出國報告（出國類別：其它-參訪交流）

與日本JST召開NSC(MOST)-JST合作計畫研究成果發表會

服務機關：科技部
姓名職稱：馮展華　司長
鄭慧娟　研究員
派赴國家：日本
出國期間：103年4月7日至4月11日
報告日期：103年6月26日

目 次

摘要
壹、目的……………………… 3
貳、過程……………………… 3
參、心得及建議事項………… 7
肆、附錄 ………………………8

摘要：

2014 年 4 月 7 日-11 日，科技部與日本獨立行政法人科學技術振興機構(Japan Science and Technology Agency, JST)在東京大學 Kumaba 校區舉辦 MOST (改組前為 NSC)和 JST，2013 及 2014 年所執行合作研究計畫的研究成果發表會，由台日雙方各 7 位計畫主持人出席發表研究成果，會後進行計畫主持人的實驗室參訪和人員交流。

壹、目的

2014 年 4 月 7 日至 11 日，科技部與日本獨立行政法人科學技術振興機構 (Japan Science and Technology Agency, JST)，在東京 Kumaba 校區舉辦第二期共同研究計畫重點領域-“Bioelectronics and Biophotonics” 的研究計畫成果發表會，由科技部工程司馮展華司長及科國司承辦人陪同台方講員出席參與，以瞭解科技部與 JST 在本期合作的成果，俾利作為評估該領域合作效益的參考。

貳、過程

■主要行程/

1.出席與日本 JST 合作計畫成果發表會

科技部(前身為行政院國家科學委員會)於 2007 年與 JST 簽署科學合作備忘錄，本次研究成果發表會係以雙方合作第二期計

畫執行成果舉辦發表會。

4 月 8 日的成果發表會首先由台日主辦單位致詞，JST 由 Toshitaka Kuroki 代表，台方由科技部工程司馮展華司長代表，並由日方召集人 Prof. Hiroyuki Fujita 介紹本次研討會的進行方式。上午第一組，由中原大學機械系劉益宏副教授及 Waseda University Prof. Masakatsu G. Fujie 發表論文，主題為" Development of a Brain-Machine Interface-based Biofeedback Robotic Rehabilitation System"。第二組由清華大學化學工程系呂世源教授和 Tokyo Institute of Technology Associate Prof. Nobuhiro Matsushita 發表論文，內容為" Electrochemical biosensors based on novel nanostructures of fluorine-doped tin oxide for detecting myocardial infarction marker"。 第三組由台灣大學化學工程系何國川教授和日本獨立行政法人物質.材料研究機構 Independent Scientist Yusuke Yamauchi，主題為" Hierarchically Organized and Multiresponsive Mesoporous Materials for Biosensor and Controlled Release Platforms"。第四組由交通大學電子工程系吳重雨教授和 Nara Institute of Science and Technology Prof. Jun Ohta 發表，內容為" The Research on Self-Powered Sub-Retinal Devices for Visual Prostheses"。 第五組由清華大學奈米工程與微系統研究所葉國良教授和 The University of Tokyo Prof. Hiroyuki Fujita 發表，主題為" Neuron-on-CMOS-MEMS"。第六組由中央研究院生物研究所鍾邦柱特聘研究員和 The University of Tokyo Prof. Suguru Kawato 發表，內容為" Analysis of neurosteroid effects on hippocampal neural circuits using novel multi-electrode probe methods"。當日最後一場由台灣師範大學光電研究所洪姮娥教授和 Toyohashi university of technology Prof. Tanaka Saburo 發表，主題為" Imaging of Magnetic Nanoparticles and Low-field

Magnetic Resonance Imaging for Bio-applications”。

在當日研究成果發表結束，接著進行 Poster Presentation，由日本大學的教授和學生們展示海報並說明，與會教授參與評分，評分後選出 Best Poster Paper Award 進行頒獎。得獎第一名為 NAIST Prof. Toshihiko Noda，為吳重雨教授的合作團隊。

2. 參訪東京大學生產技術研究所(Institute of Industrial Science)

訪團參訪東京大學 Institute of Industrial Science，由 Prof. Hiroyuki Fujita 簡報該單位的概況，並參觀實驗室。生產技術研究所是東京大學成立甚早的單位，1949 年即設立；全職的教職員約 300 名、學生約 700 名、有 5 個研究部門、1 個特別研究部門、1 個客座研究部門、10 個研究中心，以及 6 個共同合作研究中心，是日本大學規模最大的研究所。此研究所從事工程領域的研究極為寬廣，從基礎科學到應用科學都有，約有 160 個實驗室。訪團在參觀 Prof. Hiroyuki Fujita 研究團隊後並進行綜合討論。

3. 參訪東京工業大學生駒俊之准教授實驗室 (Ikoma Lab, Tokyo Institute of Technology)

訪團參訪東京工業大學 Ikoma 准教授實驗室，由 Toshiyuki Ikoma 准教授簡報其生醫材料方面的研究成果，並參觀實驗室。Ikoma 和該實驗室主持人 Junzo Tanaka 發展新的技術，能夠以魚鱗與磷灰石作為製作人工骨骼的材料。Ikoma 介紹他們的研究團隊可以在短期內即完成新骨頭組織的製造，並且由於新材

料是取自魚鱗，相對也減輕從其他原料來源，例如從動物身體取得外皮感染病毒的可能性，而且因為這種人造軟骨的密度更高更堅硬，對於患有骨癌的中老年人而言，若能進一步利用魚膠原蛋白，增加再生的能力，他們的骨骼能有更多的時間可以重新再造。

4. 参訪日本獨立行政法人物質.材料研究機構MANA- International Center for Materials Nanoarchitectonics

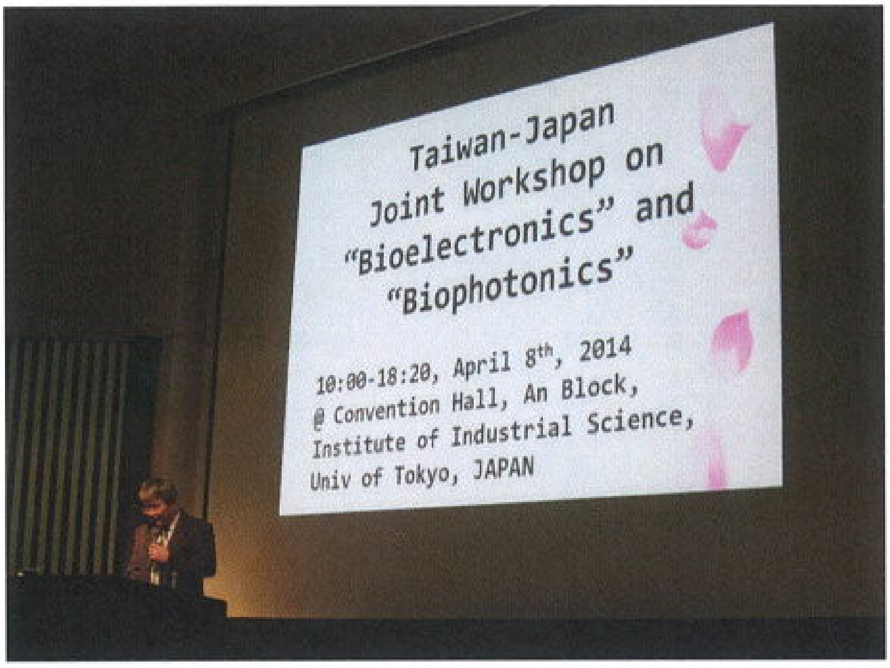
日本集合NIMS與四所大學(東京大學、京都大學、東北大學及大阪大學)成立MANA，以積極培育世界級的科研人才。MANA由Yamuchi 研究員簡報NIMS與MANA的發展概況。MANA有完善的儀器設施，其新大樓亦以智慧型及綠色建築為其特色。MANA是日本文部科學省(Ministry of Education, Culture, Sports, Science and Technology, MEXT)在2007年為引導建構日本成為世界級的9個研究中心之一，MANA提供來自全球各地尖端的科研人員在此進行國際合作研究，特別是對年青研究人才的培訓。MANA鼓勵日本在地年青學者與國際優秀的科學家團隊共同合作研究，其使用語言多以英語為主，對於日本國際化科研人才的提昇具有卓越成效

參、心得與建議

此次研究成果發表會，主要是台日參與 MOST&JST 合作計畫主持人發表近二年在 Bioelectronics 和 Biophotonics 領域合作研究計畫的成果，在 7 件合作計畫中以光電領域為多，生物領域為少，有生物專長的學者原本耽心，理工背景是否會瞭解他們的研究內容，但發現工學也很複雜，對於其他計畫主持人研究計畫的內容，其實也可瞭解，並且可自其他計畫主持人的報告，增補後續執行計畫的內容，並對生物電子的發展，有更深度瞭解，這亦是舉辦研究計畫成果發表會的目的，提供同期執行計畫人員相互激盪，他山之石可以攻錯。

台日可以互補互利合作的科研領域頗多，目前雙方合作計畫更新的週期為三年，應縮短此周期為 2 年，並開拓不同的合作模式，以增進台日合作項目的質量。

附件:研討會論文摘要及參訪照片



科技部工程司馮展華司長代表台方主辦單位致詞

Prof. Hiroyuki Fujita 介紹東京大學生產技術研究所

交通大學吳重雨教授代表大會頒贈海報競賽獲獎人員

參訪 NIMS MANA

Neuron on CMOS-MEMS

J. Andrew Yeh
Institute of NanoEngineering and MicroSystems, National Tsing Hua University
Hsinchu, Taiwan

Abstract

This work aims to develop a bio-based CMOS-MEMS technology to serve as the implementation platform for the NSC-JST neuron on CMOS-MEMS project. To monitor cell growth, behavior, and interaction on chip, a fully integrated CMOS bio-MEMS sensor system is designed and taped out through a commercially-available 0.35μm 2-poly-4-metal CMOS technology node fabricated using the largest CMOS foundry in the world – TSMC service. The sensor system includes: (i) ion-selective field effect transistors (ISFETs) for calcium ions sensing, (ii) CMOS interface/readout circuits to amplify the weak sensor signals and to enhance the signal to noise ratio, and (iii) different types of gold electrodes for later comparison. The gold layer deposition in CMOS bio-MEMS process features the improvement of cell adhesion. Note that the gold deposition, an attractive feature for bio applications, is also carried out by the TSMC, leading to very high fabrication yield and facilitating our sensing scheme without the need of additional post-CMOS processes. Understanding how taste cell interact with taste stimuli and identifying the patterns of taste receptors expressed in taste cells should shed light on coding of taste information by nervous system. We have developed an optics setup capable of performing Ca^{2+} imaging on acute cultures of mouse taste bud epithelium. Double-label fluorescent immunohistochemical confocal images revealed the mutually exclusive expression patterns of NCAM (neural cell adhesion molecule) and PLCβ2 (phospholipase C, β2), two taste cell type specific markers, confirming the general belief that distinct cell types express unique receptors. 30% and 42% of total 267 taste cells in 30 taste buds examined were stained by anti-NCAM and anti-PLCβ2 antibodies, respectively. In the meanwhile, to achieve selective cell patterning, we developed a robust and easy-to-use photolithography-based nanofabrication method that allowed us to place hydrophobic nanosponges on a silicon surface to pattern mammalian cells. We also developed various physically and chemically based approaches to functionalize chitosan membranes, one of the US FDA/US EPA-approved biomaterials. This nanofabrication method can be easily merged with the current IC-based manufacturing approach and has a great potential for mass production of patterns at the nanometeric scale. Future works will be focus on the process integration for fabricating nanostructures on CMOS-MEMS chips.

Development of a Brain-Machine Interface-based Biofeedback Robotic Rehabilitation System

Masakatsu G. Fujie[1] and Yi-Hung Liu[2]

[1]Faculty of Science and Engineering, Waseda University, Tokyo, Japan

[2]Department of Mechanical Engineering, Chung Yuan Christian University, Chungli, Taiwan

Abstracts: Stroke is the leading cause of motor disability. It causes several impairments, such as hemiparesis and cognition deficits. Such stroke patients need a large amount of healthcare and social service to improve their quality in activities of daily living (ADL). Moreover, among the impairments after strokes, hemiplegia significantly makes stroke patient's gait performance degenerate. Therefore, their returning to society and restarting normal lives by means of rehabilitation is an issue meriting much research effort.

For stroke patients, gait recovery is the main objective in the rehabilitation program. Classic neurological gait rehabilitation can be achieved by various techniques, including neurophysiological and motor learning. Robotic devices have recently gained wide acceptance in gait rehabilitation because these devices not only provide intensive and task-oriented rehabilitation to stroke patients but also have good repeatability. In addition, more recently, some researchers further combined MI training technique and brain-computer interface (BC) techniques to improve upper-limb motor recovery. However, lower limb and gait function recovery have not been studied in combination with BCIs yet. Therefore, the combination of MI training and BCI techniques is a novel approach for gait rehabilitation.

Motivated by these findings, this international collaborative research between Taiwan and Japan aims to develop a BCI-based biofeedback robotic rehabilitation system for improving gait functions for hemiplegic stroke patients. Waseda University Team from Japan and the Chung Yuan Christian University (CYCU) Team from Taiwan join this collaborative study. Wasada team is focused on the development of a robotic rehabilitation system (Fig. 1) for gait training, the gait analysis and safety controller design. The CYCU team is focused on the development of a multi-functional MI-based BCI system (Fig. 2) for gait training and MI monitoring. Both teams conduct assessment of the gait function recovery on stroke patients to validate the effectiveness of the proposed BCI-based biofeedback robotic rehabilitation system in gate rehabilitation.

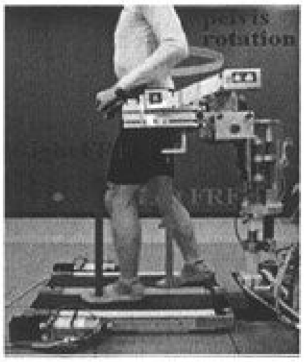


Fig. 1 The robotic rehabilitation system

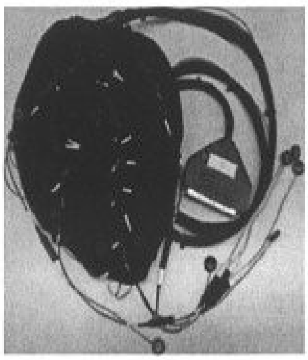


Fig. 2 EEG device for BCI

Hierarchically Organized and Multiresponsive Mesoporous Materials for Biosensor and Controlled Release Platforms

Yusuke Yamauchi[1], Kuo-Chuan Ho[2], Kevin Chia-Wen Wu[2]

[1]International Center for Materials Nanoarchitectonics, National Institute for Materials Science (NIMS), 1-1 Namiki, Tsukuba, Ibaraki 305-0044, Japan; [2]Department of Chemical Engineering, National Taiwan University, Taipei 10617, Taiwan

Abstract:

Fabrication of hierarchically ordered nanoporous materials (Yusuke Yamauchi)

The first topic of this proposal is to create hierarchically ordered (from macroscopic to nanoscopic range) mesoporous silica and non-silica (titania or metals) materials including nanoparticles, thin films and nanopatterns through the combination of top-down lithographic technologies and bottom-up surfactant-templated processes.

Synthesis of redox polymer nanocomposite for glucose biosensor (Kuo-Chuan Ho)

Redox polymer nanobeads of branched polyethylenimine binding with ferrocene (BPEI–Fc) were synthesized for glucose sensor. After incorporating conductive poly(3,4-ethylenedioxythiophene) poly(styrenesulfonate) (PEDOT:PSS), the sensing performance of a redox polymer nanobead–based enzyme electrode could be further improved. Based on this system, we intend to fabricate a hybrid electrode by impregnating enzyme into the mesoporous material with an aim to replace the conducting polymer. The ordered functional mesopores are expected to provide more efficient pathway for electron transfer.

Controlled drug release of hierarchically ordered nanoporous materials (Kevin C.-W. Wu)

Various kinds of multi-functionalized, hierarchically ordered mesostructured/mesoporous materials will be fabricated according to different bio-applications. In this proposal, several bio-application platforms will be emphasized, namely, biosensor, biofuel cell, controlled drug release, and cell culture. In the controlled drug release, a smart multi-functionalized nanodevice that can release drugs based on any stimulus (light, temperature, chemicals, etc.) of environment in a controlled manner was fabricated and reported here.

The Research on Self-Powered Sub-Retinal Devices for Visual Prostheses

Chung-Yu Wu[1], Jun Ohta[2], and Po-Kang Lin[3,4,5]

[1]National Chiao Tung University, Hsinchu City, Taiwan

[2]Nara Institute of Science and Technology, Nara, Japan

[3]National Yang-Ming University, Taipei City, Taiwan

[4]Taipei Veterans General Hospital, Taipei City, Taiwan

[5]National Taiwan University, Taipei City, Taiwan

Abstracts:

The objective of this joint research is to develop a vision prosthetic device consisted of a subretinal implantation chip with high-performance on-chip stimulus electrodes and a head-mounted goggle for image capture, display, and projection. National Chia Tung University (NCTU) which has been developing a novel type of a subretinal implantation chip, and Nara Institute of Science and Technology (NAIST) which has been developing a high-performance stimulus electrode, are to establish collaboration for the research. NCTU will develop an 256-pixel artificial retina chip that can generate stimulation currents by sensing the incident visible light and powered by the on-chip solar cells under infra-red illumination. Thus no wire through the eyeball is required. The goggle can provide both enhanced images from the camera and the IR light. NAIST will develop the technology of three-dimensional stimulus electrode with IrOx film coating, and fabricate the electrodes on the chip that NCTU will develop. The whole device will be tested in vitro. Finally, NCTU will implant the fabricated chip into a pig's eye and demonstrate the effectiveness in vivo. NAIST and NCTU will collaborate together and pave the way to human trial by using the developed devices..

This research will realize a high-performance electrode with 3-D shape on an implantable semiconductor chip. The developed technology can be applied to not only a retinal prosthetic device but also a neural prosthetic device. This joint research will develop solar-cell self-powered sub-retinal prosthetic devices which will provide a high QOL to blind patients.

Analysis of neurosteroid effects on hippocampal neural circuits using novel multi-electrode probe methods

Suguru Kawato[1] and Bon-chu Chung[2]

[1]Dept. Biophysics & Life Sciences, Grad School of Arts & Sciences, Univ. of Tokyo
Tokyo, Japan

[2]Institute of Molecular Biology, Academia Sinica
Taipei, Taiwan

Abstracts: Neurosteroids are small steroid molecules that enhance learning and memory, promote neuron recovery after spinal cord injury, and decrease anxiety. Neurosteroids have been tested in clinical trials for the treatment of chronic neurodisorders and neural injuries. However, the mechanism of neurosteroid action is still unclear. By using multi-electrode analysis, we have investigated rapid neurosteroid action in the hippocampal slices. We blocked the synthesis of a major neurosteroid, pregnenolone, by inhibiting the activity of its synthetic enzyme, cytochrome P450scc, with an inhibitor AG (aminoglutethimide). AG perfusion into rat slices for 20 min suppressed the long-term potentiation (LTP) of signal transmission between neurons. AG perfusion also rapidly decreased EPSP (excitatory postsynaptic potentiation). We can rescue the suppression of LTP and EPSP by supplementation of exogenous pregnenolone. This result shows that the effect of pregnenolone to rapidly (< 20 min) potentiate neuronal activities. We also searched for pregnenolone receptor that mediates its action in the brain. Although MAP-2 is known to be a pregnenolone receptor in solution, MAP-2 is not a good receptor inside cells. We found a new pregnenolone receptor, CLIP-170. We found that pregnenolone binds to and changes the conformation of CLIP-170 into an active form. When activated by pregnenolone, CLIP-170 could bind to microtubules and increased microtubule polymerization. We also showed that pregnenolone and CLIP-170 functioned synergistically to promote cell migration. Since CLIP-170 regulates dendrite morphology and promote neuron motility, we will analyze the function of CLIP170 in the hippocampus. We will also search other steroids that can rescue LTP suppression in addition to pregnenolone. We are also generating mice that are knocked out of P450scc selectively in the brain to address the functions of pregnenolone in vivo.

Imaging of Magnetic Nanoparticles and Low-field Magnetic Resonance Imaging for Bio-applications

Saburo Tanaka, Hayaki Murata, Tomoya Ohishi

Department of Environmental and Life Sciences, Toyohashi University of Technology

Japan

Herng-Er Horng, Shu-Hsien Liao, Jen-Jie Chieh, Hong-Chang Yang

Institute of Electro-Optical Science and Technology, National Taiwan Normal University

Taipei, Taiwan

In this work, we report ultra-low field nuclear magnetic resonance/magnetic resonance imaging (NMR/MRI) and magnetic particle imaging (MPI) system for bio-application. In the MPI study, the magnetic response, M, of magnetic nanoparticle (MNP) to an applied magnetic field, H (M–H characteristics) could be divided into a linear region and a saturation region, which are separated at a transition point H_k. When applying an excitation AC magnetic field (H_{ac}) and an additional DC bias field $H_{dc} = H_k$ as shown in Fig.1, the second harmonic of M reaches the maximum due to the nonlinearity of the M–H characteristics. It is stronger than any other harmonics including a third harmonic [1]. The advantage of the use of the second harmonic response is that the response can be taken for even in small H_{ac}. The M response of MNP was systematically analyzed and experimentally proven. In the case of the conventional detection using a third harmonic, the amplitude of the H_{ac} must be larger than the threshold level, which is almost the same as H_k. The detection method using a second harmonic can be applied to MPI. A high sensitive device, Superconducting Quantum Interference Device (SQUID) magnetometer was also applied to the MPI. Then we could successfully demonstrate the 1D image of two separated bottle-shaped phantoms filled with MNP using the method with a lock-in amplifier. The magnetic nanoparticles made by NTNU (National Taiwan Normal University) and Resovist (obtainable at market) were used.

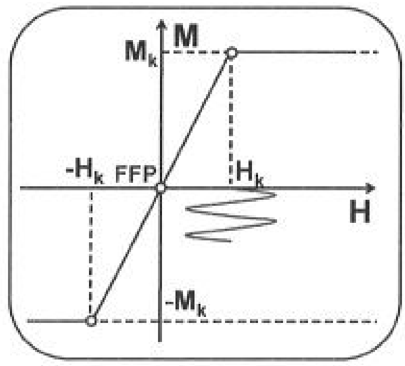


Fig.1. Principle of the detection using a 2nd harmonic with dc bias field of H_k.

Additionally highly-balanced first-harmonic detection was invented to improve the detection sensitivity. We applied a compensation coil to enhance the balance of the pick-up coil. The sensing coils of MPI system are consisted of excitation coil, pick-up coil and a compensation coil. The pick-up coil was wound in a gradiometer configuration to cancel the induced voltage from excitation coil. Thus the magnetic signal generated by MNPs can be resolved. Although the balance could be adjusted by modifying the position of excitation coil and pick-up coil, the induced voltage from excitation field is difficult to cancel completely. Therefore a compensation field was used to optimize the balance of pick-up coil. By adjusting the strength and phase of compensation field, it's easy to cancel the induced voltage from excitation field and further improve the balance of pick-up coil. Then we can obtain a high signal-to-noise ratio signal from MNPs. We also demonstrated the 1D-image of MNPs.

For low-field NMR/MRI, a high-T_c SQUID based low-field NMR and MRI system without μ-metal shielding was established. The field coils and SQUID are put inside a shielded box and shielded cylinder which were made out of aluminum to reduce the surrounding noise. For NMR and MRI measurement we apply three dimensional gradient fields to cancel the field inhomogeneity to obtain a narrow linewidth NMR spectrum of 0.8 Hz from a 10-ml water specimen. The 2-dimensional images of water specimen, mini tomato and human finger are performed by using our low-field MRI system. For tumor detection, the T_1 relaxation time of normal tissue and tumor tissue were obtained. The high-T_c SQUID based low-field MRI system shows the feasibility for biomedical application in microtesla magnetic fields

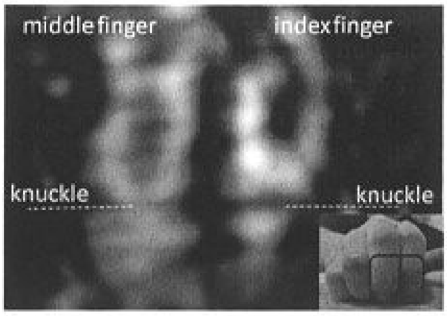


Fig.2. 2-dimensional image of human finger obtained by our high-T_c SQUID based low-field MRI system

[1] Yi Zhang, Hayaki Murata, Yoshimi Hatsukade and Saburo Tanaka, "Superparamagnetic nanoparticle detection using second harmonic of magnetization response", Review of Scientific Instruments 84, 094702 (2013).

Electrochemical biosensors based on novel nanostructures of fluorine-doped tin oxide for detecting myocardial infarction marker

Part I: Porous fluorine-doped tin oxide as a promising substrate for electrochemical biosensors – demonstration in hydrogen peroxide sensing

Part II: Electrochemical detection of immobilized Biotin-Avidin system on porous fluorine-doped tin oxide electrode

Kuan-Ting Lee[1], Dai-Min Liu[1], Yung-Yung Liang[1], Fumihiko Chimoto[2], Yuta Katayanagi[2], Tomohiko Yoshioka[3], Toshiyuki Ikoma[3], Nobuhiro Matsushita[2], Shih-Yuan Lu[1*]

1: Dept. of Chem. Eng., National Tsing Hua Univ., Hsinchu, 30013, Taiwan;

2: Mater. & Structures Lab., Tokyo Institute of Technology, Yokohama, 226-8503, Japan;

3: Dept. of Inorganic Mater., Tokyo Institute of Technology, Tokyo, 152-8550, Japan

Abstracts: Conducting porous substrates of high hydrophilicity are advantageous in applications of electrochemical biosensors as hosting electrodes, offering not only fast charge transport and large sensing surface areas but also necessary wetting ability in aqueous analytes. In this study, inexpensive, highly hydrophilic (contact angle<5°), conducting (17 Ω/□) porous fluorine-doped tin oxide (PFTO) glass was created from commercial FTO glass with a novel, facile, one-step Sn^{4+}-based anodic treatment process, and used as a hosting electrode for electrochemical biosensors. We demonstrated its application advantages, as compared with commercial FTO glass (CFTO), by hydrogen peroxide sensing. The Pt-loaded PFTO outperformed Pt-loaded CFTO in sensitivity (25.6 vs 2.7 mA/M) and response time (1 vs 36 sec).

Avidin-biotin system sensor was fabricated using this PFTO. In order to immobilize the avidin and biotin on the FTO electrodes, (3-Aminopropyl)triethoxysilane (APS) was used for silane coupling agent. Four type electrodes, 1) biotin immobilized CFTO, 2) biotin+avidin immobilized CFTO, 3) biotin immobilized PFTO and 4) biotin+avidin immobilized PFTO respectively were prepared. 2 mmol/dm^3 $K_3[Fe(CN)_6]$ and $K_4[Fe(CN)_6]$ were used as electrochemical reactant, and 0.01 mol/dm^3 phosphate buffered saline (PBS) was used as electrolyte solution. An Ag/AgCl was used for reference electrode. Cyclic voltammograms of redox current of $[Fe(CN)_6]^{4-}$ and $[Fe(CN)_6]^{3-}$ couple were obtained using above four type FTO electrodes. The scan rate and scan range of cyclic voltammetry were 0.1V s^{-1} and -0.2 to +0.8V, respectively.

Fig. 1 shows the cyclic voltammograms of above four types of CFTO and PFTO electrodes. The peak currents corresponding $[Fe(CN)_6]^{4-}$ oxidation at near 0.4V and $[Fe(CN)_6]^{3-}$ reduction at near 0.1V were decreased with immobilizing biotin and avidin on the FTO electrodes. Especially, in the case of PFTO, the decreased amount of peak current was larger than the case of CFTO. This is because that PFTO has large electrode surface area, therefore the inhibition effect of electrode reaction by biotin and avidin molecules was clearly appeared.

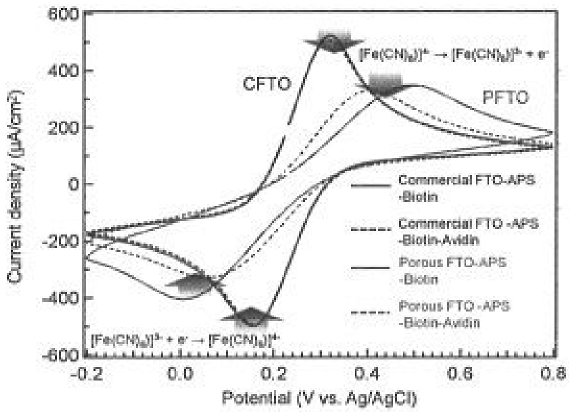


Fig. 1 Cyclic voltammograms of 1) biotin immobilized CFTO, 2) biotin and avidin immobilized CFTO, 3) biotin immobilized PFTO and 4) biotin and avidin immobilized PFTO. Peak current difference between biotin immobilized PFTO and biotin+avidin immobilized PFTO was larger than that of CFTO.