion to evaluate oocyte quality for the selection of top quality mature oocyte before in vitro			

八、附件二（論文發表）

Nucleic Acid Sandwich Hybridization Assay with Quantum Dot-Induced Fluorescence Resonance Energy Transfer for Pathogen Detection

Cheng-Chung Chou*, Yi-Han Huang

***Abstract*— This study is to use bioinformatics, nucleic acid sandwich hybridization assay with a quantum dot (QD)-induced fluorescence resonance energy transfer (FRET) reporter system and optical sensing technologies for developing a highly sensitive/specific, rapid, real-time and portable detection device to identify avian influenza and human pandemic influenza viruses within 30-90 minutes**

I. Introduction

Zoonoses have continuously threatened public health and economics worldwide. A notable example is avian influenza (AI), caused by the infection of type A influenza viruses of the family Orthomyxoviridae. Since the outbreak of the highly pathogenic H5N1 avian influenza in Hong Kong in 1997, growing evidence has been showing that avian influenza viruses (AIVs) can cross the species barrier to directly infect humans [1]. Early identification of the highly pathogenic AIVs and other zoonotic pathogens in the field can help control zoonosis spread and reduce the risk of development into an epidemic. Therefore, rapid, highly specific and sensitive detection methods for routine surveillance are keys to the efficient prevention and control of AIVs

II. Methods and Results

A label-free hemagglutinin H5 sequences (60-mer DNA) of avian influenza viruses were used as the targets in this work. Two oligonucleotides (16 mers and 18 mers) that specifically recognize two separate but neighboring regions of the H5 sequences were served as the capturing and reporter probes, respectively. The capturing probe was conjugated to QD655 (donor), and the reporter probe was labeled with Alexa Fluor 660 dye (acceptor) during synthesis. The sandwich hybridization assay was done on a disposable, temperature- adjustable indium tin oxide (ITO) glass slide. The FRET signal in response to the sandwich hybridization was monitored by a LED-based UV optical sensor. Figure 1 shows the setup of the FRET detection device. The 20 μL, transparent microchamber on the ITO glass slide was constructed by applying a sticky 25 μL Microarray Gene Frame onto the ITO conductive surface along with a transparent, plastic cover slip. The assembly of Gene Frame and cover slip were thermally stable and remained well-sealed up to 97 °C. The hybridization mixture was transferred to the microchamber with a micropipette. Then the miniature CCD-array spectrophotometer, connected to a laptop computer, was used to collect the emission spectra detected by the optical sensor system. The target with a concentration ranging from 0.5 nM to 1 μM was successfully correlated with both QD emission decrease at 653 nm and dye emission increase at 690 nm. To sum up, this work is beneficial for developing a portable QD-based nucleic acid sensor for on-site pathogen detection.

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III. Conclusion

The sandwich hybridization assay with a QD-induced FRET reporter system has been successfully integrated with a homemade optical sensor composed of an UV LED, a miniature CCD spectrophotometer and a disposable ITO glass slide. With the prototype sensor, label-free H5 target sequences (60-mer DNA) have been successfully detected. The target concentrations ranging from 0.5 nM to 1 μM has been correlated with both the QD emission decrease at 653 nm and dye emission increase at 690 nm. In summary, a new QD-induced FRET sensor platform well-suited for both nucleic acid analysis and on-site zoonosis surveillance is accomplished.

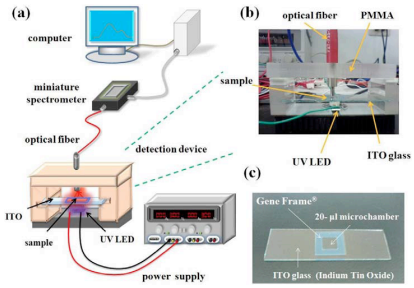

Figure 1. The homemade FRET detection system based on a single 400 nm UV LED, a disposable ITO glass slide, a miniature 16-bit CCD-array spectrophotometer, and optical fibers: (**a**) schematic diagram of the detection system setup; (**b**) picture of the detection device setup (the main body of the device was made of PMMA with dimensions of 8.4 °— 4.5 °— 4.3 cm3); (**c**) ITO with a transparent, 20 μL microchamber created by theMicroarray Gene Frame®.

References

[1] J. H. Beigel, J. Farrar, A. M. Han, F. G. R. Hyer, M. D. de Jong, S. Lochindarat, et al. *"Avian influenza A (H5N1) infection in humans"*. N. Engl. J. Med. Vol. 353, pp. 1374–1385, 2005.