國立臺灣大學生醫電子與資訊學研究所

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國立臺灣大學生醫電子與資訊學研究所

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序言 Preface

在過去一年中，我們持續地推動生醫電資跨領域的研究與教學工作。其中在師資方面，特別合聘醫工所林發暄副教授、醫學院 孫維仁教授、腫瘤醫學研究所 吳文超助理教授加入本所陣容，以提昇本所在生物醫學工程及臨床醫學的研究能量，林發暄副教授的專長主要是神經影像、神經系統模擬，其研究成果非常傑出；孫維仁教授是疼痛醫學權威，麻醉的研究在國內居於領先地位；吳文超助理教授，專長是功能性磁振造影、磁振微灌流影像、醫學影像處理、生醫信號分析，其研究成果傑出。

為培育臺灣高階醫療器材的跨領域人才，本所與永齡生醫工程中心及進修推廣部共同開設醫療器材人才培訓課程，其內容強調跨領域合作、臨床需求導向、創新產品研發與新事業開創等核心精神，以期能協助建立台灣醫療器材產業之優勢，並促進產學合作成效。

此外我們也舉辦了第四屆台大生醫電資營，本活動的主要對象是國內各系所之大學生及研究生，本活動報名踴躍，人數遠遠超過預期，顯見經過了連續四屆的活動舉辦，本所推動的跨領域學習已獲得共鳴與成效。

各項所務工作的推展需要持續不斷、與時俱進。在此理念之下，我們落實執行跨學門課程改善計畫，將本所現有之基礎與核心課程，透過各項資源的支持，持續改善，提升教學成效。此外，以所上教師既有之優異研究成果為基礎，加強推動整合性研究，向校內外爭取研究經費，也是重點推動的工作。

為了持續提昇本所教學的品質，我們申請IEET工程及科技教育認證，並於今年三月通過認證，在師資、教學、研究、經費及設備上的表現均獲得非常好的評價。另外，本所也與醫學院、國立台南藝術大學、國立新竹教育大學共同舉辦2010音樂與健康促進國際研討會 (International Symposium of Music and Health Promotion 2010) 增加本所在醫學資訊研究的國際地位及知名度。

本所成立至今已四年，非常感謝大家的努力及團隊合作，我們希望所有同仁都能積極參與所務，共同合作執行計畫，對外更要加強學門間的合作關係，讓本所研究成果能夠成為亞洲的標竿。生醫電資領域的研究從沒有像今日這樣充滿史無前例的機會及挑戰，讓我們攜手並進，勇於承擔這個偉大的使命及責任。

賴飛羆

2010年9月

In the past year, promoting multidisciplinary research and teaching in the areas of Biomedical Electronics and Bioinformatics continued to be our main mission. Three new faculty members joined our institute, including Associate Professor Fa-Hsuan Lin, Professor Wei-Zen Sun, and Assistant Prof. Wen-Chau Wu. The related research interests of Prof. Lin include Magnetocephalography electroencephalography, Magnetic resonance imaging, Functional magnetic resonance imaging, Large-scale neuronal modeling. Prof. Sun is a leading expert in anesthesiology, his research interests include pain management, acupuncture. Prof. Wu's expertise includes Functional Magnetic Resonance Imaging and Perfusion Magnetic Resonance Imaging: Arterial Spin Labeling and Bolus Tracking. With the addition of these new faculty members, we are sure that the multidisciplinary research and teaching efforts can be better integrated and consolidated.

To educate multidisciplinary talents for the advanced medical device industry in Taiwan, YongLin Biomedical Engineering Center, School of Professional and Continuing Studies and our institute have been executing Talents Cultivation Program for Advanced Medical Devices. This program emphasizes on cross-disciplinary collaboration, clinical needs finding, innovative product developments, and entrepreneurship, hoping that it can assist in building the competitive edge of Taiwan's medical device industry, and promote the synergy of collaboration between academia and industry.

We also held the fourth annual NTU Biomedical Electronics and Bioinformatics Camp. The target recipients of this event are undergraduate and graduate students regardless of their academic backgrounds. As it turned out, the number of attendees far exceeded our expectation and this encourages us to continue to fully support this annual event in the future.

As part of the continuing efforts towards research and teaching excellence, we have also been executing a cross-disciplinary curriculum improvement project. Under this project, the six core courses in biomedical electronics and bioinformatics at both undergraduate and graduate levels will be re-examined and refined. On the other hand, by seeking research funding from both government and industry, we continued to promote integrated research projects that aim to address important biomedical problems.

In order to keep promoting our teaching quality, we applied for the accreditation of engineering and technology education programs from The Institute of Engineering Education Taiwan (IEET). In the last March, we received a pass approval. We have very good reputation and performance in the review categories of faculty, teaching, research, funding and equipments. We and our partners from Tainan National University of the Arts, National Taiwan University Hospital, National Hsinchu University of Education, College of Medicine, National Taiwan University together held an International Symposium of Music and Health Promotion 2010 at Taipei in last April. Through this effort, it helped to promote the international reputation of our distinguished researches in medical informatics.

As always, we are very thankful for all the supports that we have received. It has been four years since our institute was founded, and we had opportunities to recruit new staff members and expanded our office space. With these, we hope that all the faculty members can do joint projects and have more cooperation in the teaching and research activities. Together we are heading to be a leading biomedical institute in Asia. These have never been such an opportunity and challenge lie ahead of us. Let us march ahead hand in hand together to fulfill this great mission and responsibilities.

Feipei Lai

September, 2010.

目錄 Contents

壹 生醫電子與資訊學研究所簡介
Introduction of BEBI

國立臺灣大學生醫電子與資訊學研究所（簡稱生醫電資所）於2006年8月1日正式成立，本所的獨特性在於電機與資訊兩大領域的結合，進行生物醫學之前瞻研究及跨領域教學。換言之，生醫電資所的主要使命在於提升跨領域的研究及教學，以因應生物科技的快速發展，這些領域有：生醫電子、分子/細胞/組織影像、生醫訊號處理、生醫光電、感測器、微陣列分析、電腦輔助診斷、生物資訊學、系統生物學以及醫學資訊學等，為了在此專業領域中追求卓越，並謀求進一步的研究合作，整合來自不同領域的專業是相當必要的。

2006年8月，生醫電資所開始招收博士班，目前每年招收17名博士生加入生醫電資所的行列，碩士班也於2007年8月開始招生，每年有44名碩士新生加入（含2名在職專班）。本所有35位教師，來自不同領域的背景，包含了電機工程、資訊科學、生物、藥學、生醫工程、醫學以及生命科學。本所的課程設計也提供學生有足夠的跨領域訓練，以迎合生物科技此一領域的挑戰，目前，我們針對重要的生醫問題進行整合性的研究，同時也和生醫電子及生物資訊相關產業合作，及進行跨領域的訓練和教育，我們期待本所持續的成長茁壯，並對生物科技與健康照護領域做出貢獻。

The Graduate Institute of Biomedical Electronics and Bioinformatics (BEBI) at National Taiwan University was formally founded on August 1, 2006. In a way, it is a very unique institute among those in College of Electrical Engineering and Computer Science, NationalTaiwan University, in that the fields of expertise are diversified but our efforts remain extremely focused. The main mission of the institute is to promote multidisciplinary research and education in respond to the rapid advancement of biotechnology. In this regard, the following areas have been identified as our focus areas which we have been putting our major efforts in: biomedical electronics, molecular/cellular/tissue imaging, biomedical signal processing, biophotonics, sensors, microarrays, computer aideddiagnosis, bioinformatics, systems biology and medical informatics. To excel in these areas and to bring up research synergy, integrative efforts from different disciplines are necessary.

The BEBI institute started the doctoral program in August, 2006 and now we admit 17 new Ph.D. students every year. Our master program started in August, 2007 with 44 new students entering the institute annually. There are 35 faculty members, among those 8 are with primary appointments. As our main mission mandates, our faculty members come from different trainings, including electrical engineering, computer science, biology, pharmacy, biomedical engineering, medicine and life sciences. Our curriculum is also designed to provide students with sufficient cross-disciplinary training to meet the challenges in biotechnology. Currently resources are used to promote integrated research projects aiming at important biomedical problems, collaboration with local industry in biomedical electronics and bioinformatics, as well as multidisciplinary training and education. As a result, research teams have been formed and several integrated program projects are underway. New courses have also been developed and a core lab is also being established to provide students with hands-on training. We look forward to continuing growth and contributions to this exciting field of biotechnology.

貳 新進教師介紹 New Faculty

一、田維誠助理教授 Wei-Cheng Tian, Assistant Professor

田維誠助理教授出生於臺北市。1995年畢業於臺灣大學電機系，並分別於2000年及2003年於美國密西根大學 (The University of Michigan, Ann Arbor) 取得電機及計算機碩士及博士學位。田教授於2009年8月返台，目前擔任臺大電機系、電子所、暨生醫電資所合聘教師，並擔任微奈米分析技術與系統實驗室主持人。

田教授於取得博士學位後，於美國奇異全球研發中心 (GE Global Research) 擔任領導工程師暨計畫主持 (2003-2009)。他的研究專長包括「生醫微奈米系統」、「生物化學偵測及生命科學應用」，並成功於生醫領域，工業領域發展微奈米系統科技；更因為這些傑出的研究表現，除每年獲得奇異總公司及事業部研發經費，並獲得包括美國國防部微氣相層析儀 (Micro Gas Chromatography)，微奈米氣體分析系統 (Micro Multi-Gas Sensing System)，與高速微流體核酸定序樣本處理平台 (High Throughput Microfluidic Platform for DNA Sequencing) 等數項美國政府研究補助並擔任總計畫主持人。他自2006年起開始固定擔任美國真空協會 (America Vacuum Society) 微奈米機電 (MEMS/NEMS) 研究群常任及技術委員，並多次獲邀擔任知名國際會議主持人及演講。他已發表超過20篇微奈米系統期刊及國際會議論文，並擁有12項專利，此外另有20項微奈米機電及微奈米流體力學專利待核定中，他擔任專書“感測器薄膜及奈米結構：合成、物理及應用 (Functional Thin Films And Nanostructures For Sensors: Synthesis, Physics And Applications)”章節作者，並擔任專書“微流體力學在生物學之應用 (Microfluidics for Biological Applications)”主編。

他未來的研究方向希望能延續微奈米系統在生醫檢測、醫療技術及生物化學應用之研究。並將微奈米系統與系統晶片相結合，期能在More Than Moore領域做出貢獻。

Dr. Wei-Cheng Tian was born in Taipei, Taiwan. He received the B.S. degree in electrical engineering from the National Taiwan University, Taipei, Taiwan, in 1995, and the M.S. and Ph.D. degrees in electrical engineering and computer sciences from The University of Michigan, Ann Arbor, MI, USA, in 2000 and 2003, respectively. He is currently an Assistant Professor of the Graduate Institute of Electronics Engineering, Graduate Institute of Biomedical Electronics and Bioinformatics, and the Department of Electrical Engineering, National Taiwan University, Taipei, Taiwan.

During 2003-2009, Dr. Tian worked for GE Global Research at Niskayuna, NY, USA and served as a lead engineer/project leader/principal investigator. His research efforts include development of various Micro/Nano system and technologies for bio/chemical detection & life science applications. Dr. Tian has not only successfully led and delivered biomedical, industrial, and security programs in Micro/Nano system and technologies within GE, but he lead and won several government grants, including the DARPA program in Micro Gas Chromatography and the DTRA program in the area of integrated sample preparation for high throughput DNA sequencing. Dr. Tian has been serving as committees in various conferences or consortiums and he currently serves on the program committee of AVS conference-MEMS/NEMS topic group (2006-present). Dr. Tian published and presented 20+ peer-reviewed articles in the major MEMS/NEMS & micro/nanofluidics journals and conferences, owns 12 issued patents, with 20 patents pending. He is the author of one book chapter and edited a book "Microfluidics for Biological Applications".

貳 新進教師介紹 New Faculty

二、孫維仁教授 Wei-Zen Sun，Professor

學經歷

- 1984 Jun.　臺灣大學 醫學系 學士
- 2009 Jun.　臺灣大學 高階管理 碩士
- 2005~迄今　臺灣大學 醫學院麻醉科 教授
- 2008~迄今　臺灣大學 神經科學及認知中心 副主任
- 2009~迄今　臺灣大學 醫學院緊急醫療研究中心 主任
- 2009~迄今　臺灣大學 腦與心智科學研究所 合聘教授
- 2010~迄今　臺灣大學 生醫電子與資訊學研究所 合聘教授

研究領域

疼痛醫學與緊急醫療相關之基礎、臨床、儀器、資訊研究與產業化開發

Current position and relevant experience

- 1984 Jun.　M.D., College of Medicine, National Taiwan University
- 2009 Jun.　EMBA, National Taiwan University
- 2005~　Professor, Department of Anesthesiology, College of Medicine, National Taiwan University
- 2008~　Vice Chair, Neurobiology and Cognitive Science Center, College of Medicine, National Taiwan University
- 2009~　Chair, Center for Emergency Medical Service (CEMS), College of Medicine, National Taiwan University
- 2009~　Adjunct Professor, Brain and Mind Research Institute (BMRI), National Taiwan University
- 2010~　Adjunct Professor, Graduate Institute of Biomedical Electronics and Bioinformatics (BEBI), National Taiwan University

Research

Pain medicine and emergent medical service related researches on basic sciences, clinical service, bioinformatics and medical instrument integration design and development into market.

a frequently invited lecturer and has published more than 300 original articles and reviews in cardiovascular field.

三、林發暄副教授 Fa-Hsuan Lin, Associate Professor

林發暄於1994年與1996年分別獲得國立臺灣大學電機工程系學士與電機工程研究所碩士。在兩年兵役後於1998年進入美國麻省理工學院與哈佛大學合辦之衛生科技研究所(Harvard-MIT Division of Health Sciences and Technology) ，於2004年獲得兩校聯合頒發之電機工程與醫學工程博士學位。2004年至2006年間在美國麻省總醫院與哈佛大學醫學院之A. A. Martinos Center從事兩年博士後研究，並於2006年與2007年晉升為哈佛大學醫學院講師與助理教授。主要研究領域為利用非侵入式神經影像工具，包括核磁共振影像、腦電波圖和腦磁波圖，了解人腦感官與認知歷程。在生理層次上探討神經系統血液動力學、解剖形態、與神經活動之間的交互作用，並結合各種神經影像資料已達到高時間與空間解析度對人腦活動的了解。

林發暄於2006年獲頒國際磁振醫學學會(International Society of Magnetic Resonance in Medicine)年輕研究者獎(I. I. Rabi Young Investigator Award) ，同年並獲頒國際生物磁學雙年會BIOMAG 2006之Sam Williamson's Prize以表彰結合核磁共振影像以提升腦磁圖的空間解析度的共獻。

Dr. Fa-Hsuan Lin received his B.S and the M.S degree from the Department of Electrical Engineering in National Taiwan University in 1994 and 1996 respectively. After two-year military service, Dr. Lin received the Ph.D degree in electrical and medical engineering from Harvard-MIT Division of Health Sciences and Technology in spring 2004. From 2004 to 2006, Dr. Lin was a post-doctoral fellow at the A. A. Martinos Center for Biomedical Imaging in Massachusetts General Hospital. Dr. Lin was promoted to the Instructor and the Assistant Professor of Radiology in Harvard Medical School in 2006 and 2007 respectively. Dr. Lin's research focuses on non-invasive multimodal neural imaging to integrate structural and functional information from magnetic resonance imaging, electroencephalography (EEG), and magnetoencephalography (MEG) for high spatiotemporal resolution characterization of the human brain during tasks and cognition. He is also interested in elucidating the system level interaction among morphology, hemodynamics, and neuronal activity. In 2006, Dr. Fa-Hsuan was awarded the I. I. Rabi Young Investigator Award by the International Society of Magnetic Resonance in Medicine (ISMRM) in Seattle, WA, USA for the invention of ultra-fast magnetic resonance inverse imaging. He was also awarded the Sam Willamson's prize in BIOMAG 2006 in Vancouver, Canada for his contribution in integrating magnetic resonance imaging and MEG analysis for dynamic brain imaging and modeling with high spatiotemporal resolution.

貳 新進教師介紹 New Faculty

四、 吳文超助理教授 Chia-Hsien Cheng, Assistant Professor

吳文超於1995年畢業於臺灣大學電機工程系，隨即入中華民國陸軍服役，退伍前考取臺灣大學電機工程研究所醫工組碩士班，修業一年後，通過成績審查逕行攻讀博士班，並於2003年初取得學位，之後前往美國加州大學聖地牙哥分校進修，擔任功能性磁振造影中心博士後研究員。2006年初，轉往美國賓州大學醫學院擔任助理研究員，負責動脈氫質子標記技術之研發與臨床應用，2007年返國，擔任台灣大學醫學院助理教授迄今。

主要研究專長為：微灌流磁振影像、功能性磁振造影、醫學影像處理、生醫信號分析。開授課程：醫用磁振造影技術、磁共振頻譜與生理性影像、快速磁共振成像技術、腫瘤影像學、醫學影像研究方法、生醫信號系統與分析方法。

Wen-Chau Wu graduated from the Department of Electrical Engineering in National Taiwan University in 1995, and then enlisted in the ROC Army. After discharged, he entered the Graduate Institute of Electrical Engineering in National Taiwan University. Approved of direct pursuit of the Ph.D. degree after finishing the first year of M.S. program, Wen-Chau graduated in early 2003 and headed for the University of California at San Diego where he worked as a postdoctoral fellow in the Center for Functional Magnetic Resonance Imaging. In 2006, he relocated to the College of Medicine at University of Pennsylvania and had been intensively involved in the technical development and clinical applications of various arterial spin labeling techniques. In 2007, he returned to Taiwan and took the faculty position in the College of Medicine at National Taiwan University.

Dr. Wu's main academic expertise and research interests include perfusion magnetic resonance imaging, functional magnetic resonance imaging, medical image processing, and biomedical signal analysis. He has been providing the following courses: magnetic resonance imaging in medicine, magnetic resonance spectroscopy and physiological imaging, fast magnetic resonance imaging technique, oncologic imaging, medical image investigation, and biomedical signal systems and analysis.

investigator of two clinical trials in Taiwan: a nationwide randomized trial of breast cancer screening using ultrasound and mammography for women aged 40–49; and a multi-center trial of tailored neoadjuvant chemotherapy for breast cancer.

參 研究領域 Research Fields

一、生醫電子組 Biomedical Electronics Group

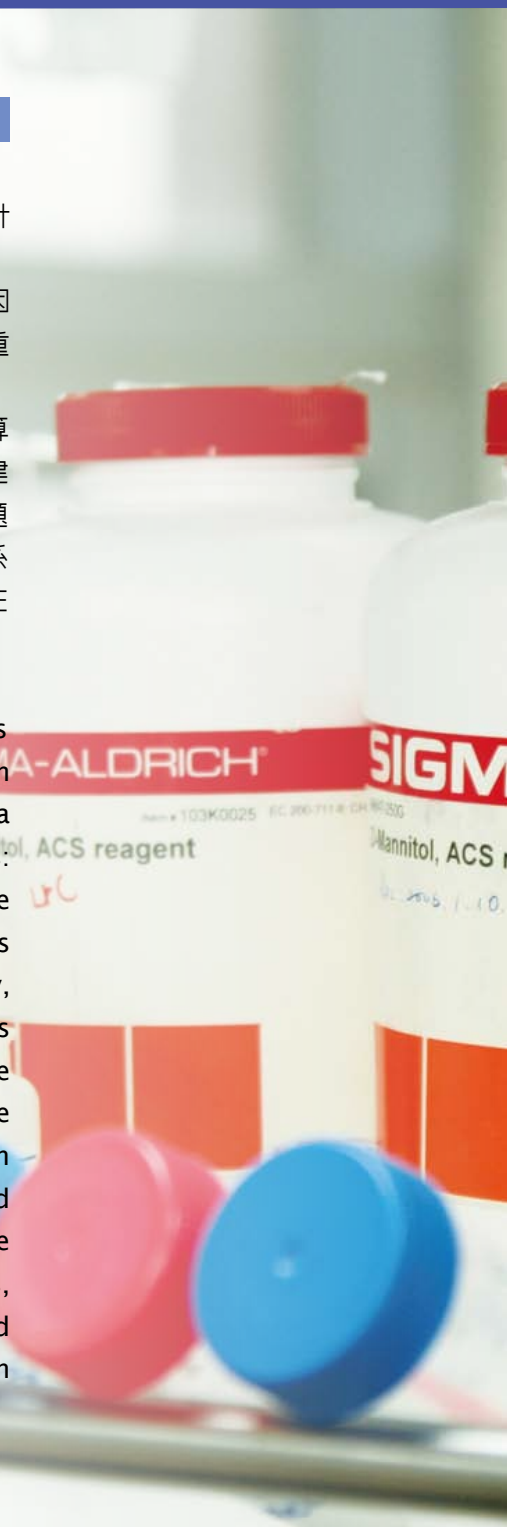
本組研究主題涵蓋醫學影像、醫療儀器與生醫信號處理、生物晶片與生醫微感測器、生醫光電等數個領域。在醫學影像方面，主要重點是針對核磁共振與超音波造影技術，提升影像的品質、速度與功能性，並發展分子影像技術，應用於臨床醫學診斷、治療以及神經認知科學等方面。在醫療儀器與生醫信號處理方面，重點在開發或利用現有的醫療儀器，擷取各種生理訊號，並且以數位信號處理技術，將有助於疾病的診斷或生理監測的資訊提供給醫療人員。生物晶片的研究重點包括DNA微陣列晶片及之製程、感測技術與資料分析方法，以及以光電蝕刻技術控制生物分子、細胞及微組織之排列，並應用上述晶片進行生物醫學上的研究。在生醫微感測器方面，主要是發展表面電漿共振光學檢測技術與利用標準半導體製程方式，進行生物分子的感測，並進一步將檢測元件微小化。在生醫光電領域，發展高解析度光學顯微影像以及各種光譜技術，提供生物分子、細胞與組織的分析、成像與操控工具，進而輔助疾病的診斷與生醫相關的研究。

Faculty members in this group have diverse research interests including “medical imaging”, “medical instrumentation and biomedical signal processing”, “biochips and biomedical sensors”, and “biomedical optics”. In the area of “medical imaging”, research efforts are focused on magnetic resonance imaging (MRI) and ultrasound imaging techniques. The goals are to improve the quality, acquisition speed and functionality of imaging, as well as to apply these techniques for diagnosis and treatment of disease. In the area of “medical instrumentation and biomedical signal processing”, digital signal processing techniques are used to extract information that is useful for diagnosis or monitoring of physiological status. Research efforts in the area of “biochips and biomedical sensors” are focused on improving the manufacture and detection of DNA and protein microarrays, arranging biomolecules and culture tissue using micro-patterning techniques, development of new data analysis methods for DNA microarrays, and development of miniature biosensors based on surface plasmon resonance (SPR) and nanowire biomolecular sensing devices based on standard CMOS fabrication. The emphasis of research in “biomedical optics” is to use optical microscopy and spectroscopy techniques to detect, image, analyze, and manipulate biological molecules, cells, and tissues. The ultimate goal is to provide information relevant to diagnosis and useful tools for the general biomedical research community.

二、生醫資訊組 Bioinformatics Group

本組研究主題為「生醫資料分析與探勘」、「計算系統生物學」、「計算藥物學及計算化學」以及「醫學資訊系統」。在生醫資料分析與探勘方面，研究重點包括生物晶片（微陣列）資料分析、DNA與蛋白質序列分析、基因及蛋白質結構與功能分析、生醫資料探勘等。在計算系統生物學方面，研究重點則是針對生物醫學及生命科學問題，建構數學分析及模擬計算的系統模型，以作為分析及模擬尖端生物醫學及生命科學現象的基礎。在計算藥物學及計算化學部分，將針對藥物及疫苗開發所涉及的量子化學計算及化學動力學計算建構新的計算模型以及設計更有效率的演算法。在醫學資訊系統方面，研究主題涵蓋層面極廣，舉凡醫學資訊應用所涉及的網路系統、多媒體系統、資料庫系統以及平行計算、分散式計算、即時計算之軟硬體設計與演算法分析均包含在內。

We dedicate our resources on the cutting-edge topics such as “biomedical data analysis and mining”, “computational system biology”, “computational pharmacology and chemistry”. In the area of biomedical data analysis and mining, our major research includes: biochip (Micro-array) data analysis, DNA and protein sequence analysis, gene and protein structure and function analysis, as well as biomedical data mining. In the area of computational system biology, we focused on advanced mathematical system models or simulations we developed to describe behaviors found in biomedicine and life science. In the area of computational pharmacology and chemistry, we are designing new computational models and efficient algorithms in quantum chemistry and molecular dynamics simulation for drugs and vaccine development. In medical informatics, we cover such as a wide range of topics in building the infrastructure for medical informatics, networking, multimedia, database, parallel processing, distributed computing, real-time computing, and algorithms as well as decision making and policy in current national health insurance database.



肆 學術活動 Academic Activities

一、大學跨學門科學人才培育銜接計畫 The Interdisciplinary Training Program for Talented College Students in Science

計劃簡介 Project Description:

本計畫目標為電機資訊二大學群之整合，為工程背景同學提供跨領域課程，為日後進入生醫資訊、生物科技相關研究之銜接準備。透過本計畫之訓練，學生們於未來可以從事以下相關之前瞻研究：生醫訊號處理、生醫光電、微陣列分析、電腦輔助診斷、生物資訊學、系統生物學以及醫學資訊學等。為達此目標，並為前二年所開設過的跨領域課程作延伸，本子計畫開設以下進階課程：

- 醫療資訊系統
- 微奈米生物科技專題

本計畫之預期成效包括加強課程內容、精進課程教材，結合生物醫學、生物科技、醫學資訊、生醫資訊四大主軸，緊密銜接跨領域知識。

此外，本計劃亦將於暑假期間舉行生醫電資營之營隊活動，作為本計畫之輔助，積極發揮不同領域之專業，透過此學術交流風氣，養成未來跨領域人才必備之團隊合作能力，引領同學進入跨領域之學習。

The sub-project is a collaboration of teachers in College of Electrical Engineering and Computer Science of National Taiwan University. Through integration, consolidation and participation, we will provide a series of interdisciplinary courses to the engineering students (especially with electrical engineering and computer science backgrounds), so that they will be ready to enter research fields such as: computer aided diagnosis, bioinformatics, systems biology and medical informatics. To continue our previous work during 2008-2009 and achieve the main goal, we offer two advanced courses:

- Medical Information System
- Special Topics In Micro And Nano Biotechnology

In addition, we will also organize a summer camp for students to provide them opportunities of learning in an interdisciplinary circumstance. We expect that students can interact with teachers and peers freely through the academic activity.

二、博士班招生說明會
BEBI introduction to prospective students: College of Medicine (2010/3/17)

三、期末聚會活動 Year-end Gathering

Bowling Game

Farewell Party

Year-end Party

肆 學術活動 Academic Activities

四、所務發展諮詢會議 The advisory commitee of BEBI (2010/4/23)

五、演講 Lectures

1. 98.09.14
   陳維超 博士，Nokia Research Center
   Senior Research Scientist
   Topic: Mobile Visual Computing
   Research and Applications

2. 98.09.21
   熊田雅之 客座教授，中央研究院 物理研究所
   Topic: Status of the advanced particle therapy
   of deep-seated malignant tumor

3. 98.09.28
范龍生 教授，清華大學 奈米工程與微系統研究所
Topic: From Component Technology to Microsystems –Research Activities of CMBL for Biomedical Applications

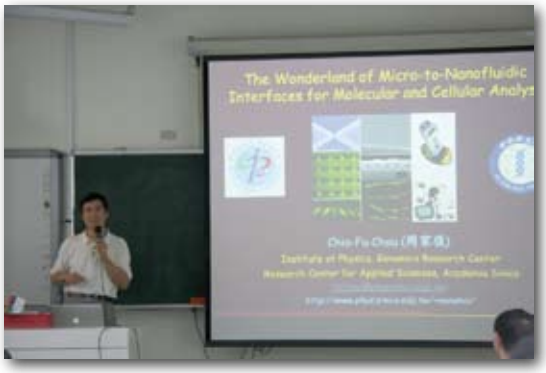
4. 98.10.05
廖英君 小姐，歌劇演唱家
Topic: 歌劇之美

5. 98.10.12
林發暄 教授，臺灣大學 醫學工程學研究所
Topic: Spatiotemporal imaging of human brain function using combined magnetic resonance imaging (MRI) and magnetoencephalography(MEG)

6. 98.10.19
Mr. Barrett Comiskey, Co-Founder & Executive Advisor at E Ink
Topic: The invention and mmercialization of electronic ink and thoughts on innovation in Taiwan

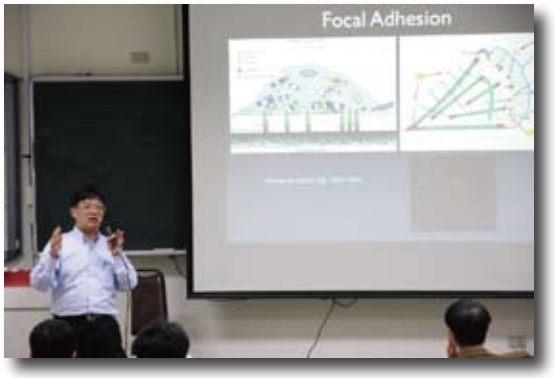
7. 98.10.26
Dr. Jung-chih Chiao, Professor of Electrical Engineering, UT-Arlington
Topic: Implantable Wireless Medical Devices and Systems

8. 98.10.26
周家復 教授，中央研究院 物理研究所
Topic: The Wonderland of Micro-Nanofluidic Interfaces for Molecular and Cellular Analysis



9. 98.11.02
張韻詩 教授，中央研究院 資訊科學研究所
Topic: Information Technology and LOHAS (Lifestyles for Health and Sustainability)

10. 98.11.09
邱大剛 董事長，美商現觀科技公司
Topic: Innovation, Entrepreneurship, and MIT



11. 98.11.16
陳培菱 教授，中央研究院 應用科學研究中心
Topic: Investigation of Focal Adhesion Using Polymeric Nanopillars and Super-resolution Microscopy

12. 98.11.23
劉承愚 律師，益思科技法律事務所
Topic: 醫工產業的創業與投資

13. 98.11.30
王家俊 執行長，IAdea
Topic: 台大人的產業機會與責任：以美國高中教育為背景之觀點

14. 98.12.07
田維誠 教授，臺灣大學 生醫電資所
Topic：Micro / Nano Analytical Technologies & Systems for Biomedical & Life Science Applications

15. 98.12.14
陳鈴津 副主任，中央研究院 基因體研究中心
Topic：Glycan Targeted Cancer Immunotherapy: an Example of Translational Medicine

16. 98.12.21
何弘能 副院長，臺大醫院
Topic：幹細胞研究的新境界

17. 98.12.28
陳怡茹 小姐，NSO 小提琴演奏家
Topic：弦外之音

18. 98.01.04
游正博 教授，中央研究院 基因體研究中心
Topic：Searching for novel stem cell markers and differentiation regulators using emerging new technologies

19. 99.02.22
陳培哲 教授，臺灣大學 臨床醫學研究所
Topic：Translational Research--- Liver Disease as an example

20. 99.03.01
孔祥重 教授，哈佛大學
Topic：Cloud Computing: An Exploration and Discussion

21. 99.03.08
黃杉榕 董事長，倚天資訊股份有限公司
Topic：倚天創業經驗分享

22. 99.03.15
路寒袖 老師，彰化師範大學 台灣文學研究所 駐校作家
Topic：愛戀去流浪—談旅行的攝影與詩寫

23. 99.03.22
林俊彬 院長，臺大牙醫專業學院
Topic：口腔醫療器械及生醫材料研發之現況及與未來

24. 99.03.29
黃森煌 董事長，原相科技股份有限公司
Topic：CMOS Image Sensor在人機介面上的應用-原相科技簡介

25. 99.04.12
劉惠玲 顧問，台灣自殺防治學會 自殺防治中心
Topic：珍愛生命守門人

26. 99.04.19
李文雄 主任，中央研究院 生物多樣性研究中心
Topic：Applications of Modern Sequencing Technology to Genetics and Evolution

27. 99.04.26
陳贊鴻 技術長，研華科技股份有限公司
Topic：啓動智能生活

28. 99.05.03
游本中 所長，中央研究院 資訊科學研究所
Topic：Challenges and Opportunities in the Era of Multi-cores

29. 99.05.10
陳嫦芬 理事，中華公司治理協會 常務理事
Topic：做個有價值的上班族

30. 99.05.17
林芳郁 院長，台北榮民總醫院
Topic：問蒼茫大地 誰主浮沈？

31. 99.05.24
楊志忠 教授，臺灣大學 電機工程學系
Topic：光學同調斷層掃瞄之原理與生醫應用

32. 99.05.31
林子珊 教授，屏東教育大學 音樂學系
Topic：琴感再現—小提琴奏鳴曲的百年旅程

33. 99.06.07
楊文光 教授，中國醫藥大學 臨床醫學研究所
Topic：Cell-/gene-based therapeutic approaches to lethal human cancer: from laboratory investigations to clinical trials

34. 99.06.14
賴麗純 館長，天使學園網路股份有限公司（天使美術館）
Topic：創意與生活

六、國立臺灣大學電機資訊學院九十八學年度畢業典禮
2010 Commencement of College of Electrical Engineering and Computer Science, NTU

肆 學術活動 Academic Activities

七、2010/07/05~07/07生醫電子資訊營 / Biomedical Electronics and Bioinformatics Camp

2010臺大生醫電資營於7/5(一)~7/7(三)假臺大博理館舉行，活動透過規畫設計的課程及課後的創意競賽活動，介紹如何運用尖端電子資訊技術，協助生命科學基礎研究與改進疾病的診斷與治療品質。今年主題訂為「個人化健康照護」，透過主題課程的設計，使學員對此跨領域學門有一深入的認識，並培養其興趣，作為進入相關領域之準備。

本次活動共69人報名參加，大學生及研究生佔八成以上。活動結束後請學員們填寫滿意度問卷調查，認為活動內容充實、課程多元，對活動規劃的滿意度高達90%，再次參加意願亦高達95%，整體而言頗受好評，給予本所辦理跨領域交流活動相當大的鼓勵。明年亦將本持培養生物科技與醫療電子資訊之學術與產業人才，繼續舉辦相關研習課程。

2010 Biomedical Electronics and Bioinformatics Summer Camp, known as BEBI summer camp, was held on 7/5-7/7 at Barry building in NTU. The main theme of this year was “personalized healthcare”, and based on the course designs and innovation contest in the camp, the interdisciplinary knowledge were covered and introduced to the participants. Utilizing these introductory curriculums, the interests for developing biotechnology and bioinformatics can be stimulated and identified. We had a total of 69 participants with diverse backgrounds and a 90% satisfaction rate was achieved.

National Taiwan University

伍 國際交流 International Exchanges

一、2010「音樂演奏健康促進」國際研討會/ 2010 International Symposium of Music and Health Promotion

本研討會以「促進音樂與醫學的跨領域研究」為宗旨，除了進行音樂醫學、音樂生心理與相關社會議題之研討外，並將討論音樂療育如何應用於健康促進、音樂多媒體與遠距健康照護議題。

本次研討會主題講者Dr. Professor Eckart Altenmüller，為德國「漢諾威音樂與戲劇大學」附設「音樂生理學暨音樂家醫學研究中心」主任，其為神經生物學教授及醫師，同時具備長笛演奏背景。

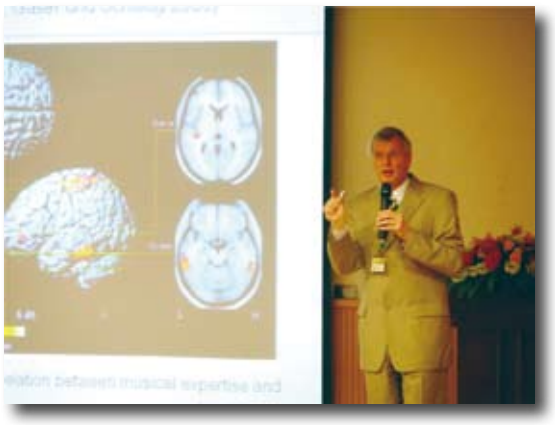
本會同步徵求國內外學者專家，就「音樂與健康促進」議題進行學理性的論文發表研討，及舉辦亞歷山大技巧工作坊之實務演練，研討會理論與實務的結合，提供給關心音樂醫學、音樂療育及遠距健康科技議題之相關人士，一個學術交流研討的重要機會。

In this International Symposium of Music and Health Promotion (ISMHP2010), the goal is to promote the collaboration and researches between music and medicine. Besides the main themes of music medicine, music psychophysiology and related social issues, panel discussions also cover implementation of music therapy in health promotion, music multimedia and e-health technology.

The distinguished keynote speaker, Prof. Eckart Altenmüller, is the director of Institute of Music Physiology and Musicians' Medicine at university of Hannover for music and theater performance. Prof. Altenmüller is a renowned neurologist and a professional flutist.

ISHMP 2010 is expected to provide an opportunity to researchers, specialists and scientists to interact and get a comprehensive, fully integrated picture of musicians' medicine, music therapy and e-health technology. The hands-on workshop incorporated to forums and paper presentations provide an integration of theory and practice on the main theme "Music and health promotion". We kindly invite domestic and international participants to submit papers to present research work and experience.

National Taiwan University



伍 國際交流 International Exchanges

二、外賓參訪 International Visits

1. 2010/01/15 - 02/15
Prof. Erdenebaatar. A and Prof. Dashdorj. J, Mongolian University of Science and Technology

2. 2010/03/22 Professor Chung-Kang Peng, Harvard Medical School

3. 2010/04/09　Professor Eckart Altenmüller, Hanover University of Music and Drama, Germany

4. 2010/04/12　Professor Tzyh-Chang Hwang, University of Missouri

5. 2010/06/07　Professor Nian-Feng Tzeng, University of Louisiana at Lafayette

陸 實驗室及教師
Laboratories and Faculty

生醫電子組實驗室 Laboratory of Biomedical Electronic Group

實驗室名稱 Name	主持教授 Advising professor	地點 Room
超大型積體電路系統晶片電腦輔助設計實驗室 SOC VLSI-EDA Lab.	陳中平 Chung-Ping Chen	博理館405 Barry Lam Hall, Room 405
醫學影像實驗室/磁共振影像頻譜實驗室 Medical Imaging Lab./Magnetic Resonance Imaging Lab.	陳志宏 Jyh-Horng Chen	明達館706 MingDa Building, Room 706
智慧型與精密運動控制實驗室 IPMC Lab.	陳永耀 Yung-Yaw Chen	明達館604 MingDa Building, Room 604
放射物理生物實驗室 Radiation Physics and Biology Lab.	成佳憲 Chia-Hsien Cheng	臺大醫院 NTUH
生醫系統與電磁實驗室 Biomedical System and Electromagnetism Lab.	張璞曾 Fok-Ching Chong	明達館702 MingDa Building, Room 702
生物資訊暨生物統計核心實驗室 Bioinformatics and Biostatistics Lab.	莊曜宇 Eric Y. Chuang	明達館701 MingDa Building, Room 701
醫用磁振造影實驗室 Magnetic Resonance in Medicine Lab.	鍾孝文 Hsiao-Wen Chung	明達館704 MingDa Building, Room 704
紅外線暨生醫奈米元件實驗室 Infrared and Bio-Chemical Nano-Device Lab.	管傑雄 Chieh-Hsiung Kuan	電機二館426 EE 2, Room 426
細胞行為實驗室 Cell Behavior Lab.	郭柏齡 Po-Ling Kuo	明達館707 MingDa Building, Room 707
生物醫學信號實驗室 Biomedical Signal Lab.	郭德盛 Te-Son Kuo	明達館 705 MingDa Building, Room 705
統計信號處理實驗室 Statistical Signal Processing Lab.	李枝宏 Ju-Hong Lee	電機二館553 EE 2, Room 553
薄膜電晶體實驗室 TFT Lab.	李嗣涔 Si-Chen Lee	電機二館451 EE 2, Room 451

超音波影像實驗室 Ultrasonic Imaging Lab.	李百祺 Pai-Chi Li	明達館731 MingDa Building, Room 731
無線生醫晶片系統實驗室 Wireless Bio-Electronics-System Lab.	林致廷 Chih-Ting Lin	電機二館450 EE 2, Room 450
醫用微感測器暨系統實驗室 Medical Micro Sensor and System Lab.	林啓萬 Chii-Wann Lin	展書樓605/608 Jan Su Hall, Room 605/608
人腦實驗室 Brain Imaging and Modeling Lab.	林發暄 Fa-Hsuan Lin	展書樓703 Jan Su Hall, Room 703
整合神經生理學實驗室 Integrative Neurophysiology Lab.	林則彬 Tzer-Bin Lin	中國醫藥大學附設醫院I棟6樓 China Medical University Hospital
生醫光譜與影像實驗室 Biomedical Optical Spectroscopy and Imaging Lab.	宋孔彬 Kung- Bin Sung	明達館703 MingDa Building, Room 703
微奈米分析技術及系統實驗室 Micro/Nano Analytical Technologies & Systems Lab.	田維誠 Wei-Cheng Tian	明達館509 MingDa Building, Room 509
數位信號處理實驗室 Digital Signal Processing Lab.	曹建和 Jen-Ho Tsao	電機二館552 EE 2, Room 552
心臟輔助器實驗室 Ventricular Assist Device Lab.	王水深 Shoei-Shen Wang	臺大醫院 NTUH
非侵入式生理量測實驗室 Non-invasive physiological measurements Lab.	王唯工 Wei-Kung Wang	明達館 705 MingDa Building, Room 705
臨床磁振影像實驗室 Clinical Magnetic Resonance Imaging Lab.	吳文超 Wen-Chau Wu	明達館 704 MingDa Building, Room 704
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Laboratories and Faculty

生醫資訊組實驗室 Laboratory of Bioinformatics Group

實驗室名稱 Name	主持教授 Advising professor	地點 Room
醫學影像處理實驗室 Medical Image Processing Lab.	張瑞峰 Ruey-Feng Chang	資訊館402 CSIE Building, Room 402
演算法與計算生物學實驗室 Algorithms and Computational Biology Lab.	趙坤茂 Kun-Mao Chao	資訊館432 CSIE Building, Room 432
數位相機與電腦視覺實驗室 Digital camera and Computer Vision Lab.	傅楸善 Chiou-Shann Fuh	資訊館328 CSIE Building, Room 328
	黃俊升 Chiun-Sheng Huang	臺大醫院 NTUH
系統生物學研究室 Systems Biology Lab.	阮雪芬 Hsueh-Fen Juan	生命科學館1105 Life Science Building, Room 1105
生物資訊實驗室 Bioinformatics Lab.	高成炎 Cheng-Yan Kao	資訊館401 CSIE Building, Room 401
醫學資訊實驗室 Medical Informatics Lab.	賴飛羆 Fei-pei Lai	資訊館346 CSIE Building, Room 346
演算法實驗室 Algorithmic Research Lab.	呂學一 Hsueh-I Lu	資訊館406 CSIE Building, Room 406
分子生醫資訊實驗室 Knowledge Engineering and Bioinformatics Lab.	歐陽彥正 Yen-Jen Oyang	資訊館410 CSIE Building, Room 431
臨床-生物醫學工程-產業融合實驗室 Merger Laboratory for Clinical Sciences, Biomedical Engineering and Industry	孫維仁 We-Zen Sun	臺大醫院 NTUH
計算分子之設計與偵測實驗室 Computational Molecular Design & Detection Lab.	曾宇鳳 Y. Jane Tseng	資訊館404 CSIE Building, Room 404

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醫學影像處理實驗室
Medical Image Processing Lab.

乳癌是近年來已全球化的婦女死亡的主要原因，如果可以及早查出腫瘤的存在，乳癌治癒的機會將大增不少。在臨床上，電腦輔助診斷系統(CAD)可以幫助醫師分辨惡性和良性的乳房腫瘤，如果電腦輔助診斷系統可以提供更高的準確率，便可以大幅減少乳房切片檢查的需求。從1998年開始，我們致力於發展超音波電腦輔助診斷系統，也有了不錯的研究經驗與成果，成果計有2D/3D超音波診斷系統、彩色超音波診斷系統、超音波篩檢診斷系統、PC-based超音波診斷系統。合作研究單位有美國芝加哥大學，美國U-Systems超音波公司，法國INT/ARTEMIS雙聯博士計畫暨中法幽蘭計畫，並與韓國漢城大學醫院、日本獨協大學醫院、臺大醫院、台北榮總、中國醫大醫院、彰化基督教醫院醫師均有密切合作研究。

In recent years, the breast cancer is globally the main causes of death for women. If a cancer can be found out earlier, the curability of the breast cancer will increase greatly. Clinically, the computer-aided diagnosis (CAD) systems can help physicians to differentiate the benign and malignant tumors. If the computer-aided diagnosis systems have higher accuracy, the demand of the breast biopsy can be reduced. Since 1998, we are devoted to develop the ultrasound (US) CAD systems including 2D/3D US CAD, color Doppler US CAD, whole breast US screening system, color elastography CAD, and PC-based US CAD. The laboratory also collaborates with The University of Chicago and U-systems Inc., USA, and has a double Ph.D. program and the Taiwanese-French orchid project with INT/ARTMIS, Paris, France. We closely collaborate with physicians from Seoul National University Hospital, Dokkyo Medical University Hospital, National Taiwan University Hospital, Taipei Veterans General Hospital, China Medical University Hospital, and Changhua Christian Hospital.

主要研究領域 Major Research Areas

醫學影像電腦輔助診斷、影像視訊處理、多媒體系統及通訊

Medical Image Computer Aided Diagnosis、Image Processing、Multimedia Systems and Communication

研究計畫 Research Projects

1. 利用多重掃瞄及影像套合的大區域乳房超音波系統
   Large Area Breast Ultrasound Using Multi-Pass Scanning and Image Registration
2. 3-D 彩色乳房超音波之電腦輔助診斷
   Computer-aided Diagnosis for 3-D Doppler Breast Ultrasound

計畫名稱：3-D 彩色乳房超音波之電腦輔助診斷
補助單位：行政院國家科學委員會
計畫期間：2007/08/01-2010/07/31

血管新生作用在惡性腫瘤之生長、惡化與轉移過程中扮演著重要的角色。在最近幾年，和乳癌相關的血管新生作用已經非常廣泛地被研究並且對於血管新生行為模式、所影響的腫瘤發展結果和病人的預先診斷，乳癌所引發的血管新生被當成是一種去了解這些過程的標準範例。以往的相關研究，只是利用血管點數的多寡來診斷腫瘤。然而，對於乳癌而言，血管型態上和曲度上的特徵應能再提供更多的診斷資訊並且輔助醫生做更精密的診斷。本子計畫將研究一個全自動輔助診斷系統，這個系統是針對乳房腫瘤利用3-D Power 都卜勒超音波成像技術去取得血管超音波影像，最後再量化血管的型態及曲度特徵。為了從血管影像中取出型態和曲度特徵必須有一3-D的細化(Thinning)演算法來取得血管的骨幹(Skeleton)，然後再必須有一方法利用骨幹資訊建立出一個血管樹(Vessel tree)，如此即可由這些血管樹中取出型態上的特徵。而這些特徵將可利用來進行腫瘤診斷。3-D 彩色都卜勒超音波的資料可被解碼成兩種連續的影像，分別是紀錄腫瘤結構的灰階影像與保存血管資訊的血管影像。上述利用血管資訊的研究並沒有採用到B-mode灰階影像，因此如果此資訊可加入灰階診斷，因可再提高診斷及治療的準確度，例如可再考慮血管相對於腫瘤的位置關係，亦即新血管是否位於腫瘤內。為了量化此一特徵，腫瘤區域首先必須切割出來，以利分析血管與腫瘤位置之關係。我們將採用模糊理論演算法來切割腫瘤區域。完成腫瘤區域切割後，即可將原提出的血管特徵再區分成腫瘤內、外二種。

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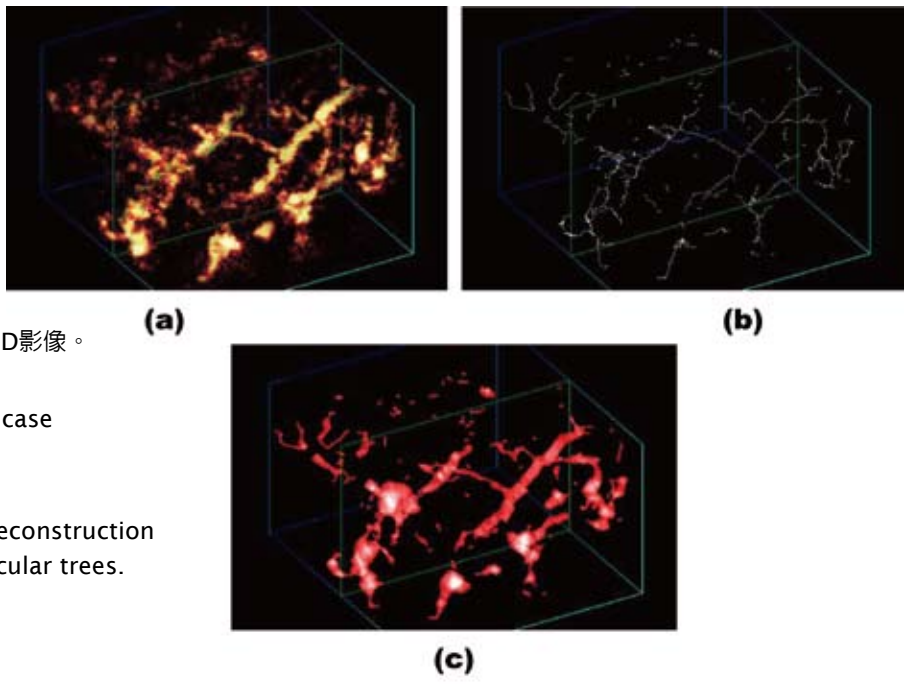
Project title: Computer-aided Diagnosis for 3-D Doppler Breast Ultrasound
Supported by: National Science Council
Project period: 2007/08/01-2010/07/31

Tumor angiogenesis is the process that correlates to tumor growth, invasion, and metastasis. Breast cancer angiogenesis has been the most widely studied and now serves as a paradigm for understanding the biology of angiogenesis and its effects on tumor outcome and the patient's prognosis. Most studies on characterization of tumor angiogenesis focus on pixel/voxel counts. However, in breast cancer, vascular morphology and tortuosity can provide more information that helps the physician diagnose more accurately. This project presents a computer-aided diagnostic (CAD) that can quantify vascular morphology and tortuosity using 3-D power Doppler ultrasound (US) on breast tumors. The method to extract morphological and tortuous information from angiography and to relate them to tumor diagnosis results is proposed. At first, a 3-D thinning algorithm helps narrow down the vessels into their skeletons and then the vascular trees could be produced from these skeletons. These measurements of vascular morphology will be used for the tumor diagnosis. A 3-D power Doppler ultrasound dataset could be decoded into two kinds of sequential images, grey and vessel images. The above study based on the vessel images does not use the information of grey images. Hence, if the grey images could be used in the system, the diagnosis accuracy might be improved. For example, the position relation of vessels to the tumor could be a good feature. For obtaining the feature, the grey images are applied by a fuzzy unit, a defuzzier unit, and connected component labeling techniques to determine the tumor region. Then, the vessels could be classified into inside or outside the tumor.



3-D彩色都卜勒超音波。
(a) 為原彩色超音波資料,
(b) 細線化結果,
(c) 利用血管樹重建出的3-D影像。

3-D Doppler ultrasound case
(a) Original data.
(b) The thinning result.
(c) Three-dimensional reconstruction via the obtained vascular trees.

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演算法與計算生物學實驗室
Algorithms and Computational Biology Lab.

演算法與計算生物學實驗室創立於2002年8月。我們對於組合演算法的設計與分析很感興趣，尤其是關於解決計算分子生物學領域及網路應用上所產生的計算問題。在過去幾年裡，我們的研究主軸是關於序列及樹狀結構上的有效演算法設計與分析。在序列方面，包括生物序列分析，如：單套體預測問題、標記SNP、複製數目變異問題、各種不同評分準則等，以及數列分析，如：最大總和區段問題、最大平均區段問題、不同條件的最佳化問題等。在樹狀結構方面，包括樹的建構問題，如：演化樹建構、最小繞線代價伸張樹問題等，以及樹的探索問題，如：樹邊分割問題、樹的查詢問題、樹邊置換問題等。這是非常有樂趣及成果的研究歷程，我們最終的目標是開發更多關於序列及樹狀結構的基本性質，並充分運用它們來設計解決這方面計算難題的實用演算法。

The Algorithms and Computational Biology Laboratory was established in August, 2002. We are interested in all aspects of the design and analysis of combinatorial algorithms. In particular, we solve algorithmic problems arising in computational molecular biology and networking. For the past few years, we have been mostly focused on the design and analysis of efficient algorithms for analyzing sequences and trees. For sequences, we mainly work on problems related to biological sequence analysis (haplotype vs. genotype; tag SNPs; copy number variations; variant scoring schemes), and numerical sequence analysis (maximum-sum segments; maximum-average segments; other maximization criteria). For trees, we mainly work on some tree construction problems (evolutionary trees; minimum routing cost spanning trees), and tree exploring problems (tree edge partition; tree querying; swap edges). This has been a joyful and fruitful journey to us. Our ultimate goal is to reveal more properties related to sequences and trees, and fully utilize them to design practical algorithms for solving hard problems in that line of investigation.

主要研究領域 Major Research Areas

計算生物學及生物資訊學、演算法、套裝軟體
Computational Biology and Bioinformatics, Algorithms, Software Tools

研究計畫 Research Projects

1. 單一核苷酸多型性資訊運用的演算法設計
   Efficient Algorithms for Utilizing SNP information
2. 線上拓撲排序問題之快速演算法
   Fast Algorithms for Online Topological Ordering
3. 多重基因複製問題的快速演算法
   Faster Algorithms for the Multiple Gene Duplication Problems

計畫名稱：多重基因複製問題的快速演算法
補助單位：行政院國家科學委員會
計畫期間：2009/08/01-2012/07/31

在演化分子生物學裡，種系發展分析可協助理解不同生物間的演化關係。一棵種族樹可以用來代表一個種族集合之親緣關係；一棵基因樹則描繪出一群種族就某個基因家族所建立之親緣關係。由於複雜的演化過程，如：基因複製、水平基因轉移、染色體重組等，基因樹和種族樹之間可能產生不一致的地方，演化生物學家必須能進一步解釋這些不一致的地方。

前人以對應基因樹與種族樹的調和模式，來解釋這些不一致產生的原因。這方面有個重要的問題稱為「多重基因複製問題」，它將基因複製事件，從基因樹對應到種族樹。本計劃將探討多重基因複製問題上的兩個主題：一個主題稱為「事件叢集問題」，該問題要在種族樹上找出最少的地方，來放置所有應該產生的複製事件；另一個主題稱為「最少事件問題」，該問題要在種族樹上決定發生複製事件的樹點，使得複製事件的總數為最少。

我們將設計解決「事件叢集問題」的更快速解法，這問題已被證明是「樹區間覆蓋問題」的特例，透過調整整個樹的拜訪順序，我們希望能設計出這兩個問題的最佳解法。我們也將設計解決「最少事件問題」的更快速解法，主要是要加速下面四個步驟：(1) 計算最低共同祖先對應關係；(2) 找出所有帶頭的樹點；(3) 檢查帶頭樹點是否自由；(4) 修訂對應關係。我們進一步檢驗基因叢集裡的資料，從而建立一套更合適的模組，希望能有統一的理論可處理各式各樣的演化事件，如此得到的重建過程將更貼近實務需求。

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Project title: Faster Algorithms for the Multiple Gene Duplication Problemsn
Supported by: National Science Council
Project period: 2009/08/01-2012/07/31

In the evolutionary molecular biology, phylogenetic analyses help to realize the evolutionary relationship among various organisms. A species tree represents the phylogeny of a set of species, and a gene tree depicts the phylogeny among a gene family for a set of species. Due to complicated evolutionary processes such as gene duplication, horizontal gene transfer, recombination, etc., gene trees and species trees may be inconsistent. It is important for evolutionary biologists to explain the inconsistency between gene trees and species trees.

The reconciled tree provides the mapping between genes trees and a species tree that explains the inconsistency in the evolutionary history. The Multiple Gene Duplication (MGD) problem is to map gene duplications from the gene trees into the species tree and to cluster such mapped duplications into a few genome duplications. In this project, we study two variants of the MGD problems with different cost function measurements. Given are a set of gene trees and a species tree. The first problem, called the Episode-Clustering problem, is to find a minimum number of locations in the species tree for placing all duplications in the gene trees. The other problem, called the Minimum Episodes problem, is to assign duplication events to nodes in a species tree such that the total number of episodes is minimized.

We will design faster algorithms for the Episode-Clustering problem, which has been shown to be a special case of the Tree Interval Cover problem. By traversing the tree in an appropriate order, we wish to design an optimal algorithm for both problems. We will also design faster algorithms for the Minimum Episodes problem. We need to speed up the following four steps: (1) computing the LCA-mapping, (2) finding all leading nodes, (3) checking if these leading nodes are free, and (4) updating the mapping. We will examine the data in the gene clusters more closely and establish a more robust model for them. We will set up a unified theory for handling all evolutionary operations in order to make the reconstruction work in practice.

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超大型積體電路系統晶片電腦輔助設計實驗室
SOC VLSI-EDA Lab.

自2003年成立至今，本實驗室一向是一個不斷追求創新及擴展知識的一個的國際化研究團隊，其研究領域包括了生醫電子，電腦輔助設計及數位IC設計實驗室，其研究重點在於針對電路實體設計及時序之最佳化以及線路模擬，及在針對製造時所產生之製程移之影響及解決方案。最近，我們又極力發展生醫MRI及PEI影像及血管模擬以及半導體光學製程之模擬之最佳化。在IC設計方面，我們主力在發展在高速低功率之微處理機所須之電路。本實驗室目前的研究方向主要可分為六大領域

- 生醫MRI、PET影像處理
- 可製造性設計
- 數位電路之最佳化
- 統計型時序分析
- 高效能電路設計
- 半導體光學製程影像之模擬與處理

Established in 2003, BIO-EDA-VLSI Lab has been relentlessly pursuing new challenges and enrich knowledge in the field of EDA, VLSI circuit design, and BIO/Optical Microlithography Image Simulation and Processing. The focus of our research field include the following 6 major projects:

- Biomedical MRI, PET Imaging processing
- Digital Circuit Optimization
- Design for Manufacturabiliy
- Statistical Static Timing Analysis
- High Performance Circuit Design
- BIO and Optical Microlithography Imaging Simulation and Processing

主要研究領域 Major Research Areas

生醫及半導體光學製程影像處理、微處理機設計、VLSI電腦輔助設計、微波通訊線路設計
BIO/Optical Microlithography Image Processing, VLSI CAD, Microprocessor Design, RF Mix/Signal Circuit Design

研究計畫 Research Projects

1. 次微米下之高速電路及低耗電最佳化
   Deep-Sub-Micron High-speed Low Power Optimization
2. 動態邏輯加法器設計及自動化
   Domino Adder Design and Automa
3. 次微米級干涉週期量測之診斷演算法
   Efficient and Accurate Optical Scatterometry Diagnosis of Grating Variation Based on Segmented Moment Matching and Singular Value Decomposition Method

計畫名稱：基於分段式動差比對法以及奇異值分解之快速且準確的散射儀光柵變異診斷
補助單位：行政院國家科學委員會
計畫期間：2007/08/01-2010/07/31

在奈米科技中，光柵 (Optical Grating) 的良率是相當重要的。為了要確保製作出的光柵良率，使用散射儀 (Optical Scatterometry) 去診斷實際光柵的形狀是一個有效率且實際的方法。大致來說，散射儀使用了不同的波長 (200nm ~ 700nm)去掃描光柵，並且收集在不同波長的反射波強度 (reflection spectrum)。如果我們事先能針對不同幾何形狀的光柵建立出對應的反射波資料庫，那透過比對此資料庫我們就能夠得知最有可能的光柵幾何形狀。

然而，因為製程不斷的縮小，物理的參數可能會產生很嚴重的偏差（圖1a為光學散射儀實驗的建置模型，圖1b為SEM的實際圖形）。因此，為了要涵蓋所有可能因製程偏差產生的光柵形狀，我們需要非常大量的模擬（數量大於10^{12}）。由此可知，建立一個可行的資料庫本身就是一見即為困難的事情，更不要說從資料庫裡面去比對出可能的光柵形狀了。為了要解決上述的問題，我們發展了數個有效的技術去建置一個壓縮的資料庫，更重要的是從這個資料庫搜尋的技術。這幾個演算法簡述如下：

首先，我們建置了分段式動差比對的方法去初步過濾出可能的光柵。在一開始，我們的資料庫會根據反射波強度的前幾個動差（平均、變異、偏態、峰態）階層式的(hierarchically)分類成數個子資料庫。一旦我們得到一個未知的反射波強度，我們就可以根據他們的動差去找到對應的子資料庫，並且在子資料庫中搜尋可能的光柵形狀（如圖2）。分段式動差主要有幾個好處，其一是動差很容易被分佈兩端的一些極值所影響，另一個是透過分段式的計算動差，我們可以處理只有量測到部分反射波強度的情形。另外，為了要確保我們可以有效率的壓縮資料庫以及找到最佳的結果，我們使用了奇異值分解(Singular Value Decomposition)加上最小平方法的技術。

結合了上述的幾種技術，我們提出的演算法可以相當有效的減少儲存的空間而且資料比對的時間也得到了大幅的提升。我們的實驗結果顯示在一個如此大的資料庫裡做搜尋，僅僅需要數秒的時間，並且我們較原始的資料庫有超過100倍的壓縮率。

Project title: Efficient and Accurate Optical Scatterometry Diagnosis of Grating Variation Based on Segmented Moment Matching and Singular Value Decomposition Method
Supported by: National Science Council
Project period: 2007/08/01-2010/07/31

The quality of optical gratings is of great importance to the nanoimprint technology. To ensure the quality of the fabricated optical gratings, optical scatterometry (OS) is an efficient and effective mean to diagnose the actual fabricated geometry. Generally speaking, OS scans the reflection light spectrums of the gratings on varieties of light wavelengths range from 200nm to 700nm and more. If a comprehensive database of the reflection spectrum has been built, one can use the measured spectrum to search the matched pattern and finally find out the most possible fabricated shape.

However, due to the everlasting shrinking process feature sizes, the values for the physical parameters of a grating may deviate significantly from the original design in our SEM chart as shown in fig. 1a (fig. 1b demonstrate the Optical Scatterometry Experimental Setup). Therefore, enormous amounts (more than 10^{12}) of simulations are required to cover all the possible parameters variation ranges. As a result, there are tremendous difficulties to even build the database, not to mention to efficient query the matched patterns. To resolve this issue, we develop several effective techniques not only to build compact databases and most importantly the efficient searching methods. The highlights of our novel algorithms are as follow:

First, a segmented statistical moment matching method has been developed to do a first filtering for possible matching patterns. In the beginning, all of the spectrum in the database will be classified and hierarchically sorted according to the values of the first few segmented moments such as mean, variance, skewness and kurtosis. The definition of the ith moment can be represented as:□□=1□ □□□□□=1. Therefore, once the spectrum of an unknown grating is measured, the calculated moments of the spectrum can be used as hierarchical indices to find the corresponding sub-database and the comparison for a similar spectrum can then be done. (see fig. 2) The novelty of our method is that since the standard definition of statistical moments often put more emphasis on the far end of the distributions, we first chop the spectrum into segments according to the ranges of the wavelengths (say 50nm). Another benefit of this method is that when only limited portions of the reflection spectrums are available, our method can still function correctly.

Second, to ensure the best fit (minimum error) of the result, the Singular Value Decomposition (SVD) technique has been employed. After applied SVD to the original database, a, the database can be decomposed into a product of 3 matrices, USVT, where U and V are orthonormalized basis and S contains singular values on the diagonal. We then reduce the database sizes according to the singular values as shown in fig. 3. In this way, with a measured spectrum, b, the search process can be fundamentally mapped to a least square fitting problem which can be mathematically expressed as follow: find the i-th basis which minimizes □□□−□□□ 2.

Combing the two above mentioned methods, our proposed algorithm can effectively compact the storage and thus the overall comparison time can be significantly improved. Our experimental result shows that the search time for a large database case only needs less than a few seconds where more than 100X storage reductions has been achieved.

Acknowledgements

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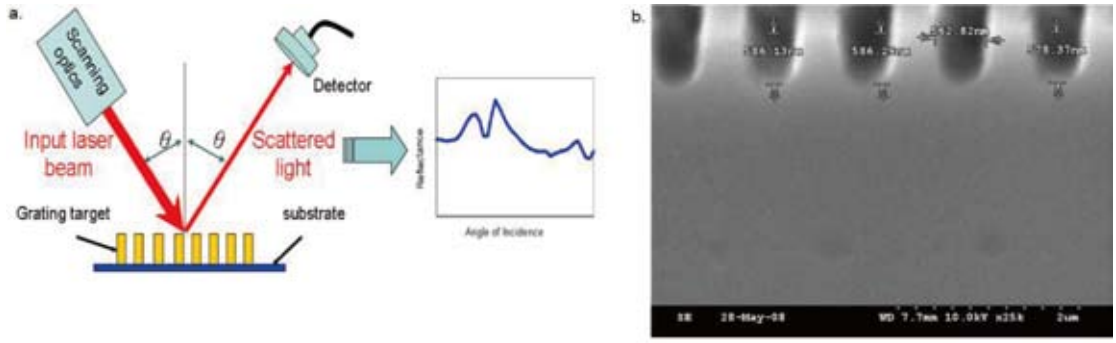
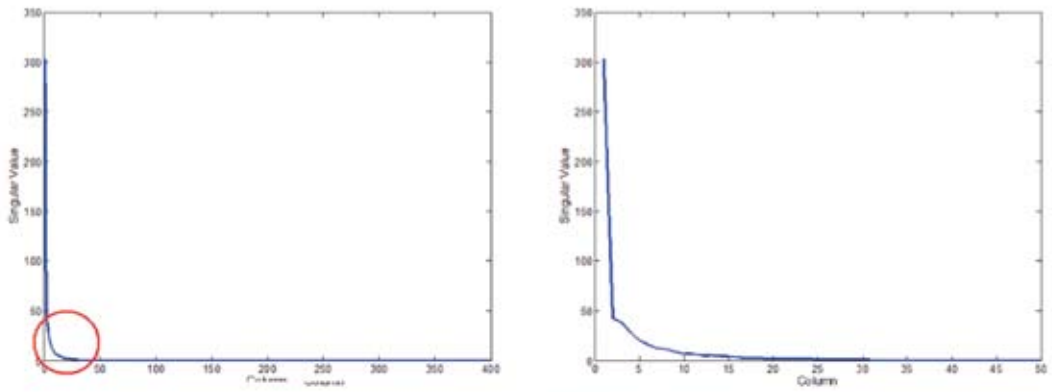
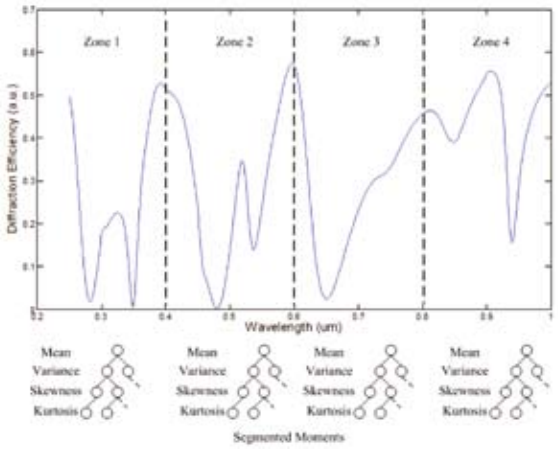




Singular Value Distribution



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醫學影像實驗室
Medical Imaging Lab.

醫學影像實驗室目前位於臺灣大學明達館七樓 (room706)。負責人為陳志宏(Jyh-Horng Chen)教授，助理一人，研究生六人，博士班學生一人。主要研究方向為核磁共振造影(MRI)、殘障者人機介面與噪音抑制(Noise cancelation)等研究主題。在電機一館一樓設有MRI/MRS實驗室，設有一台Bruker 3.0 Tesla MR，平時提供校園內學術單位做研究，以及本實驗室研究造影技術之用。

核磁共振影像頻譜實驗室
Magnetic Resonance Imaging Lab.

本實驗室於1999年成立，以提供有效、可靠的成像技術及訓練課程予各研究領域之研究學者，心理學家、生理學家、動物學家，可藉由磁振光譜影像之重建方式，為未來之基因蛋白體研究、動物病變模型之評估，提供微細且精確的訊息，以成為台灣的MRI研究及人才培訓資源中心。另一方面，本實驗室亦從事新技術之研發，期能突破現有磁振造影(MRI)之成像速度限制，提升磁共振影幅系統成像能力及台灣在磁共振領域之國際知名度，並藉由國內現有MR研究資源合作，以跨學科之研究，使人文、科學、醫學、工程等不同學科得以匯整激盪，並創造21世紀之新學門科學，建立一個世界級之核磁共振卓越中心。主要研究方向包括：大腦功能性磁振造影、擴散磁振造影、MR線圈設計、MRI成像最佳化技術、超快速平行擷取MRI系統、小動物生理病理研究、分子影像。

The laboratory will apply the existing MRI / MRS techniques to interdisplinary research, including school of humanity, psychology, medicine, engineering, agriculture and food science. Its object is to combine experts in different areas to generate, hopefully, some new academic areas in 21 century. This laboratory is supported by National Taiwan University (NTU) as well as Instrumentation Center of National Science Council (NSC) in Taiwan.

生醫分子影像核心實驗室
Biomedical Molecular Imaging Core Lab.

此核心實驗室結合磁共振(MR)分子影像 、光學分子影像(Optical molecular imaging)及超音波分子影像(Ultarsonic molecular imaging)，此外，為使活體中特定的分子成像，除了要有上述高分辨率、敏感、快速的成像技術，還具備合成具有高親和力的分子探針及具有特異標定之顯影劑。

本核心實驗室主要目標之一為提供分子醫學影像之量測與生物體之醫學成像技術研究服務予台灣大學醫學院區內從事生物醫學、基礎醫學與臨床醫學研究人員，此外，本實驗室致力發展新型醫學影像之顯影劑開發，並結合分子生物之技術，開發新式具特異標定功能之奈米粒子。

This core combined MR molecular imaging, optical molecular imaging and ultrasonic molecular imaging, thence, besides above mentioned properties, high spatial resolution, sensitivity and fast imaging technology, it has the ability to synthesize high affinity molecular probe and specific-targeting contrast agent, and then in vivo specific molecular imaging will be obtained.

Our primary aim for this Biomedical molecular imaging Core is to provide research services to all the investigators within NTU medical campus, and conducting methodological research related to biomedical molecular imaging is our secondary aim. On other hand, we also develop the novel contrast agents which have specific targeting function for disease model.

主要研究領域 Major Research Areas

核磁共振影像、醫學工程

Magnetic Resonance Image, Functional MRI, Molecular imaging, Man Machine interface, Medical Engineering

1. 心智科學大型研究設備建置及共同使用服務計畫—大腦與心智文化整合性研究
   Installation and Operation of Core Facility in Mind Science: An Initiative for Integrated Research on Brain, Mind and Culture
2. 供癌細胞/幹細胞血統追蹤之基因改造鼠：研發及應用--具標定功能奈米顯影劑及複合式生醫分子影像技術平台之研究：以雙螢光基因及白喉毒素受體基因替換小鼠為模型（子計畫二）
   Genetically-Gngineered Mice for Cancer Cell / Stem Cell Lineage Tracing : Research and Application
3. 發展動態磁振造影及具標定之生醫分子影像：評估肺癌與轉移肺癌小鼠模式之治療反應－發展動態磁振造影及具標定之生醫分子影像：評估肺癌與轉移肺癌小鼠模式之治療反應
   Evaluating Therapeutic Response of Lung Cancer and Metastatic Lung Cancer in Mouse Models with DCE MRI and Targeted Molecular Imaging
4. 大腦如何調節自發性節律 平靜狀態下腦功能性連結之探討與應用
   How Does Brain Coordinate Spontaneous Fluctuation?
5. 影像導向神經幹細胞之應用於中風及週邊神經創傷－神經幹細胞之非侵入式磁振影像追蹤（子計畫三）
6. 基因體醫學研究中心
   Program for Excellence Research Teams：NTU Center for Genomic Medicine -Biomedical Molecular Imaging Core Lab

計畫名稱：發展動態磁振造影及具標定之生醫分子影像：評估肺癌與轉移肺癌小鼠模式之治療反應－發展動態磁振造影及具標定之生醫分子影像：評估肺癌與轉移肺癌小鼠模式之治療反應
Evaluating Therapeutic Response of Lung Cancer and Metastatic Lung Cancer in Mouse Models with DCE MRI and Targeted Molecular Imaging
補助單位：行政院國家科學委員會
計畫期間：2009/08/01-2012/07/31

本研究計畫將利用兩種肺癌轉移的動物模式作為研究標的：其一為受放射線治療誘發肺癌轉移的動物模式（C57BL/6品系），其腫瘤細胞為Lewis lung carcinoma(LLC-LM)；其二為SCID之動物模式，其腫瘤細胞為CL1-0、CL1-5、與Mock 189來探討腫瘤轉移形成機轉。在針對細胞分子表現特異性鑑別之奈米顯影劑的發展平台部份，可藉由測試修改奈米表面以改良並同時具有正子斷層掃瞄與磁振造影之對比顯影的效果。藉由發展新型態之奈米粒子作為吸收近紅外光誘發熱治療之雙效奈米藥物。根據過去的文獻報導，為新生血管之表面受器，其可被RGD-4C特異標定其腫瘤新生血管。而同時EFGR(Epidermal growth factor receptor)為一腫瘤生長激素表面受器，其功能可被抗EGFR抗體抑制，因此未來將進一步連結抗腫瘤及新生血管特異性表面抗原分子，如EGFR及RGD-4C，以作為融合標的投遞之導向器及攻擊武器於一體之多功製劑。

在磁振造影之分子影像擷取部份，此計畫將整合跨領域的磁振造影技術，包括擴散磁振造影、微灌流磁振造影、顯微磁振造影以建立一個宏觀且領先的磁振分子影像造影技術。此外，本團隊將發展出高效率改良式的高速成像序列及高溫超導射頻線圈造影技術並使用具有強梯度磁場的顯微造影線圈及平行影像技術及其重建演算法，藉以大幅提升影像敏感度、解析度、訊雜比、及取像速度。為了適用於活體動物實驗，本計畫將結合上述改良造影技術於3T (Tesla)以及7T 磁振造影系統並結合動物正子斷層掃瞄以建立小鼠實驗影像技術整合平台。有了此一最佳化之小動物平台，將有助於研究奈米顆粒顯影劑的對比特性、建立適合於磁振照影對比強化的肺癌動物模型之造影平台、並評估動態顯影之核磁共振照影技術與合成之奈米顆粒顯影劑之體內生物分佈及標記之功效。

本研究整合一流之生醫及理工研究團隊以從事動態顯影、奈米顯影粒子、顯微磁振造影、及動物正子斷層掃瞄等結合上中下游之整合研究建立活體動態追蹤動物腫瘤治療評估及轉移過程的分子影像模式，分析放射線引發肺癌肺臟轉移過程中血管新生與缺氧誘發因子的動態表現情況，以釐清血管新生與缺氧誘發因子對應其標靶藥物在抑制小鼠腫瘤肺部轉移治療之應用潛力，以期密切的交流互動及研究成果達成預期研究目標，提升在國際上的能見度，達到生醫分子磁振造影技術之領先地位。

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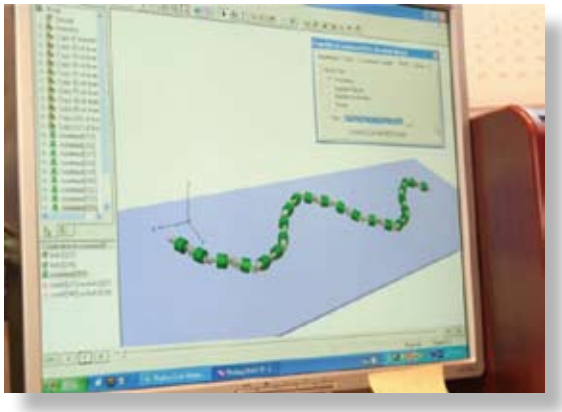
智慧型及精密運動控制實驗室
IPMC Lab.

本實驗室「智慧型精密運動控制實驗室」由陳永耀教授領導，位於明達館604室，其研究的主要方向為智慧型控制與超音波熱療。實驗室的近期研究領域分成反向光學微影技術、電子束微影系統、姿態辨識聲音的分析與處理、仿生機械人、及超音波熱療等五大主題。

反向光學微影技術的研究是針對在IC製程上小尺度的光罩所產生的繞射現象，在光罩設計時將繞射現象考慮進去，設計出最佳的光罩形狀。電子束微影系統的研究是在IC製程中的電子束蝕刻時，對電子束做位置的訊號回授控制以修正電子移動時所產生的漂移現象。姿態辨識的研究是利用人工智慧的方式來處理影像中的資訊，本實驗室建立影像的監視系統應用在老人看護上。另外在聲音處理的方面是利用訊號處理的方式將聲音中的雜訊濾除，進而研究聲音本質與語者分析。仿生機械人的研究是模仿生物的運動模式，將生物的優點轉換成電機領域的應用，近期的研究是將蛇的運動設計成新型的載具。超音波熱療的研究是發展新的預測方式，來追蹤人體中因呼吸而上下運動的腫瘤細胞，使得聚焦的超音波能夠正確的加熱在腫瘤細胞上，殺死腫瘤細胞。

本實驗室致力於將智慧型控制嘗試應用在各方領域，將機械自動化，改良儀器控制法，改善人類生活。



Intelligent Precision Motion Control Laboratory is lead by Prof. Yung-Yaw Chan and located in room 604, Minda building. Researches included inverse optical micro-lithography, electron beam lithography, motion identification, sound Analysis, biomimetics, and high intensity focus ultrasound.

Inverse optical micro-lithography is to design the optimal from of the mask, due to the diffraction of light changes. Electron Beam Lithography is to write on wafers by electron beam directly. We use sensors to feedback control the system to reduce beam broadening and proximity effect. In motion identify, we analyze the human activities for the home care systems. Biomimetics is to study the biological structure and the locomotion of real snakes, and to develop and design advanced platform actuation systems. Our laboratory applies Intelligent Control to automate machine and to improve the system performance.

主要研究領域 Major Research Areas

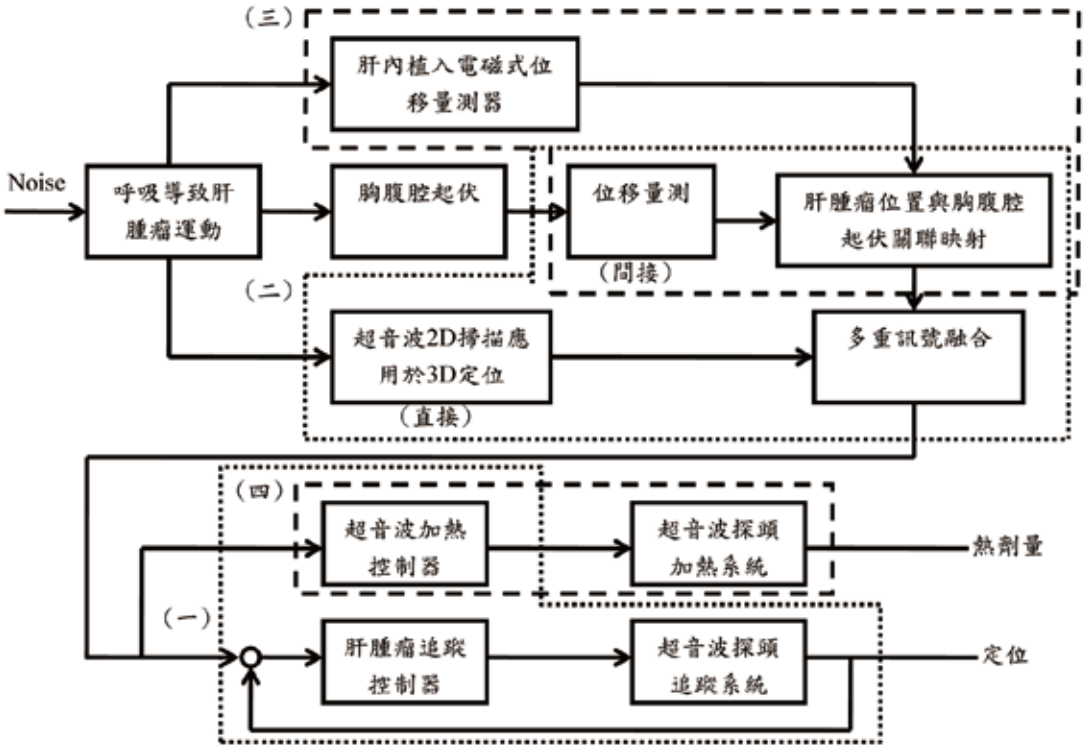
智慧型控制、居家看護、精密伺服控制、超音波加熱治療

Intelligent control, Home care, Precision servo control, Hyperthermia treatment planning

研究計畫 Research Projects

1. 智慧型居家看護影像監控系統(II)
   Intelligent video surveillance on home care system(II)
2. 應用於熱手術與熱治療之高強度聚焦超音波患能器開發(I)
   Effects of HIFU cavitation and nonlinearity on the thermal lesion formation and its pplications for thermal therapy(I)
3. 蛇形仿生運動機制及前瞻載具驅動系統之研究-總計畫：蛇形仿生運動機制及前瞻載具驅動系統之研究
   Biomimetic snake locomotion and its application to advanced platform actuation systems—master plan
4. 蛇形仿生運動機制及前瞻載具驅動系統研究-子計畫四：蛇形運動控制方法及前瞻載具驅動器設計
   Biomimetic snake locomotion and its application to advanced platform actuation systems—sub plan
5. 智慧型居家看護影像監控系統(Ⅲ)
   Intelligent video surveillance on home care system(Ⅲ)
6. 座艙聲紋分析系統之研發
   Development of voiceprint analytical systems for cockpit voice recorders
7. 高強度聚焦超音波穴蝕化與非線性對熱治療區形成之影響及其在熱治療應用之研究(II)
   Investigation of high intensity focused ultrasound for moving tumor thermal therapy

8. 高強度聚焦超音波應用於運動中腫瘤之熱治療探討
   The beating effect of confocal ultrasound on the thermal lesion formation
9. 共焦聚集超音波熱治療時聲拍作用對熱燒灼區形成之影響
   Development of HIFU transducer for thermal therapy and surgery
10. 以影像為基礎之智慧型動作辨識
    Vision-based Multi-target Intelligent Human Motion Identification
11. 由呼吸導致週期性位移肝腫瘤之超音波熱劑量控制方法研發（總計畫）
    Development on High Intensity Focused Ultrasound Thermal Therapy Tracking Control on Liver Tumor with Respiration-induced Periodic Motion
12. 肝腫瘤位置追蹤及高強度聚焦超音波熱療控制系統研發（子計畫一）
    Development on Liver Tumor Tracking and High Intensity Focused Ultrasound Thermal Therapy Control System

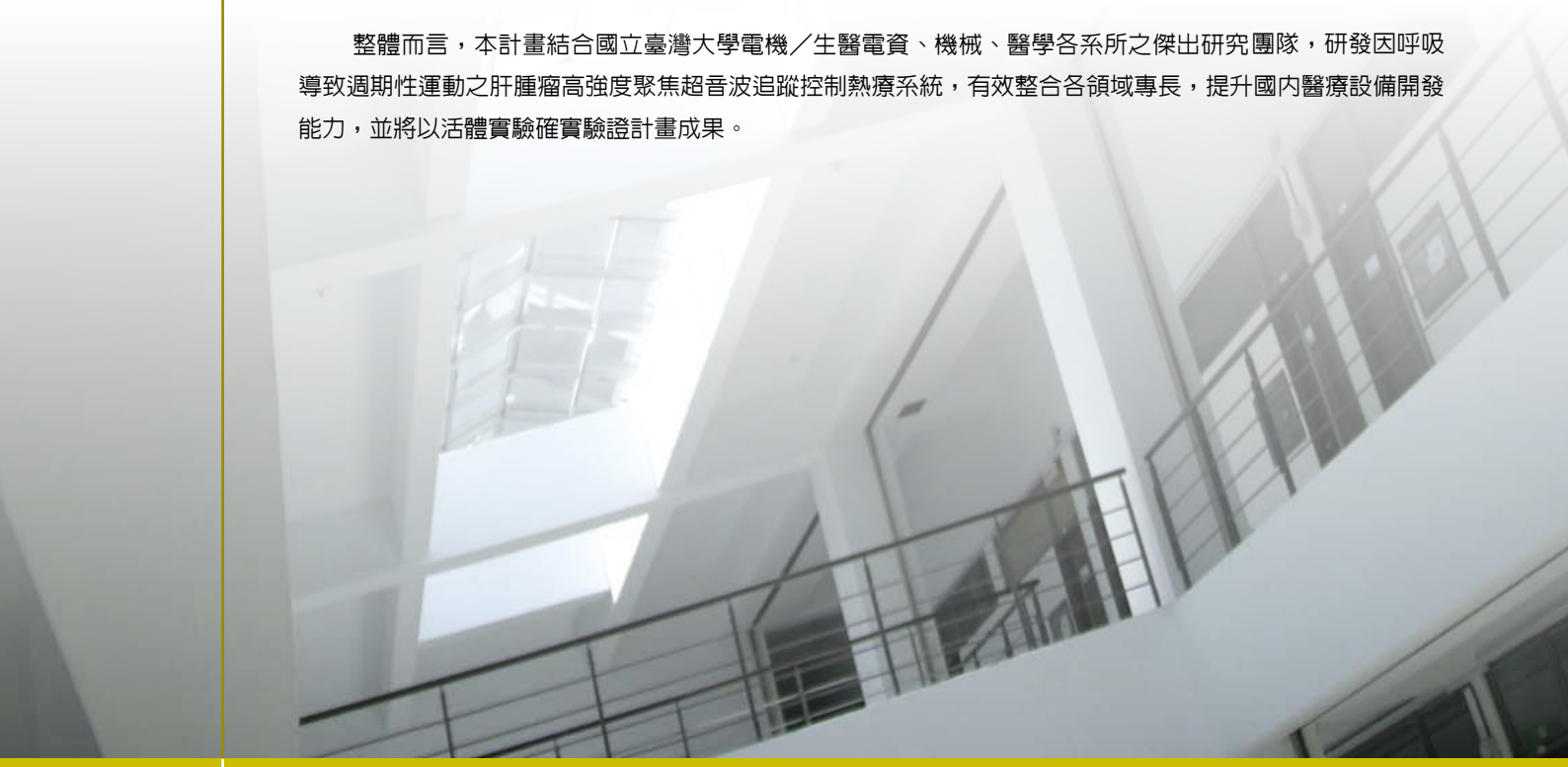


圖一 子計畫關聯性之控制方塊圖

計畫名稱：由呼吸導致週期性位移肝腫瘤之超音波熱劑量控制方法研發（總計畫）
補助單位：行政院國家科學委員會
計畫期間：2009/08/01-2011/07/31

惡性腫瘤高居台灣十大死因之首，而有效的治療方式中，超音波加熱治療較外科手術切除、放射線療法、栓塞法與化學療法等方法有更低的副作用及非侵入性，而為極有潛力之腫瘤治療方法。以高強度聚焦超音波進行治療時，必須準確地聚焦在所要治療的患部，以避免在正常的組織形成過多的熱劑量分布。動態腫瘤如肺癌、肝癌，由於呼吸及橫膈膜的影響產生週期性的往復運動。為了能夠準確的定位運動中的肝腫瘤，並施以適當的加熱治療，本計畫將依量測、控制、探頭、及生理等多領域進行研究。在子計畫二主要研究的量測方面，將分為間接量測與直接量測。由於肝臟位於人體腹腔內，現有之掃描技術雖然可以取得非常精細之圖像，但速度遠低於即時控制所需。因此計畫將同時推動以量測胸腹腔起伏關聯至肝臟運動之間接量測方法與分析，進行多重感測訊號融合，以及以二維超音波掃描轉換為三維定位資訊之量測技術。在子計畫三之生理實驗相關研究上，將以活體實驗方式量測肝臟位置，以進行間接量測之關聯性分析，同時多方面探討各項生理參數與限制條件對肝臟位置關聯性之影響。此外子計畫三最後將進行超音波熱療之活體實驗，確認計畫執行成效。在子計畫四主要研究之探頭設計方面，將發展順型(conforming)加熱之探頭設計，以期能夠在最短時間內達成有效之加熱療效，並阻抗控制觀念下進行探頭理論之開發。子計畫一之主要任務在完成高強度超音波熱療之肝腫瘤追蹤控制系統設計與建構，除了系統整合與協調各子計畫研究工作進行外，預計探討即時之智慧型重複控制方法(Intelligent Repetitive Control)，以及以較慢之三維定位資訊進行即時控制系統之週期性校正。

整體而言，本計畫結合國立臺灣大學電機／生醫電資、機械、醫學各系所之傑出研究團隊，研發因呼吸導致週期性運動之肝腫瘤高強度聚焦超音波追蹤控制熱療系統，有效整合各領域專長，提升國內醫療設備開發能力，並將以活體實驗確實驗證計畫成果。



Project Title: Development on High Intensity Focused Ultrasound Thermal Therapy Tracking Control on Liver Tumor with Respiration-induced Periodic Motion

Supported by: National Science Council
Project Period: 2009/08/01-2011/07/31

Cancer has been the top cause of death for people in Taiwan for many years. Among its possible treatments, such as surgery, radiation, blocking, and chemical therapies, the High Intensity Focused Ultrasound (HIFU) thermal therapy is regarded as one with great potential due to its low side-effect and noninvasiveness. With HIFU, the target area has to be quite accurate to avoid the possible damage of normal tissues from the excessive thermal distributions. Some of the tumors, such as liver or lung cancers, will have periodic motions from the respirations. Our project is focused on the sensing, heating, in vitro experiment, control and system integration so that an effective thermal therapy methodology can be achieved. In project II, indirect sensing of liver motion through the chest and abdomen motion will be conducted and studied. Also from the fact that current imaging technology is not fast enough for real-time control, a technology by utilizing the 2D ultrasound images and transform to the 3D liver position will be developed. Project III will conduct in vitro experiments for liver motion data acquisition and analysis. And will also investigate the relationship between possible factors with the liver tumor position. At the final stage, project III will conduct an in vitro experiment with integration of the sensing, heating, and control of all the other projects for verifications. Project IV will study the conforming transducer design with the concept of impedance control and optimal heating strategies. Finally, project I will be mainly on the tracking control system design. Intelligent repetitive control will be studied to combine the repetitive control theory and the neural networks to form a real-time control system with periodic updating mechanism. Project I will also be responsible for system integrations.

Overall, an excellent research team is integrated with members from the NTU EE/BMEI, ME, and Medical departments to make joint efforts on this project. This project is expected to have excellent results academically and promote the domestic research capability of medical therapy equipments.

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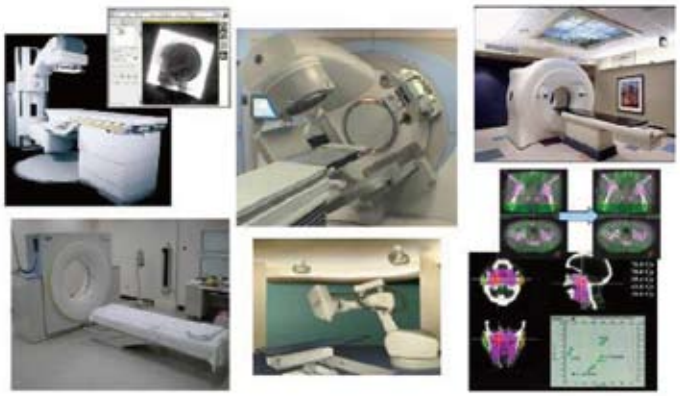
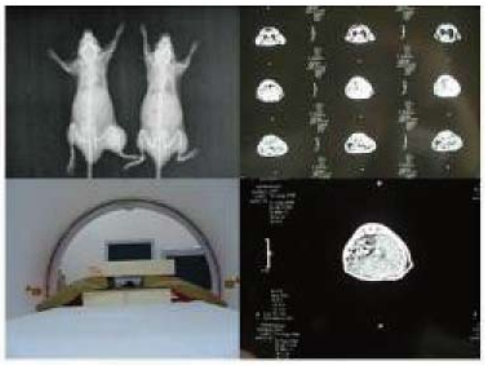
Adjunct Associate Professor, Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine
Attending Physician and Division Chief, Division of Radiation Oncology, Department of Oncology, National Taiwan University Hospital

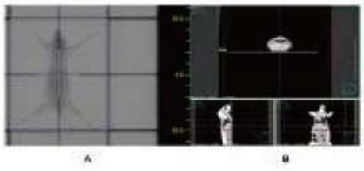
放射物理生物實驗室
Laboratory for Radiation Physics and Biology Lab.

本實驗室由成佳憲副教授於2002年起隨同整建臺大醫院腫瘤醫學部放射腫瘤科時設立，主要從事放射治療物理學與放射生物學相關研究，目前以設備技術物理與腫瘤放射治療轉譯醫學等領域為研究重點。本實驗室在影像導引放射治療領域與肝癌放射治療領域已產出許多具體貢獻。本實驗室之成員來自臺大醫院腫瘤醫學部放射腫瘤科醫學物理師、放射師及放射生物醫學領域研究人員，多年來亦積極與國內外單位進行合作。

The laboratory for radiation physics and biology was established by Jason Chia-Hsien Cheng, M.D., M.S., Ph.D., with the reconstruction of Division of Radiation Oncology, Department of Oncology, National Taiwan University Hospital. The main research directions are radiation physics related to equipment and technique, as well as translational medicine of radiation oncology. Our research team has been contributing significantly the progress in image-guided radiation therapy and radiotherapy to hepatocellular carcinoma. The team members of our laboratory include the radiation physicists, radiation technologists, and radiation biologists from Division of Radiation Oncology. The laboratory also has the collaboration with the other research teams in Taiwan and in the other countries.







主要研究領域 Major Research Areas

放射腫瘤學、放射物理學、放射生物學、癌症轉譯醫學
Radiation Oncology, Radiation Physics, Radiation Biology, Cancer Translational Medicine

研究計畫 Research Projects

1. 肝臟放射治療激發之介白素6 於肝癌控制與副作用預防的功能與機轉研究
   The functional and mechanism study of interleukin-6 from liver radiotherapy for therapeutic intervention on hepatocellular carcinoma control and side effect prevention
2. 以小鼠肺癌模式作為放射線活化癌症轉移之MMP-9/MMP-2角色
   Mechanism study of radiation induced lung metastasis-the role of MMP-9/MMP-2
3. 放射線引發血管內皮細胞產生介白素-8的作用機轉及其生物效應研究
   Biological effect and mechanism of radiation-induced interleukin-8 from endothelial cells
4. Cetuximab與Bevacizumab合併FOLFOX化療與放射線治療對直腸癌治療協同效果之分子機轉探討
   Molecular Mechanism Study of Synergism with Combined Radiation, FOLFOX, and Cetuximab versus Bevacizumab on Rectal Cancer
5. 食道鱗狀上皮細胞癌表皮生長因子接受體之訊息途徑與放射治療抵抗性之機轉研究
   Mechanisms of radiation resistance by epidermal growth factor receptor signaling pathway in esophageal squamous cell carcinoma

計畫名稱：以小鼠肺癌模式作為放射線活化癌症轉移之 MMP-9/MMP-2 角色探討

補助單位：行政院國家科學委員會

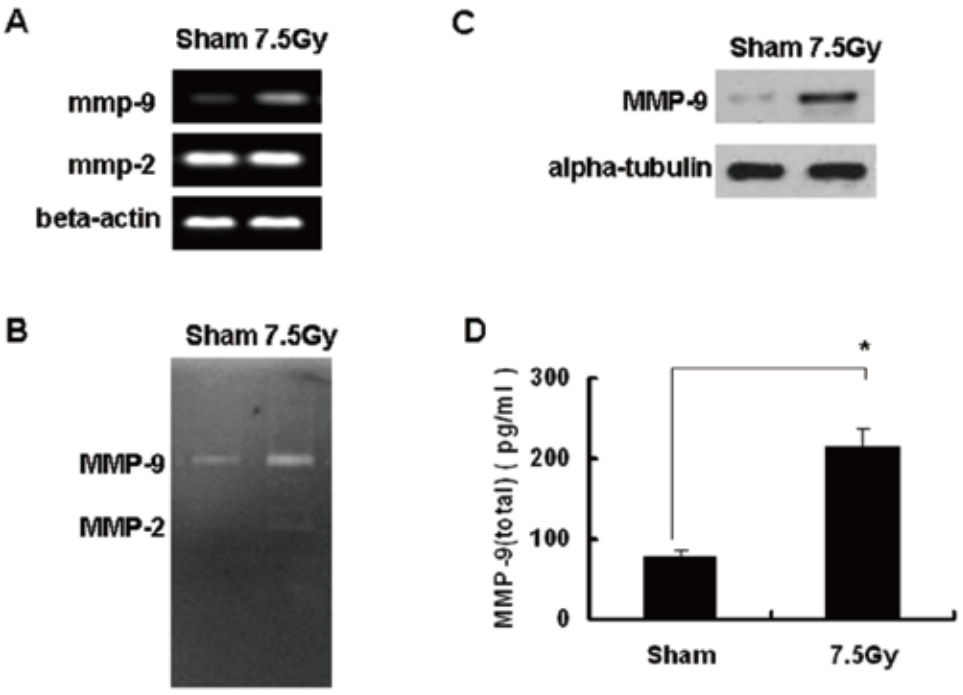
計畫期間：2008/08/01-2011/07/31

腫瘤細胞轉移為目前臨床癌症治療最棘手的問題，因為轉移包含了侵襲、移行、抗懸浮性凋亡、固著、血管新生等現象。現行關於腫瘤轉移的活體研究模式，大多牽涉多個變項同時影響轉移與否的情況，而無法在個別因素控制下於實驗動物模式下形成穩定的轉移，與人體內腫瘤轉移的現象有很大的差別。本研究計畫主要將利用一種受放射線治療誘發肺癌腫瘤轉移的動物模式（C57BL/6 品系），其腫瘤細胞 (Lewis lung carcinoma，LLC-LM) 之肺臟轉移現象會在放射線治療原發部位腫瘤後自然發生，來探討腫瘤轉移形成機轉。此模式為哈佛大學於2001 年建立，當時理論著重於血管新生與轉移的關連性，但也發現轉移過程與動物尿液中MMP-2/MMP-9 增加相關。本研究室也在肝癌細胞侵襲轉移能力的研究中發現放射線治療誘發之MMP-9 與增加肝癌細胞侵襲能力有高度關連（發表於2006 年Oncogene）。我們已於LLC-LM 細胞學及動物肺臟轉移模式初步研究成果呈現放射線治療中細胞培養液及小鼠血清及尿液中MMP-2/MMP-9的蛋白質濃度與活性增加反應，證實其在腫瘤肺部轉移過程中扮演了關鍵的角色。本三年期計畫主要將以這個放射線治療穩定引發動物腫瘤轉移的方式釐清MMP-2/MMP-9 在癌症侵襲轉移機轉中的介入角色。第一年的研究重點為運用細胞分子生物學方法，分別以已分別建立核酸干擾技術(RNA interference)的MMP-2 knockout、MMP-9 knockout、MMP-2/MMP-9 double knockout 之LLC-LM 肺癌細胞株，驗證MMP-2與MMP-9 基因knockout 有否影響細胞活性及放射線敏感性，以及影響放射線引發之肺臟轉移現象與血管新生的關係。第二年的研究重點為以這些LLC-LM 肺癌細胞株，配合放射線引發體內動物腫瘤轉移模式，驗證MMP-2/MMP-9 在活體轉移現象是否有差別，以確認MMP-2/MMP-9 對放射線引發LLC-LM 轉移的真正影響，並進一步探討MMP-2/MMP-9 對放射線引發LLC-LM 轉移的訊息傳導路徑。第三年的研究重點為運用轉殖螢光基因的LLC-LM 方式進行動物實驗與時序性的血液及肺臟組織基因針測，同時以小型動物正子/電腦斷層掃描設備建立活體追蹤動物腫瘤轉移過程的影像模式，分析放射線引發肺臟轉移過程中，除原發腫瘤受控制使其分析血管新生抑制因子減少引起之轉移機轉外，MMP-2/MMP-9 是否亦參與血管新生前期機轉而使原發腫瘤散至血液的另一機制，以完整此轉移模式的確實路徑。並將前兩年之基礎研究結果進行轉譯研究，探討以MMP-2/MMP-9 或其活化過程中重要之訊息傳遞分子為標的的藥物在抑制小鼠腫瘤肺部轉移治療之應用潛力。釐清此模式之轉移發生的機轉，將有助於對相關於MMP-2/MMP-9 的人類腫瘤細胞轉移機轉有更多瞭解。也能更妥善運用此模式進行其他腫瘤轉移的類似路徑研究及抗腫瘤轉移之藥物開發。

Project title: Mechanism study of radiation induced lung metastasis-the role of MMP-9/MMP-2
Supported by: National Science Council
Project period: 2008/08/01-2011/07/31

Metastasis has been the most difficult problem in clinical cancer treatment. It has been found that metastasis involves invasion, migration, anti-apoptosis, adhesion, and angiogenesis. The current in vivo animal model with metastasis is confounded by multi-factorial impact on metastasis, limiting the single-factor induced metastasis. The stable metastasis modelcontrolled by univariate factor is lacking. Difference exists between animal model with metastasis and clinical metastasis. This project is to use an animal model (C57Bl/6 mouse) with radiation-induced metastasis of Lewis lung carcinoma (LLC-LM). The spontaneous radiation-accelerated pulmonary metastasis after irradiation to the primary tumor is to be used for investigating the mechanism of cancer metastasis. This mouse model was established by Camphausen et al. in 2001. They emphasized the correlation between angiogenesis and metastasis. The additional findings included the increased urinary MMP-2/MMP-9 concentrations related to the metastatic process. Our laboratory similarly found the correlation of radiation-activated MMP-9 with the radiation-enhanced invasiveness in human hepatoma cells (published in Oncogene 2006). Our preliminary data on LLC-LM showed the critical roles of the increased activities and concentrations of MMP-2/MMP-9 proteins in mouse serum and urine in the radiation-accelerated LLC-LM metastasis. This 3-year project is to investigate the integrated roles of MMP-2/MMP-9 in the mechanism of cancer invasiveness and metastasis, by use of the stable mouse model of radiation-induced pulmonary metastasis of LLC-LM. The first-year goal is to verify the impact on the radiation sensitivity and viability with the established RNA interference-expression clones of MMP-2 and/or MMP-9 knockout LLC-LM cells. The relationship between the angiogenesis and metastasis is also studied from these cell lines. The second-year goal is to use these MMP-2 and/or MMP-9 knockout cell lines and conduct in vivo experiments for pulmonary metastasis, to confirm the exact roles of MMP-2 and/or MMP-9 in radiation accelerated metastasis. The signal transduction pathway of radiation activated MMP-2/MMP-9 and induced metastasis of LLC-LM is to be studied. The third-year goal is to trace the in vivo time-dependent manner of LLC-LM cell metastasis from the circulation and the lungs by using the established Green fluorescent protein-transfected cell lines. We also apply the micro-PET/CT system to set up the sequential imaging models of metastasis in this animal model. This work may help understand the mechanism of MMP-2/MMP-9 involved pre-angiogenesis phase with spread of LLC-LM into the circulation, which is different from the reported theory of decreased angiostatin secretion with the controlled primary tumor and the resultant angiogenesis. Therefore, the pathway of radiation accelerated LLC-LM metastasis could be uncovered. Based on the first two-year data we will conduct the translational research to test the potential drugs targeting the signaling factors in radiation-induced MMP-2/MMP-9 activation, and to verify the effect on suppressing the radiation-accelerated pulmonary metastasis. With elucidation of this metastatic model, it would be helpful in further understanding the MMP-2/MMP-9 related human cancer metastasis, and in developing the anti-metastasis drug.

代表圖及中英文說明：



Radiation enhances LLC-LM cell invasiveness through increased MMP-9 protein expression. (A) LLC-LM cells were irradiated with 7.5 Gy or not (sham). After 6 hours, total RNA was isolated and reverse-transcribed to cDNA for mmp-2 and mmp-9 mRNA detection by PCR, with actin as a loading control. (B) After 12 hours, cell culture supernatant was collected and MMP-9 as well as MMP-2 activities were measured using gelatin zymography. (C) Total cell lysate protein was collected. The expression of MMP-9 was detected by Western blot with specific antibodies, with alpha-tubulin as a loading control. (D) The cell culture supernatant was collected for the total MMP-9 measurement. “*”, $p<0.01$, irradiation group compared with the sham group.

本圖顯示放射照射LLC-LM細胞引發經由MMP-9蛋白質增強的侵襲能力，分別在基因轉譯轉錄及細胞內與培養液蛋白質表現的增加。

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主要研究領域 Major Research Areas

生醫信號處理、醫學資訊系統及醫學健康教育數位學習

biomedical signal processing ,medical information system, e-learning in medical and health education

研究計畫 Research Projects

1. 家庭式攜帶型(homecare)健康檢測儀之開發-功能指標AST(GOT)/ALT(GPT)監測系統
   The development of the homecare health detector – function indicator AST (GOT) /ALT(GPT) monitoring system

2.跌倒防制之雙六軸平衡訓練系統整合研
   The Integration and Development of Dual Stewart's Balance Training System for Prevention of Fall

計畫名稱：跌倒防制之雙六軸平衡訓練系統整合研
The Integration and Development of Dual Stewart's Balance Training System for Prevention of Fall
補助單位：行政院國家科學委員會

根據多份研究，平衡訓練系統對於老年人、中風患者以及麻痺患者有著相當程度的幫助，除了有助於提升病患的生活品質，更藉著訓練以降低跌倒的發生率，進而節省整體醫療成本的付出。

就國內外文獻，評估老年人平衡狀態可分為三大指標模式，「堅硬平台模式(Hard Plat, HP)」、「柔軟平台模式(Soft Plat, SP)」、「移動干擾模式(Sway-Referenced Support, SRS)」。然而在現有的平衡儀對於上述三大指標模式無法作有效且客觀的評估，在老人跌倒預防上著力有限。

本計劃欲建構一復健系統，以史都華平台作為基礎硬體，利用其穩定與精密的特性，製造出不同的平衡環境。並使六自由度力與力矩感測器(6 DOF force/torque sensor) 與3D追蹤器(3D tracker) 詳細記錄平衡時的二維壓力中心(Center of Pressure, COP)與重力中心(Center of Gravity, COG)，以提供客觀的平衡數據，為老人跌倒防制尋找一個更有系統的評估機制。再者，搭配者虛擬實境(Virtual Reality, VR)並輔以視覺與聽覺的回饋，使本系統的發展與應用範圍更加的廣泛。

相較於坊間的平衡系統，本計畫系統具有下列優點：
(1)相較於一般平衡儀，本系統具有更多元的平衡環境選擇。
(2)相較於已上市機械式平衡儀，本系統造價較低，且軟體配合度更高。
(3)本系統可搭配虛擬實境，並可藉由家用電腦擴充為遠距復健系統。
(4)本系統硬體自由度高，可藉由撰寫驅動軟體滿足多元復健需求。
(5)本系統採雙平台系統，相較於單平台系統，在硬體效能與靈活度更具優勢。
關鍵詞：平衡系統、平衡表現、站立平衡

Previous reports in the literature demonstrated balance training can help improve the quality of life for elderly people, stroke survivors, and paraplegic patients. In addition, balance training can decrease the occurrence of falling and then decrease the cost of the whole health system.

It has been documented that balance assessment for elderly can classify into three standard models: Hard Plat (PH), Soft Plat (SP), and Sway-Referenced Support (SRS). However, current balance equipments can't provide sensitive effective and objective evaluation for the three models, so it's hard to avoid efficiently falling of the elderly.

Our project is to set up a rehabilitation system with Stewart-Platform which can be set into different balance situations. Static and precise are the advantages of this system.6 DOF force/ torque sensor and 3D tracker are used to record the path of Center of Pressure (COP) and Center of Gravity (COG) in plane for objective database about balance assessment. This database can help us to develop the better system for balance assessment about flopping of the elder. Beside, combining with Virtual Reality (VR) and the feedback of vision and auditory can increase the development and application of our system.

Comparing with others, the advantages of our system are：
1. Our system has more diversified balance situation than present ones.
2. Comparing with present mechanical devices, our system with software is more economic and more friendly.
3. Our system can combine with virtual reality to become a distant rehabilitation system by personal computer.
4. For different requirements of rehabilitation, our system can work easily with other hardware by custom-made drivers.
5. Our project use two-plats system which can improve the efficiency of hardware and adaptability.

Keyword：Balance System,Balance performance,Standing Balancelue.

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生物資訊暨生物統計核心實驗室
Bioinformatics and Biostatistics Core Lab.

本實驗室研究是以基因體學探討癌症形成機制為主軸。近年來基因晶片 (DNA microarray) 已經被廣泛應用在同時觀察大量的基因表現，為研究特定基因調控極為方便、快速與可靠的方法。因此實驗室的研究方向乃致力於增進基因晶片技術在生物醫學領域上的研究，研究範疇涵蓋晶片製備技術、影像擷取與分析、生物資訊學、資料管理，以及利用基因晶片分析技術來解析致癌基因複雜的調控關係，探討基因表現或基因突變與細胞反應的關連。長遠的目標為藉由基因體研究找尋特定的癌症分子指標，將來作為癌症治療與診斷的標的。

The focus of our laboratory is using genomic approaches to investigate the mechanisms of carcinogenesis. DNA microarray has been applied widely in simultaneously monitoring a large quantity of gene expression patterns and served as a convenient, quick, and reliable method to investigate specific gene regulation. Therefore, our lab devotes to the application of microarray technology in the biomedical field. Interests in our laboratory include microarray fabrication, image capture and analysis, bioinformatics, database management, and analytic technique to understand the complicated regulatory mechanisms of cancer related genes as well as the correlation between gene expression or gene mutation and cellular response. Our long-term goals are via genomic study to identify specific cancer molecules as biomarkers for the targets of cancer therapy and diagnosis.

主要研究領域 Major Research Areas

生物晶片、生物資訊、癌症生物、輻射生物
Biochip, Bioinformatics, Cancer Biology, Radiation Biology

研究計畫 Research Projects

1. 研究不同輻射敏感性之肺癌細胞受輻射誘導後之基因表現改變以及探討 Notch pathway 如何影響肺癌細胞CL1-0與CL1-5 之輻射敏感性
2. 微核醣核酸調控機制與其作用標的之預測
   Target prediction and regulation of microRNAs
3. 乳癌經放射治療、化學治療或合併治療後分子特徵之比較
   Comparison of molecular signatures in Breast cancer following chemo- and/or radiotherapies
4. 優勢重點領域拔尖計畫-醫學卓越研究中心-生物資訊暨生物統計核心實驗室
   Bioinformatics and Biostatistics Core Facility
5. 以基因體方式篩選台灣非吸菸女性肺癌病患染色體上變異及基因表現改變
   Genome-wide screening of genomic alteration and transcriptional modulation in non-smoking female lung cancer in Taiwan.

計畫名稱：以基因體方式篩選台灣非吸菸女性肺癌病患染色體上變異及基因表現改變
補助單位：行政院衛生署
計畫期間：2007/05-2010/04

肺癌是國人十大死因之一，也是國人最常罹患的癌症，在台灣的肺癌死亡率更高居世界之冠。吸菸經常被認為是導致肺癌的主要因素。但研究結果發現，只有大約7%的台灣女性肺癌病患有抽菸的病歷，明顯低於美國女性肺癌病患抽菸的比例。因此吸菸行為不能解釋台灣女性之高肺癌發生率，也因此台灣非吸菸女性肺癌之病因仍需進一步探討。雖然有研究證實烹煮時產生的油煙會引起細胞內的COX-2的表現，進而引起肺癌;許多研究也發現EGFR基因突變的機率在台灣非吸菸女性肺癌偏高，但也只能解釋50%左右的台灣女性肺癌病例。由於癌症的形成是由許多分子機制共同參與，因此要了解台灣非吸菸女性肺癌的病因，需要對肺癌細胞內的基因進行大尺度的分析。目前已知癌症的發生和細胞內致癌基因(Oncogene)與腫瘤抑制基因(tumor suppressor gene)的表現量改變有密切相關，而基因的複製及缺失直接影響基因的表現。此外，染色體的重組除了引起染色體倍數不平衡，也可能導致基因重組而形成具有致癌特性的蛋白質。為了進一步了解台灣非吸菸女性肺癌的致病機制，我們希望藉由microarray能進行大規模基因體的優勢，對台灣非吸菸女性肺癌組織內的基因表現及基因倍數上的變異進行篩檢。利用array CGH 搜尋染色體倍數的變異，以及利用DNA microarray來解析基因表現的改變，並利用high-resolution tiling arrays近一步鑑定發生變異的染

色體區域上特殊基因的改變及確定發生染色體轉移的位置。找到新的基因指標會用於分析新的女性肺癌病患，對指標的準確性作為近一步確認。藉由這些分析所提供的分子特徵及基因指標，用以發展更準確的診斷與預後方法，並尋找新的治療方法。

Project title: Genome-wide screening of genomic alterations and transcriptional modulation in non-smoking female lung cancer in Taiwan
Supported by: Department of Health, Executive Yuan
Project period: 2007/05-2010/04

Lung cancer is the leading cause of cancer mortality in most countries, including Taiwan. The rate of increase in the mortality of lung cancer in Taiwan is the highest in the world. Smoking is usually considered to be the major risk factor for lung cancer, since about 90% of lung cancer worldwide can be related to cigarette smoking. However, only 7% of female lung cancer patients in Taiwan have a history of cigarette smoking, extremely lower than the percentage of the female lung cancer patients in the United States. Smoking behavior cannot well explain the exceptional epidemiologic characteristics of the lung cancer women in Taiwan. Thus, the etiology of lung cancer for non-smoking females in Taiwan remains unknown. Numerous reports have shown that the patients with lung diseases history or exposure to cooking oil fumes which can induce the expression of COX-2 have high risk of tumorigenesis. Other reports have also observed that epidermal growth factor receptor (EGFR) gene mutations are frequently detected in lung cancer, especially in females and non-smoking patients. However, EGFR gene mutations are only observed in about 50% of the non-smoking lung cancer females, and thus the conclusion that a significant relationship between EGFR gene mutations and non-smoking female lung cancer patients cannot be made. Moreover, carcinogenesis appears to result from the aberrations of multiple molecular pathways, genomic- scale analyses will be essential to reveal the etiology of non-smoking female lung cancer. Cancer appears to result from the progressive accumulation of genetic aberrations and genomic rearrangements leading to fusion proteins with oncogenic properties and chromosome copy number imbalances. Microarray technology provides a powerful tool to conduct genome-wide analysis of chromosome copy number variations and gene expression profiling analysis. For better understanding of the molecular mechanisms of non-smoking female lung cancers in Taiwan, we will use aCGH to identify chromosome copy-number changes, DNA microarray to elucidate the differences of gene expression, and high-resolution tiling arrays to determine specific gene changes as well as translocation events in identified altered chromosome regions. New bio-markers identified from those analyses will be used to assay new patients for further validation. Therefore, more accurate detection methods at diagnosis and prognosis and new molecular targets for therapy of non-smoking female lung cancer patients in Taiwan can be developed based upon the molecular signatures generated from this study.

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目前已利用whole-genome sampling analysis (WGSA)，完成6個檢體初步之GeneChip Mapping 500K分析，在染色體5p附近有三組樣本在相同區域有DNA高度複製的狀況，進一步研究這些區域發現SKP2, GDNF, NF-kappaB 基因與前人研究肺癌形成有關。並依GeneChip Human Genome U133 Plus 2.0基因表現之初步結果，發現140個於肺癌檢體與正常組織表現有顯著不同表現的基因。經IPA綜合分析GeneChip Mapping 500K與基因表現的結果，顯示染色體變異區域上的基因確實與癌症的形成有相關性。

We have completed the SNP analysis of 6 specimens by Microarray GeneChip Mapping 500K chip. We found that DNA high amplification regions at the chromosome 5p in three samples. We further investigated the potential genes of these alteration regions. Genes encoding S-phase kinase-associated protein 2 (SKP2), Glial Cell Line-Derived Neurotrophic Factor (GDNF), Nuclear transcription factor kappaB (NF-kappaB) in chromosome 5p were found in previous lung cancer-related studies. Regarding the gene expression, we found that 140 genes were expressed differently between lung cancer tissue and normal tissues. By using the IPA analysis, we found that genes in high amplification regions of chromosome 5p are involved in many pathways including cancer, cellular growth and proliferation.

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成立於2000年7月，指導教授為鍾孝文教授，目前計有博士班研究生16名，碩士班研究生1名。博士班畢業生17名，碩士班畢業生12名。目前進行中的研究主要有以下幾項：

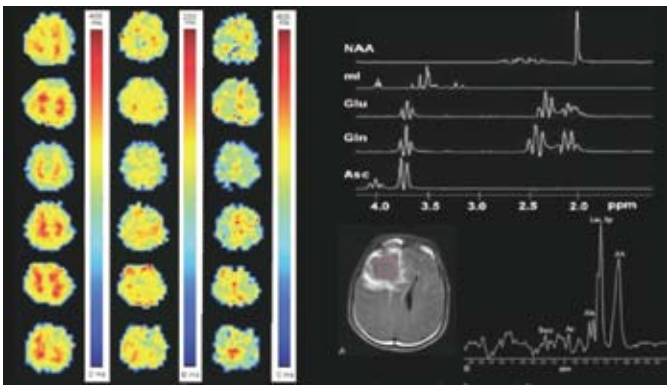
1. 抗壞血酸之臨床磁振頻譜檢測技術開發
   抗壞血酸為人體內重要的抗氧化劑。本計畫預期以虛擬滴定、純量偶合頻譜編輯、巡弋迴訊運動校正等方式進行人體氫原子核磁振頻譜之活體腦部抗壞血酸檢測，並探討其精確度。
2. 數據共享之動態磁振造影加速。

本計畫針對動態磁振造影，擬以影片壓縮演算法、多心跳週期Unpack技術等數據共享法則，研發一系列動態影像加速擷取與影像重建之技術，以加速五至八倍為目標，並適用於型態變異與對比改變兩種不同之模式。

Founded in July 2000. Supervisor: Prof. Hsiao-Wen Chung. This lab currently (2010) has 16 Ph.D. students and 1 M.S. student, plus 17 Ph.D. graduates and 12 M.S. graduates. Research topics include:

1. MR spectroscopic techniques for ascorbic acid detection.
   Ascorbic acid is an important anti-oxidant in the human body. This project aims to use virtual titration, J-coupling spectral editing, and navigator echo motion correction techniques to explore the accuracy of proton MRS for ascorbic acid detection in the human brain in vivo.
2. Acceleration of dynamic MRI via data sharing.

This project proposes data sharing methods using video compression principles and multiple cardiac phase Unpack techniques to reconstruct dynamic images with accelerated acquisition. Methods suitable for either morphological variations or contrast changes are developed, aiming at acceleration factors up to 5 or 8.



主要研究領域 Major Research Areas

醫用磁振造影
Biomedical magnetic resonance imaging

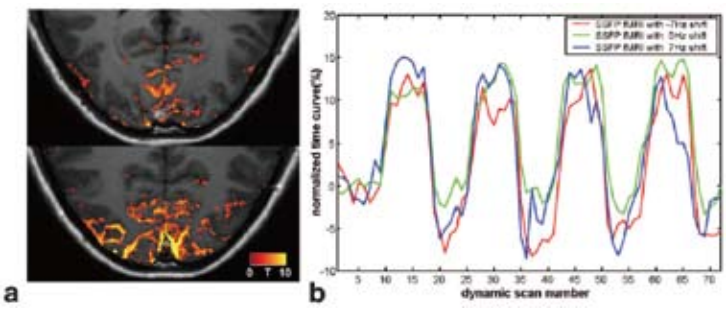
研究計畫 Research Projects

1. 快速穩定態磁振造影及其臨床應用之進階研究
   Advanced investigations on rapid steady-state free precession MRI and clinical applications.
2. 抗壞血酸之臨床磁振頻譜檢測技術開發
   Developments of clinical magnetic resonance spectroscopic techniques for the detection of ascorbic acids.

計畫名稱：平衡穩定態磁振造影之功能性神經影像
補助單位：行政院國家科學委員會
計畫期間：2007/08/01-2010/07/31

本計畫為三年期前瞻性研究。重點在於針對極小角度之平衡穩定態磁振造影(BOSS)，研發一系列可突破實驗瓶頸之關鍵技術、探討空間解析度與平行影像暫態信號響應、並以高解析度實驗驗證技術研發之潛在優勢，從而應用於高磁場(3.0 Tesla)無幾何扭曲的大腦功能性磁振造影。三年間計畫之特定目標為：一、發展出多頻率葉片式內插混成技術，以增寬BOSS fMRI之空間涵蓋度。並研發切面性頻率調整法，針對事前選擇之特定區域從事功能性對比之最佳化。本階段將以視覺皮質刺激實驗結果技術發展之優勢。二、以高解析度(像素寬度小於0.5mm)視覺BOSS fMRI 探討空間解析度對於資訊特異性、信號雜訊比、以及功能性對比之影響。並進一步以平行影像加速掃瞄，同時探究暫態響應信號之功能性影像表現。三、以研發完成之高解析度無扭曲BOSS fMRI 進行：(一)左右眼視覺之大腦皮質功能活化區分野實驗，與(二)不同手指運動之雙側大腦皮質功能活化區分野實驗，由此驗證BOSS fMRI 技術發展之重要性與優勢潛力。本計畫之預期成果，較之現行常用之面迴訊影像，將能有效提高腦功能磁振造影在探討細部活化區方面之可行性；較之以往穩定態成像法，則得以增寬空間涵蓋率、並提高實驗穩定度。因而得以協助未來神經功能影像之進一步進展。

Maximum intensity projection combination of the high-resolution brain functional activation maps from visual stimulation experiments using three interleaved frequencies, showing activation regions located exactly on the microvessels in the sulci (a). The activation signals for the high-resolution experiments reached the level of 15% for all trials, reflecting the effectiveness of partial-volume reduction by high-resolution BOSS fMRI with the infinite-impulse-response-filtered frequency stabilization (b).



（左圖）由葉片式頻率混成、經由最大亮度投影合併三次實驗所得到的高解析度視覺刺激腦功能活化區圖譜，顯示出功能活化區域均精確對位於腦溝處之小血管。（右圖）功能性活化信號靈敏度在每次實驗中都達到 15%，反映出以 IIR 濾波器作為頻率穩定技術後所達成之高解析度影像得以有效減低部分體積效應。

Project title: Balanced steady-state free precession MR imaging techniques for functional neural imaging

Supported by: National Science Council
Project period: 2007/08/01-2010/07/31

This is a three-year prospective project aiming at the exploration of distortion-free techniques for blood-oxygenation-sensitive steady-state (BOSS) functional MRI (fMRI) of the brain at 3.0 Tesla. We shall attempt technical developments to increase experimental robustness, investigate the signal behavior under different conditions, and perform high-resolution fMRI experiments to demonstrate the unique advantages of BOSS fMRI. Chronologically, the specific aims are: 1. We shall develop a multi-frequency interleaving method to widen the spatial coverage of BOSS fMRI, and a slice-dependent frequency adjustment method to optimize the functional contrast with respect to the pre-selected region of interest. Experiments using visual stimulation will be performed to visualize the technical advantages. 2. We shall explore the effects of spatial resolution on the information specificity, signal-to-noise ratio, and functional contrast in BOSS fMRI by performing visual fMRI at in-plane pixel width of 0.5mm or smaller, plus a further increase in temporal resolution using parallel imaging along with a comprehensive investigation of transient-state signal behavior. 3. We shall attempt the application of distortion-free high-resolution BOSS fMRI to examine the activation patterns in (1) ocular dominance column using visual stimulation to left and right eyes separately, and (2) bilateral motor cortex activation upon movement of different fingers, to fully explore the overall benefits of technical improvements in BOSS fMRI. Compared with EPI-based fMRI, the anticipated results from this study should substantially increase the feasibility of detailed structural examination of the fine activation pattern. Compared with current steady-state-based fMRI, the anticipated results from this project should widen the spatial coverage with increased experimental robustness. The overall advantages in BOSS fMRI provide strong potential enhancing future neural functional imaging.

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數位相機與電腦視覺實驗室
Digital Camera and Computer Vision Lab.

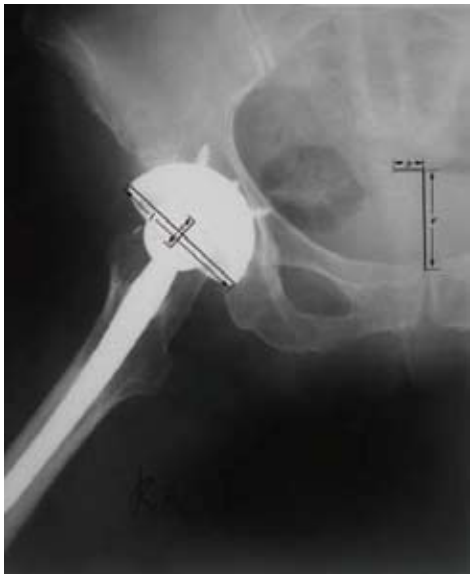
本實驗室由傅楸善教授成立於2003年，主要從事數位相機與電腦視覺相關研究。歷年來已執行多項研究計畫，目前以生醫數位相機、影像處理與自動光學檢測等領域為研究重點。本實驗室在上述領域已產出許多具體貢獻並在全世界有很高之能見度。此外，本實驗室之成員來自電子、資訊及醫學等各領域，多年來亦積極與國內外單位進行合作，合作夥伴包括產、研、學各界，例如：光寶科技、致伸科技、太欣半導體、創惟科技、由田新技、德律科技等。提升數位相機與自動光學檢測技術及其生醫應用，是本實驗室之成立宗旨與具體目標。

Digital Camera and Computer Vision Laboratory was founded by Professor Chiou-Shann Fuh in 2003, with the main research focus in digital camera and computer vision. In the past few years, we have conducted a number of research projects in digital image processing and automatic optical inspection. We have also made several critical contributions and are now one of the most visible research laboratories in this field in the world. Members of the laboratory come from various backgrounds, including electronics, informatics, and medicine. We have also been actively collaborating with research laboratories throughout the world, covering industry, research institutes and universities, from basic sciences, engineering to clinical research, such as Liteon, Primax Electronics, Genesys Logic, Syntek Semiconductor, Utechzone, and TRI. Integrating multi-disciplinary research efforts, exploring advanced digital camera with biomedical applications, and automatic optical inspection is the mission of this laboratory.

主要研究領域 Major Research Areas

數位相機、電腦視覺、自動光學檢測、數位影像處理
Digital Camera, Computer Vision, Automatic Optical Inspection, Digital Image Processing

研究計畫 Research Projects



1. 數位相機之影像處理：降低雜訊、光線補償、臉色改善
   Image Processing for Digital Cameras: Noise Reduction, Light Compensation, Facial Color Enhancement
2. 數位相機之影像處理：色彩內插、色彩校正、色彩管理
   Digital Image Processing for Camera: Color Interpolation, Color Calibration, Color Management
3. 行動視訊高畫質顯示調適技術
   High Quality Display Adaptation Technique for Mobile Video Device
4. 視訊會議使用的相機陣列
   Camera Array for Video Conferencing

計畫名稱：數位相機之影像處理: 降低雜訊,光線補償, 臉色改善
補助單位：行政院國家科學委員會
計畫期間：2009/08/01-2012/07/31

本計畫為期三年、目的是研究利用電腦視覺與數位影像處理方法，進行數位相機降低雜訊(Noise Reduction)、光線補償(Light Compensation)、臉色改善(Facial Color Enhancement)之研究。在計畫執行期間，我們將探討最佳的攝影機、光源、環境、景物及色彩的互動，第一年研究適合不同感應器(Sensor)與影像訊號處理器(ISP: Image Signal Processor)的最佳降低雜訊方法；第二年研究最適合的光線補償演算法使拍出來的影像不管是在太暗或太亮的場景下都能得到對比很清楚，層次很分明的影像；第三年研究各種臉部瑕疵及顏色的改善方法，不管是雀斑、青春痘、膚色暗沈等，改善數位相機擷取的原始影像，使得每張影像都精采，每個主角都漂亮且滿意。並突破日本及美國在這三方面的專利及技術障礙，提高我國的數位靜態相機，相機模組及視訊攝影機在國際市場的競爭力。

Project title: Image Processing for Digital Cameras: Noise Reduction, Light Compensation, Facial Color Enhancement
Supported by: National Science Council
Project period: 2009/08/01-2012/07/31

This is a three-year project to use computer vision and digital image processing methods for noise reduction, light compensation, and facial color enhancement of digital cameras. We will study the best camera, light source, environment, scene, and color interaction. In the first year, we will develop various noise rduction methods for different sensors and image and signal processors (ISPs) to achieve optimum noise reduction. In the second year, we will research the best light compensation algorithm to achieve images with good contrast and shading even under too bright or dark scenes. In the third year, we will research various facial defect and color enhancement methods to develop programs and algorithms so that freckles, acnes, skin darkness, and incorrect color and be enhanced and eliminated from digital camera raw image and achieve beautiful subject faces and satisfactory images for each shot. We would like to break the patent and technology barriers of Japanese and American companies and to enhance and competitiveness of Taiwan companies in international markets.

階層式降雜訊:

Imagenomic Noiseware、高頻、邊、金字塔、低頻、抹平滑，希望發展成適合即時內嵌式硬體實現。

Hierarchical Noise Reduction, Imagenomic Noiseware, High Frequency, Edge, Pyramid, Low Frequency, Smoothing, Aim for Real-Time Embedded Hardware Implementation.

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主要研究領域 Major Research Areas

乳房外科、乳房超音波檢查、腫瘤外科、分子流行病學
Breast Surgery, Breast Ultrasound, Tumor, Molecular Epidemiology

研究計畫 Research Projects

1. 微核醣核酸調控腫瘤進展的微環境因子與分子機制--微核醣核酸在乳癌轉移的角色探討
2. 全基因體關聯研究找到的單一核甘酸基因多形性變異與乳癌危險性，分子類型與預後的關係
3. 自動乳房超音波之電腦輔助診斷
4. 以乳房超音波及乳房攝影術進行台灣40-49歲婦女乳癌篩檢隨機試驗
5. 乳房彩色彈性超音波之電腦輔助診斷
6. 雙波段紅外線乳房影像系統之三維模型建立與血管增生定量分析
7. 乳房磁振造影電腦輔助偵測與功能性評估系統之研發
8. 家用型雙波段乳癌紅外線診斷系統
9. 微流體平台進行藥物篩選與化療療效監測
10. 經前婦女可切除乳癌之CYP19(TTTA)重複多型性研究
11. 多國多中心、開放性、分為兩組的第三期試驗，評估 bevacizumab 輔助性治療對三項標記陰性乳癌之療效
    BEATRICE (Protocol BO 20289): An international multicentre open-label 2-arm phase III trial of adjuvant bevacizumab in triple negative breast cancer
12. 隨機分配、多國多中心、第二階段的臨床試驗，針對局部晚期、發炎性，或早期 HER2 陽性之乳房腫瘤的病人， 評估trastuzumab 合併 docetaxel對trastuzumab 合併 docetaxel 及pertuzumab對trastuzumab 合併 pertuzumab治療
    A randomised, multicenter, multinational Phase II study on trastuzumab plus docetaxel versus trastuzumab plus docetaxel plus pertuzumab versus trastuzumab plus pertuzumab in patients with locally advanced, inflammatory or early stage HER2 positive breast cancer
13. 以Herceptin單一或合併Taxane療法作為第一線使用在先前HER2呈陽性初期乳癌時曾接受Herceptin輔助性治療後復發的轉移乳癌患者之第二階段臨床試驗
    Phase II study of HFerceptinÒ, alone or in combination with a taxane, as a first-line treatment for patients with metastatic breast cancer, who have relapsed after receiving Herceptin in the adjuvant setting for HER2 positive early breast cancer

14. 以Lapatinib、Trastuzumab及其組合併用paclitaxel輔助治療罹患HER2/ErbB2陽性原發性乳癌婦女之隨機、多中心、開放性第三期臨床試驗
    A randomised, multi-centre, open-label, phase III study of neoadjuvant lapatinib,trastuzumab,and their combine plus pailtaxel in women with HER-2/ErbB2 positive prrimary breast cancer
15. 一項隨機、多中心、開放性、第三期臨床試驗、研究連續與合併使永輔助性之Lapatinib與Trastuzumab於治療HER2/ErbB2陽性之原發性乳癌病患
    A randomised, multi-centre, open-label, phase III study of adjuvant lapatinib,trastuzumab, their sequence and their combination in patients with HER2/ErbB2 positive primary breast cancer
16. 第三期隨機分配之臨床試驗：比較黃體期或濾泡期進行卵巢切除術併用Tamoxifen用於停經前婦女荷爾蒙受體陽性轉移性乳癌之療效
    Phase III randomizated study of luteal phase vs follicular phase surgical oophorectomy and tamoxifen in premenopausal women with metastastic hormone receptor- positive breast cancer

計畫名稱：以乳房超音波及乳房攝影術進行台灣40-49歲婦女乳癌篩檢隨機試驗
補助單位：行政院衛生署國民健康局
計畫期間：2003/12/01-2009/12/31

台灣地區40-49歲婦女乳癌的問題相當重要，國內婦女乳癌發生率之高峰較國外年輕，主要集中在45-55歲，且年輕族群的乳癌發生率每年以相當驚人的速度在成長。然而有鑒於乳房攝影術較不適用於50歲以下之婦女，是否可使用超音波篩檢來提高效益，是相當值得探討的問題，雖然在臨床上已有許多文獻支持，不過這些發現都是基於臨床病人，而其接受超音波或乳房攝影術的原因(Indication)並非全來自篩檢，部份是因為已有症狀（如腫塊）。所以超音波檢查是否較乳房攝影術對於早期乳癌發現效益更大，亟待實證醫學評估。

本計畫之主旨在利用臨床隨機試驗證明乳房超音波與乳房攝影術對台灣地區40-49歲婦女乳癌之篩檢效益。在此研究計劃中之目的如下所述：

(一) 針對40-49歲設計一個以族群為主的隨機試驗，對乳房攝影術及乳房超音波進行下列比較：
篩檢方法敏感度及精確度比較，敏感度指標有三：
1. 相對敏感度指標：計算在診斷為乳癌個案中各種篩檢工具診斷為異常者之比例
(包括localized benign及疑似個案)
2. 計算篩檢12個月後篩檢間隔個案佔所有個案比例
3. 計算在篩檢後1年及2年內篩檢間隔個案佔基本發生率之比例

(二) 比較乳房超音波及乳房攝影術+超音波篩檢工具對於病人回診率之差異

(三) 比較兩種篩檢工具降低第二期癌症或以上之效益

(四) 比較兩種篩檢工具降低乳癌死亡率之效益

本計畫共分五年進行，內容包括進行研究中心臨床隨機分配、組織及倫理面(Organization and Ethical Aspect)、社區公共衛生資源動員(Mobilization of Community Resources)、臨床篩檢轉介、確診流程作業標準化、大規模邀請及進行乳房攝影術與超音波篩檢(Large-scale Mass Screening)、研究中心、參與醫院、及衛生局所資訊系統之建立、早期評估超音波及乳房攝影術之轉介、回診、確診狀況、敏感度及精確度、臨床隨機分配三組間早期效益（如第二期癌症以上降低）之比較、及預測兩種篩檢（乳房超音波及乳房攝影術）乳癌死亡率之降低情形。

Project title: A population-based cross-over randomized controlled trial of breast cancer screening with alternate mammography and ultrasound for women aged 40 to 49 years in Taiwan

Supported by: Bureau of Health Promotion, Department of Health
Project period: 2003/12/01-2009/12/31

Background: As there is paucity of data on population-based screening for breast cancer using mammography and ultrasound for oriental young women aged 40-49 years, the peak of incidence rate and high proportion of dense breast, we aimed to evaluate the relative performance of detecting breast cancer between ultrasound and mammography and also to assess complementary efficacy of ultrasound to mammography screening.

Methods: A total of 79,691 female residents aged 40-49 years were invited from community in Taiwan since late 2003. These participants were first randomly assigned to mammography (n=20040), ultrasound (n=20088), and control group (n=39563). The two former groups were further done by a cross-over design with mammography and ultrasound on alternate year until 2008. Detection rate and annual incidence rate of interval cancer as a percentage of the control group (I/E ratio) were compared between mammography and ultrasound.

Results: The attendance rate of the first round was 59% (11921/20040) for mammography and 56% (11249/20088) for ultrasound. The repeated attendance rate of both groups was 85% in the second round and 91% in the third round. In the first round of screen, the detection rate of breast cancer for the mammography group (0.34%) was 1.5-fold compared with the ultrasound group (0.22%). The additional detection rate was 0.16% contributed from a subsequent ultrasound screen and 0.36% contributed from a subsequent mammogram screen. The combination of mammography with ultrasound was as three to four times as likely to detect breast cancer compared with the control group (annual incidence rate was 0.17%). The I/E ratio was lower after mammography screening than that after ultrasound screening.

Conclusion: The current randomized controlled trial not only demonstrated higher detection rate and better performance using mammography but also indicated the complementary role of ultrasound applied to young Taiwanese women. This further suggests the optimal screening modality for young women in Asian country is to combine mammography with ultrasound

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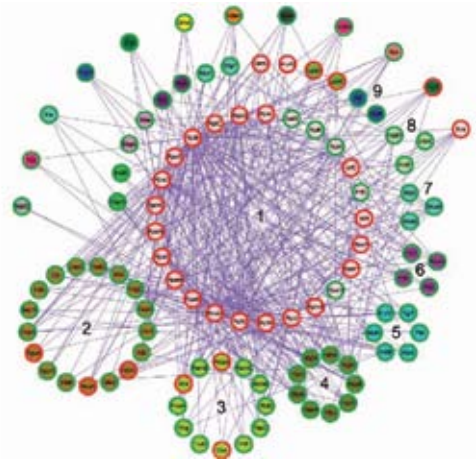
Systems Biology Lab.



本研究室主要以系統生物學探討藥物在癌細胞的作用機制，內容包括各蛋白質間交互作用的預測和建構、基因網絡的模擬和建構，及微型RNA於其調控的蛋白質間交互作用及網路關係，期望進一步達到開發新藥的目地。主要的目標是利用系統生物學研究法來研究在ATP 合成酶抑制劑誘導下乳癌及肺癌細胞進行細胞凋亡的作用機制；同時，利用系統生物學研究法來開發新的藥物。

本研究室目前也利用系統生物學於能源開發上。*Rhodopseudomonas palustris(R. palustris)*是一種紫色非硫光合細菌，能轉換二氧化碳成為體內所需能量。我們以系統生物學來研究*R. palustris*的代謝路徑，描述和了解複雜的*R. palustris*生物系統如何運作，並將之應用於生質能源技術平台之研發。

The main research in our lab is to apply systems biology for drug-discovery. We discover novel drugs for cancer therapy and investigate the molecular mechanism of apoptosis in drugs-induced cancer cells using systems biology approach.

The other topic in our lab is to apply systems biology for energy-savvy microbes. *Rhodopseudomonas palustris (R. palustris)* obtains the energy necessary for hydrogen production through photosynthesis driven by the "free" supply of sunlight. We elucidate the functional genome of *R. palustris* using systems biology approach; then apply the results to develop biomass energy technological platform.

主要研究領域 Major Research Areas

系統生物學、蛋白質體學、生物資訊
Systems Biology, Proteomics, Bioinformatics

研究計畫 Research Projects

1. 調控 ATP 合成酶基因之微RNA 功能及演化
   Evolution and functions of microRNAs that regulate ATP synthase subunit genes
2. 幽門桿菌感染胃癌細胞之基因網路研究：annexin A4相關的訊息傳遞及調控機制
   Gene network of host cell by Helicobacter: annexin A4 involved singalling and regulation in gastric cancer.
3. 利用系統生物學開發抗肺癌藥物：以ATP 合成酶抑制劑進行標靶治療及機制探討
   Applying systems biology for anti-lung cancer drug discovery: targeting therapy by ATP synthase inhibitors and molecular mechanism study

計畫名稱：調控ATP合成酶基因之微RNA 功能及演化
補助單位：行政院國家科學委員會
計畫期間：2010/08/01-2013/07/31

ATP 合成酶是由DNA解旋酶和氫離子馬達結合，藉由氫離子梯度使馬達旋轉，而驅動ATP合成，這樣的旋轉機制在演化過程中效率漸增。因為ATP合成酶是一個古老的蛋白質，探討是否早在後生動物演化時，就已出現微RNA調控ATP合成酶次單體基因的現象，是一個相當有趣的議題。這些微RNA是否對這些次單體基因的表現程度有不同的影響？此影響是否會引起這些次單體表現量的平衡？我們想知道不同的微RNA是否會在相同的時間點被啓動，而當ATP合成酶的表現大量受到微RNA抑制時對細胞造成的結果又是如何？

本計畫主要的目標是要探討在演化上微RNA於ATP合成酶次單元基因調控中所扮演的角色。

特定目標：

1. 預測並實證調控人類ATP合成酶次單體基因的微RNA。
2. 闡明這些微RNA是否對ATP合成酶次單體表現程度有不同的影響，及其所造成的生物性結果為何？是否會抑制癌細胞生長？
3. 研究在動物演化的過程中，調控ATP合成酶次單體基因的微RNA及其調控網路何時被啓動？
4. 找出影響調控ATP合成酶次單體基因的微RNA轉錄因子。在動物演化過程中，這些因子何時被啓動去調控這些微RNA？

在本研究計畫中，我們期望能夠了解調控ATP合成酶次單體基因的微RNA及其網路於動物演化過程中所扮演的角色。此研究也許有助於釐清微RNA於演化的重要性。

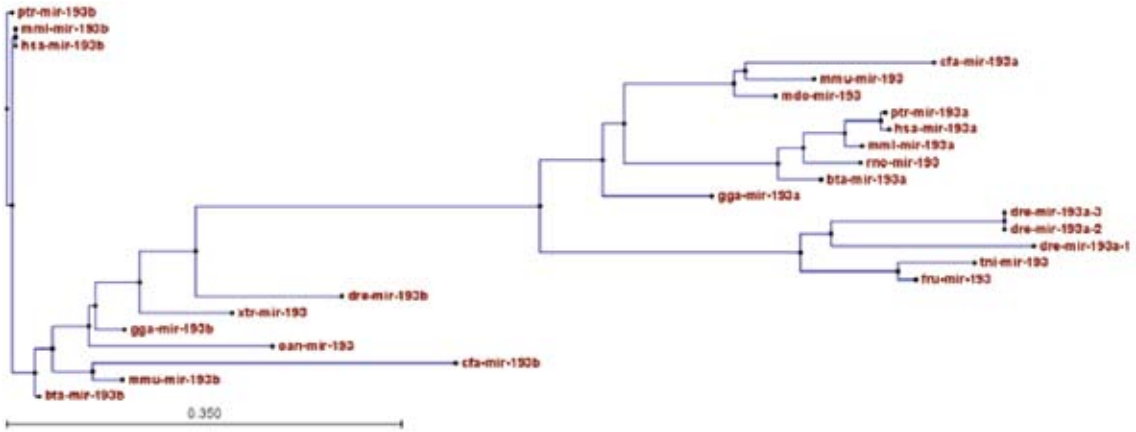
Project title: Evolution and functions of microRNAs that regulate ATP synthase subunit genes
Supported by: National Science Council
Project period: 2010/08/01-2013/07/31

ATP synthase is a multimeric protein complex that catalyzes the synthesis of ATP. It is essential for almost all organisms because ATP is the common "energy currency" of cells. The modular evolution theory for the origin of ATP synthase suggests that two subunits with independent functions, a DNA helicase with ATPase activity and a H+ motor, were able to bind together, so the rotation of the motor drive the ATPase activity of the helicase in reverse. This would then evolve to become more efficient, and eventually develop into the complex ATP synthases seen today. Since ATP synthase is such an important protein and since it is a complex with many subunits, we are curious as to whether ATP synthase is regulated by many miRNAs. Although protein complex subunit genes tend to be less regulated by miRNAs, our predictions suggest that some ATP synthase subunit genes are targets of different miRNAs. In view of the fact that ATP synthase is an ancient protein, it is interesting to ask whether the miRNA regulation of subunit genes arose early in metazoan evolution. Another question is whether these miRNAs have very different effects on the expression levels of subunit genes, a situation that would pose a problem of dosage balance among the subunits. Indeed, when a subunit gene becomes a new miRNA target, how is the dosage balance among subunits maintained? We therefore ask if the different miRNAs were recruited at similar times. A natural question to ask is what the consequences are when the express level of ATP synthase is substantially reduced by miRNAs. A simple test is to see whether it can suppress cancer growth.

Our major objective is to provide much detail on how the role of miRNAs in ATP synthase subunit gene regulation has been expanded in evolution, especially in the lineage leading to human. Our specific aims are:

1. To predict and validate miRNAs that regulate human ATP synthase subunit genes.
2. To elucidate whether these miRNAs have very different effects on ATP synthase subunit expression levels, what are the biological consequences when the ATP synthase level is significantly reduced by miRNAs and whether it can suppress cancer growth.
3. To study when these miRNAs were recruited to regulate ATP synthase subunit genes during animal evolution and how their regulatory networks have evolved?
4. To find out the transcription factors (TFs) that regulate the key miRNA genes regulating ATP synthase subunit genes. To address the questions: "when were these TFs recruited to regulate the key miRNAs?" "Were they recruited at similar times or at very different times during animal evolution?"

With the proposed study, we expect to understand the roles of the miRNAs that regulate ATP synthase subunit genes in the evolution of regulatory networks during animal evolution. It may provide in-depth information on the impact and importance of the evolution of miRNAs.



The homologous miR-193a/b precursor sequences from different species and the phylogenic tree.

本圖顯示調控ATP合成酶次單體基因的微RNA miR-193a/b前驅物在不同物種的演化關係。

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本實驗室的研究主軸為生物資訊與台語文研究。在生物資訊方面，本實驗室將遺傳演算法與組合最佳化應用到生物問題上，解決各式各樣的問題。包含微陣列分析、蛋白質結構預測、蛋白質交互作用預測、藥物探勘與設計、虛擬藥物篩選等等。這些不同的研究主題，又能夠結合成為系統生物學，從更宏觀的系統角度來看生物問題，並將研發成果，轉譯到臨床醫學與藥物開發設計上。在台語文研究方面，本實驗室致力於台語文的計算語言學研究，包含台語文的輸入（光學文字辨識）與輸出（台語文語音合成）。未來希望能加入其他的元件，讓台語文能夠和電腦密切結合，協助母語教育與文獻研究。

The research focuses of this laboratory are bioinformatics and Taiwanese research. In bioinformatics, our lab apply genetic algorithm and combinatorial optimization to biological problems, solving problems from microarray analysis, protein structure prediction, protein-protein interaction prediction, drug discovery and design, and virtual screening of drug leads. These diverse topics can also be combined into systems biology, study biological problems from a global view. We also tried to translate our researches into applications in clinical medicine and drug developments. In Taiwanese research, we have devoted to the computational linguistics of Taiwanese, including input (optical character recognition) and output (Taiwanese voice synthesis). In the future, we would like to incorporate other elements, and construct a more integrative Taiwanese-computer environment, and facilitate the education of mother tone and archival research.

主要研究領域 Major Research Areas

生物資訊、計算分子生物學、基因演算法

Bioinformatics, Computational Molecular Biology, GA- Based Computing Technologies

研究計畫 Research Projects

計畫名稱：網路生物學整合分析平台之建構與應用

Construction and Application of Intergrated Network Biology Analysis Platform

補助單位：行政院國家科學委員會

計畫期間：2009/08/01-2011/07/31

本計畫之目標為研發生物標記分析的相關技術並建立平台雛形，在這個計畫中，需要具備兩個基本功能，第一、建立性狀基因關連性資料庫，該資料庫將以生物醫學文獻為基礎，找出疾病風險／性狀－基因之間的關連；第二，提供一個微陣列資料分析平台，從公開及自行產生的生物晶片資料，分析出與檢體性狀有關的基因表現，並提供這些基因參與的訊號傳遞或代謝路徑資訊，以便於後續計畫中，發展用於基因檢測的生物標記，或治療標的。

最近幾年新發展的全基因體關連性 (whole genome association, WGA) 研究，以單一核酸變異 (single nucleic polymorphism, SNP) 為基礎，找尋哪些 SNP 與性狀之間有關連性，由於 SNP 是單一核酸的變異，因此觀察具有關連性的 SNP 位於哪些基因區段內，通常就可以推斷基因與性狀之間的關連性。

微陣列分析平台包含多項後端資料庫：蛋白質交互作用資料庫，同源蛋白質資料庫，組織特異表現資料，基因資訊與基因註解資料，訊號傳遞路徑資料等。在初期實作過程中，也應用於多項不同應用。這些應用可分為三類：致病原與宿主交互作用預測，關連性基因排序，與組織特異表現基因分析。

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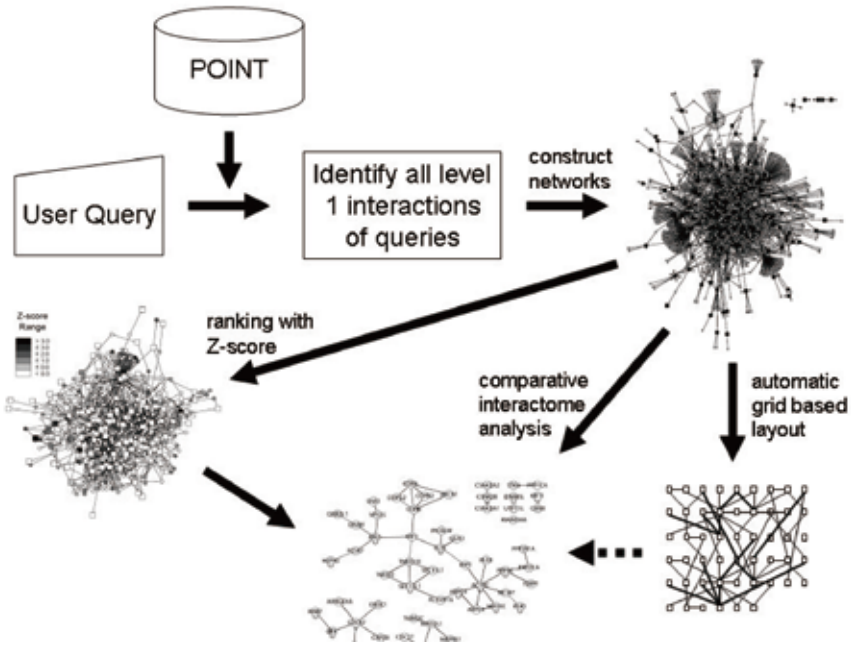
Project title: Construction and Application of Intergrated Network Biology Analysis Platform
Supported by: National Science Council
Project period: 2009/08/01-2011/07/31

This project is to build a platform for research of biomarker and its related technologies. There are two main functions in this project: one is constructing a connective database of genetic trait, groundwork from biomedical literatures, to dig out the relationship between disease and genetic trait; the other is providing a platform of microarray with its data from the public domain or the cooperators to analyze gene expression of patients' samples. It also suggests information of signal transduction or related metabolic pathway of these genes. Finally, the aim is for detection of biomarker or remedy target by these two foundations.

SNP (Single Nucleic Polymorphism) is an essential basis of WGA (Whole Genome Association) in the recent developments. An important issue is to research the relationship between SNP and genetic trait. Due to the nature of SNP, single mutation of nucleotide, the connectivity of genetic trait usually could be discovered among genetic sections on chromosome in which SNP locates.

Microarray analysis platform contains several data types of database: protein-protein interaction, protein of homologue gene, genetic data or annotation by genes and tissues, and information of signal transduction on pathway. In this project, two applications are to be provided: ranking of connective genes, genetic analysis in specific tissues of tumor.



利用 POINT 的蛋白質交互作用資料，發展數種策略以找出生物網路中的重要節點。
Starting from the protein-protein interaction data in POINT, several strategies have been developed to identify important nodes in a biological networks.

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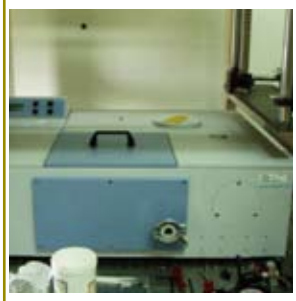
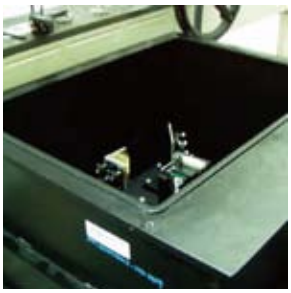
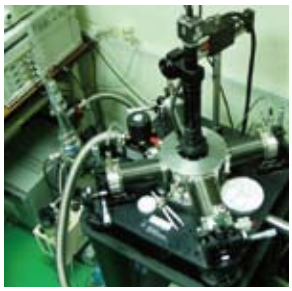
  (Direct-Writing Electron Beam Lithography System Lab., Scanning Electron Microscope Lab.)
- 微拉曼/光激發光 光譜實驗室 (Micro-Raman/PL Spectral Lab.)
- 紅外線光譜實驗室 (Infrared Spectral Lab.)

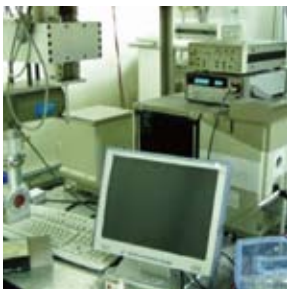


Bruker FTIR 紅外線光譜儀及變角度反射模組

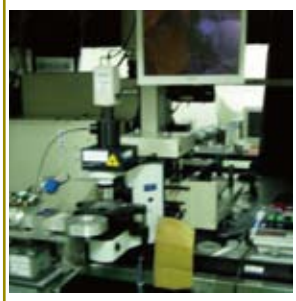




電晶體特性曲線實驗器



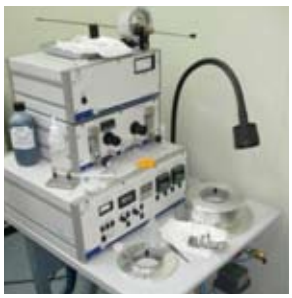
FTIR 紅外線光譜儀



具XY平面定位掃描功能之T 64000微光譜量測儀（預計新增3D共焦顯微鏡）

電子束微顯影系統

聚焦離子束顯微鏡（FIB）



Cryo-SEM

主要研究領域 Major Research Areas

光電元件、雜訊量測、奈米電子、生醫晶片、拉曼光譜分析、利用拉曼光譜做極稀薄分子之光學檢測
Optoelectronic Device, Noise Measurement, Nano-Electronics, Bio-medical Chip, Raman Spectral Analysis, Optical Detection of Ultra-Rare DNA by Raman

研究計畫 Research Projects

1. 矽鍺量子點奈米級記憶元件及陣列之製作與研究
   Nano-scale SiGe quantum-dot memory and array
2. 可低偏高溫操作且正向頂面入射的超晶格紅外線偵測器及陣列的研發
   Development of the Superlattice Infrared Photodetector and Array for Low-Bias High-Temperature Operation and Top Normal Incidence of Light
3. 光譜與電性量測於基因篩選之應用
   Application of spectrum and electrical signal measurements on gene screening
4. 窄頻紅外線光源與偵測器及其在植物與神經細胞上的應用
5. 離子的高敏感度交流電性量測並以紅外線頻譜作輔助分析(2/3)
   High-sensitivity AC electrical signal measurement and infrared spectrum assistant analysis originated from ions
6. 整合雙能障超晶格及量子井紅外線偵測器以達到高偵測率高響應及高溫操作
   Integration of double-barrier superlattice and quantum well infrared photodetectors for advantages of high detectivity, high responsivity,and high-temperature operation

計畫名稱：離子的高敏感度交流電性量測並以紅外線頻譜作輔助分析
補助單位：行政院國家科學委員會
計畫期間：2007/08/01-2010/07/31

傳統微電泳通道外加電場普遍為直流電源，在電壓持續提供下，會造成單方向電荷持續累積，此意味著量測環境將隨電荷累積持續變化，降低量測結果重複性。我們採用交留訊號量測方式使量測環境形成規律之充放電反覆循環，避免電荷持續累積，並確保量測環境不隨時間改變，以將雜訊成分降到最低，同時可大幅提高訊號／雜訊比。藉由待測分子在交流響應中表現出來之相位延遲，精準擷取出複數形式的響應延遲，再將此同一機制下產生之虛部除以實部，得到各種不同待測分子之特徵響應。此種以鎖相放大器量測系統進行之量測，可實現高敏感度，依此構想期望研發一種新型生物分子ID建立方式。

在本計畫中，我們以快速成型技術製作樹脂晶片基板，設計封閉式微電泳通道元件，以改善先前之玻璃基板半導體製程所遭遇的水溶液蒸發問題；並利用不銹鋼光罩作為阻擋，經過角度計算後，可將流道兩端之金薄膜電極作均勻且厚度精確之電子束垂直蒸鍍，確保每個微電泳槽量測結果的準確性。經過這些改良後，實部與虛部電流之趨勢均較先前穩定。而前一年度使用的樣品中，雖然分子各自具有不同的離子質量比，但由於幾何結構均不同，增加分析的困難。所以我們選用結構簡單、完全解離的鹼金屬化合物：氯化鈉、氯化鉀、溴化鈉、溴化鉀。

我們將先前推導出的模型對彈力常數項作修正，配合數值方法的計算改良，目前的模擬已經相當精準；而在我們的推導中發現，離子間存在一個隨濃度上升而增加的群聚庫侖作用力，此力會將正負離子吸引一起，我們也希望用此來解釋溶液濃度高到一個程度時，會有結晶析出之現象。另外我們利用物理觀點解釋模擬參數過程中發現，較大質量的離子阻尼因子較小；反之較小質量的離子阻尼因子大，此發現可解釋化學

界中利用水合能觀念闡述釋離子在水中的等效質量變化，以及大小離子在水中感受到不同的阻力等。這個實驗與模擬的相符性對於日後人體諸多慢性病成因的研究與體內相關結晶的形成的研究，提供一個嶄新的觀點及方向。

關鍵詞：交流訊號、訊號／雜訊比、相位延遲、鎖相放大器、快速成型技術、離子質量比、群聚庫侖作用力、阻尼因子、等效質量、微電泳通道元件、離子運動。

Project title: High-sensitivity AC electrical signal measurement and infrared spectrum assistant analysis
Supported by: National Science Council
Project period: 2007/08/01-2010/07/31

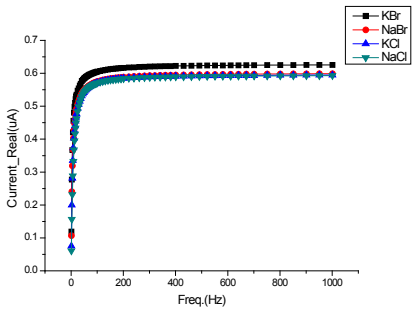
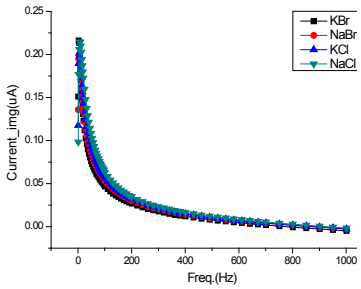
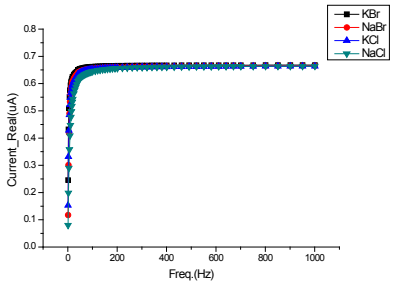
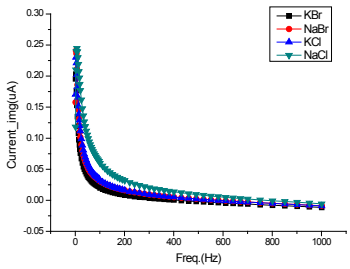
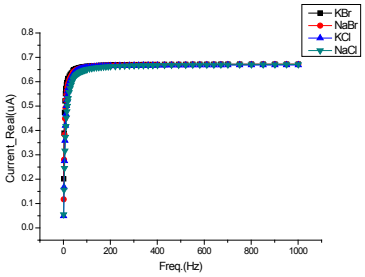
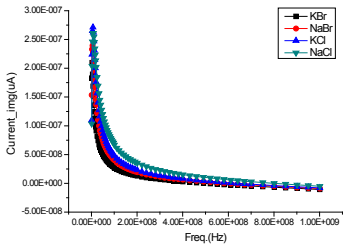
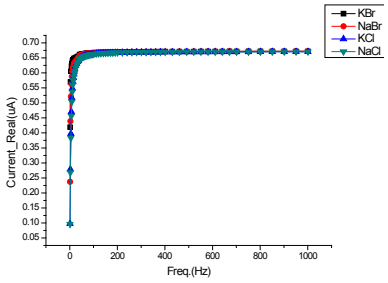
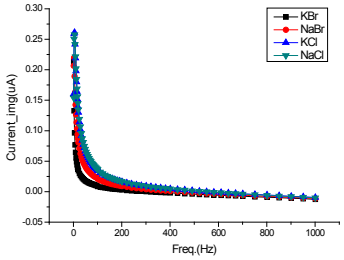
Conventional micro-electrophoresis channel devices are usually applied with DC field, with continuous voltage supply; charge accumulated at one direction, which reduces data reproducibility. We decide to utilize AC which can lead to regular charge recycling in micro-channel and avoid charge accumulation. It ensures that the lowest noise exist in this environment and therefore increase the S/N ratio. By measuring the phase delay of molecules under AC response, we can acquire data in a form of complex number. We can also calculate the individual response by dividing imaginary part with real part, both signals generated in the same mechanism. This measurement system implemented a lock-in amplifier in advance and which can measure with high-sensitivity. We expect to develop a novel biomolecular ID establishment from the new idea.

We use rapid prototyping (RP) technology to fabricate the resin chip substrate with a cover slide as a close-ended chip to avoid evaporation. We also utilize the stainless mask as a blocker, by precise angle calculation, we can evaporate uniform gold thin films as electrodes on two opposite sidewalls to guarantee the accuracy of every microchannels. In our samples used last year, each chemicals possesses individual M/m ratios, but there exists different geometrical structures; which increases analysis difficulities. So we choose an alkaline metal compound set: Sodium Chloride (NaCl), Potassium Chloride (KCl), Sodium Bromide (NaBr), and Potassium Bromide (KBr), all are simple structures and completely ionized.

We also modified our previous model in spring constant (k), combine with improvement of numerical methods calculation, we can get more accurate simulation results. In our model derivation, we have found a coulomb force between ions that will change with increasing concentration, this force will attract positive and negative ions together, we hope to use this to explain, when the high concentration to a degree, the solution will be the crystallization phenomenon.

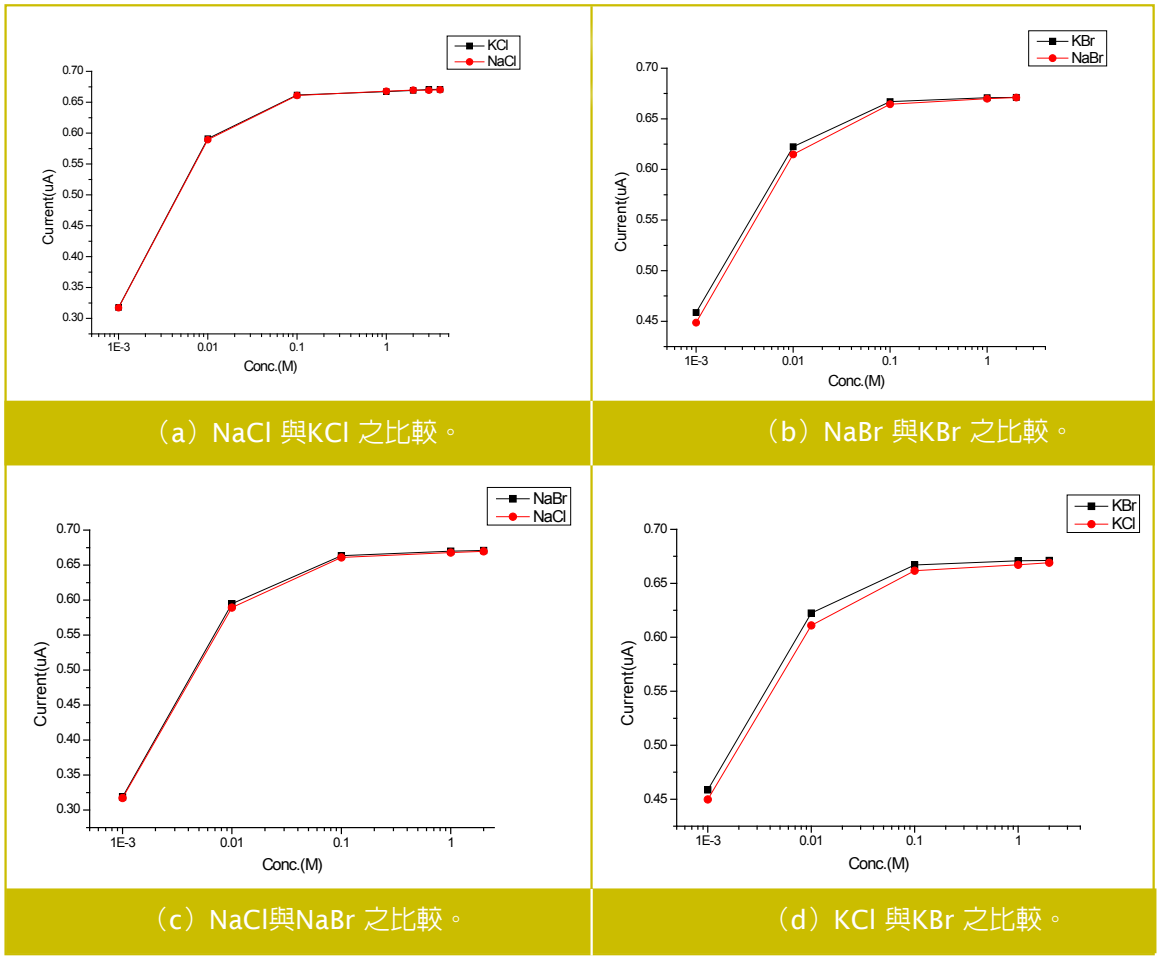
We expect to elucidate the behaviors of ion movement in solution. During the process of simulating parameters explanation, we observed that heavy ions possess smaller damping factor, and small ions possess a large one, respectively. This breakthrough can be interpreted in conventional chemical industry. The use of hydration to the concept to explain the equivalent ions in the water quality changes, and size of the ions in the water can feel a different resistance. The consistency of our experiment data and simulations provides a new version and prospects in realizing some chronic diseases due to related crystal formation in human bodies.

Keywords：AC signal, S/N ratio, phase delay, lock-in amplifier, rapid prototyping (RP) technology, M/m ratio, collective coulomb force, damping factor, micro-electrophoresis device, ion movement.

	（a）實部電流（J_x）	（b）虛部電流（J_y）
0.01 M		
0.1M		
1M		
2M		

【代表圖一】不同濃度之四種鹼金屬鹽類水溶液交流響應對時間圖：
（a）實部電流（J_x）（b）虛部電流（J_y）。

Fig.1 The AC current responses of four different alkaline metal salts solution.
（a）Real part currents（J_x）and（b）Imaginary part currents（J_y）.



（a）NaCl 與KCl 之比較。

（b）NaBr 與KBr 之比較。

（c）NaCl與NaBr 之比較。

（d）KCl 與KBr 之比較。

【代表圖二】頻率300 Hz之下，四種鹼金屬鹽類解離之電流對濃度相互比較之關係。

Fig.2 Intercomparison of AC current versus concentration of four different alkaline metal salt solutions in 300 Hz.
（a）Real part currents（J_x）and（b）Imaginary part currents（J_y）.

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細胞行為實驗室
Cell Behavior Lab.

細胞行為實驗室主要研究課題，在於瞭解細胞間如何使用物理性因子通訊，並互相調節功能。我們特別對細胞間的機械力和光學訊號傳遞感到興趣。因為相對僅能靠擴散方式作用的化學物質而言，力學和光學訊號的作用範圍更遠，傳遞速度也較快。因此在大範圍組織整合的初始過程，包括組織發育、修補、以及退化，光學和力學訊號可能扮演了具有相當決定性的角色。目前我們研究重點是同質細胞間的自我聚合及功能整合，以及異質細胞間的空間協調，特別是中、外胚層細胞間的分層現象。我們的短期目標是發展出能精確測量、並調控細胞間力學與光學通訊的實驗平台。遠程目標則是促進吾人對異質細胞間在各種生理、病理狀態下的交互作用，並對組織老化及再生的治療方針上有所啓益。

The primary interest of the cell behavior lab is to investigate cell-cell communication via various biophysical factors. Specifically, we examine how cells regulate each other using mechanical and optical signals. Compared with biochemical agents that are primarily transmitted through diffusion, mechanical and optical signals are relatively long-ranged and transmitted at a faster time scale. Hence these signals may play a deterministic role in the initiation of tissue organization at a large spatial scale such as tissue development, regeneration, and degeneration. Currently we are studying the self-aggregation and integration of homogenous cells, as well as the spatial coordination of a complicated cellular network composed of heterogeneous cells, specifically the stratification between mesenchymal and epidermal cells. Current cell model involves muscle, dermal, and endothelial cells. Our short term goal is to develop a novel platform that can detect and modulate the mechanical and optical cues communicated between cells. The long term goal is to improve our understanding in cellular interactions of heterogeneous cells in various physiological and pathological conditions, and shed light on the therapeutic strategy in tissue regeneration and degeneration.

主要研究領域 Major Research Areas

細胞交互行為、組織型態學、醫用生物物理、復健工程、組織工程

Cell-cell interactions, tissue morphogenesis, medical biophysics, rehabilitation engineering

1. 肌肉細胞間機械力通訊對細胞結構及行為之影響
   Effects of cell-cell mechanical crosstalk on the structure and behaviors of muscle cells
2. 智慧型非侵入陣列式血流監控系統晶片--子計畫六：以非侵入陣列式系統晶片監控頸動脈血流動力—力學模型及臨床評估
   Access hemodynamics of carotid arteries using a non-invasively array-based SOC — Mechanical modeling and clinical applications

計畫名稱：肌肉細胞間機械力通訊對細胞結構及行為之影響
補助單位：行政院國家科學委員會
計畫期間：2010/02/01-2011/07/31

一般認為肌肉細胞間的機械力訊息交換，在肌肉組織的整體結構、個別細胞型態表現，以及細胞之間的行為協調方面，扮演著極重要的角色。然而囿於實驗技術，科學界對肌肉細胞之間，如何以機械力訊息來互相調節結構及行為，仍所知有限。我們計畫發展一新穎的實驗系統，以研究機械力訊息交換對橫紋肌肉細胞型態學、及行為表現的影響。該系統將由二至數個未直接相連的肌肉細胞組成，並以微圖案技術控制個別細胞的初始型態、相對位置、細胞軸向等。同時以特殊方法阻斷或加強細胞之間的力學訊息交換。此外我們還將利用雷射光化學反應來激發選定細胞的自發性收縮，並據以調整其收縮頻率。我們將分析在各種機械力學條件下，細胞間機械力訊號對特定細胞動態學的影響，包括細胞遷移、細胞結構及型態重組、鈣離子波的傳遞、細胞自發性收縮的時域特徵、以及多細胞的整體性行為表現，例如循特定方位的細胞凝集、多細胞間細胞骨骼的重組耦合、以及多細胞同步收縮等。我們並將配合分子生物方法，研究細胞間力學通訊如何調節肌肉細胞的電生理活動。我們也將探討在各種拓樸環境條件下，例如改變相近細胞個數、細胞相對位置、細胞相對軸向，以及三度空間環境等，對上述細胞動態學的影響。本實驗系統初期將針對橫紋肌肉細胞研究，之後研究對象將拓展至異種細胞間的機械力相互作用，例如腫瘤細胞與纖維母細胞，內皮細胞與平滑肌肉細胞等。最後，我們將發展數學模型來解釋實驗結果，並推測機械力通訊調節細胞行為表現的生物物理機轉。本三年計畫的完成，將發展出一套專門探討肌肉細胞間機械力通訊如何影響細胞型態、以及電生理活動的特殊實驗技術與系統。我們相信這些實驗成果，將促進其他針對細胞間通訊如何影響生物型態、生物頻率等方面的基礎研究，包括瞭解在生理及病理狀態下，生物組織、器官、系統的發展過程，以及幹細胞的分化研究等。

Project title: Effects of cell-cell mechanical crosstalk on the structure and behaviors of muscle cells

Supported by: National Science Council
Project period: 2010/02/01-2011/07/31

Cell-cell mechanical communication is proposed to intimately regulate the structure and electrical behaviors of muscle cells. Our understanding in this regard however is severely limited by the technical challenging in single cell experiments. In this project we propose to develop an in vitro system to investigate the effects of intercellular mechanical crosstalk on the structure and behaviors of striated muscle cells. The system will allow manual removal and reestablishment of mechanical continuities between the cells, tuning of substrate stiffness, and controllable adjustment of the intercellular distance. Experiments are conducted on pairs of mechanically isolated cells as well as multi-cellular networks. The electrical response of a single cell resulting from mechanical cues derived from neighboring cells will be also investigated. We will initially focus our cell model on striated muscle cells. Later, the effects of mechanical interaction on heterogeneous cell culture, such as cancer cells and fibroblasts, endothelial cells and smooth muscle cells, will also be probed. Finally, we will develop a mathematical framework that can quantitatively explain the experimental observations and propose physical mechanisms underlying tissue morphogenesis in the physiological and pathological conditions.

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生物醫學信號實驗室
Biomedical Signal Lab.

生物醫學信號實驗室隸屬生醫電資所電子組，以復健科技與生物醫學信號分析為主要的研究範疇。本實驗室常年與大型醫療院所保持密切合作，並合力執行多項獲國科會高度正面評價與積極補助之跨領域整合型計劃。本實驗室將電子資訊技術引進至醫學輔具之研發中，進行電子醫學輔具之研究，並屢有佳作。本實驗室現已自行研發成功可商業化生產之肌肉功能性電刺激器，另致力於神經功能性電刺激器的研究，用於控制大鼠泌尿系統，以探討哺乳類動物泌尿控制機制。

另本實驗室在健康照護機制與系統的研究上，進行可應用於復健醫學、預防醫學、家庭醫學、急救醫學、神經醫學等方面之遠距照護系統，本實驗室於數年前即已體認到虛擬實境技術之引進將在電子醫學領域中帶來相當程度的革新。故而本實驗室早已著力於虛擬實境介面技術之開發，本實驗室除進行生物體未知信號之分析與研究，望對現代醫學診斷與分析上提供技術層面的協助外，並以人本為基石，以開發輕便、簡單、低成本的電子醫學輔具為目標。

Biomedical Signal Lab focuses on rehabilitation assistance and analysis of biomedical signals. Our lab has cooperated with medical research institutes closely for several years. In last decade, our lab had implemented the commercial functional electrical stimulation (FES) system which was proved too. With our designed muscular FES system, the paraplegics or hemiplegics with serious disabilities have greatly progressed in their activity in daily life. In addition, we are also devoted to researches of FES applications in urinary incontinence by conducting animal experiments for solutions of mammalian neurogenic detrusor overactivity.

Our lab also studies health-care mechanism and system applied in rehabilitation medicine, preventive medicine, and emergency medicine. Our lab had been aware of the potential of virtual reality applied in rehabilitation, and an innovated rehabilitation assistance combined with virtual game was developed successfully for frozen shoulder patients in past years. In biomedical signals processing and analyzing, our laboratory has made great progress. Our mission statements include not only focusing on techniques helps for modern medical diagnoses and analyses, but also keeping developing simple, easy to use, low cost electrical medical assistances.

主要研究領域 Major Research Areas

生理信號之量測與處理、以數位信號處理器為基礎之醫療儀器、復健科技輔具研發、健康照護系統

Bio-medical signal acquisition and processing, Medical instruments based on Digital Signal Processor (DSP), Technical rehabilitation assistance, Health-care system

研究計畫 Research Projects

1. 老人居家健康照護之心靈互動夥伴(healing partner)系統
   Healing Partner System for the Elderly Healthcare at Home
2. 會陰神經電刺激用於調控大白鼠排尿功能
   Modulation of voiding function by electrical stimulation of pudendal nerves in the rat

計畫名稱：老人居家健康照護之心靈互動夥伴(healing partner)系統 (II)
補助單位：行政院國家科學委員會
計畫期間： 2009/08/01-2010/07/31

面對老人易出現記憶力退化，慢性病與慢性功能障礙的出現率上升等醫療相關議題，本計劃團隊認為老人居家健康照護的重點包括如何對其日常生活中的健康提供協助居家照護的功能: 例如跌倒防治；提醒老年慢性病患須定時且正確服用藥品；協助排除老年人因慢性病痛或長期壓力而造成的失眠；或監測到睡眠時血氧若低於警戒值，則立即啓動緊急通報醫療體系或通知其家人，並注意睡眠障礙、姿勢性低血壓、發燒與早晨起床後的中風等危險。既為排解老人寂寞，同時提供完善的老人健康照護系統。本計劃針對

(1) 床旁陪伴
(2) 用藥提醒
(3) 睡眠監測
(4) 生理監測

等等老人心靈與生理方面之居家健康照護需求，建立一套功能簡便、易於操控、低成本的老人居家健康照護之心靈互動夥伴系統。此系統將整合多種生理感測器(體溫、 血壓、血氧等) 、可攜式小尺寸顯示器、下床偵測裝置、取藥偵測開關；且擁有危險分級分類制度與通報機制。將根據生理參數異常程度、正確準時用藥與否、有無下床逾時不回或自行呼救等因素來進行危險分級分類，根據不同危險級數，決定是否立即透過網路端的監控台通報醫護人員與老人家屬去電關切、前往探視或進行救護行動。本系統尚可依照個人需求進行客製化修改，透過與虛擬家人親友影像的互動，藉由聽、視、及動作來增加老人對感官的刺激，並維持老人腦部的敏感及警覺度，改善社區老人的憂鬱程度，使其擁有良好的生活品質，以及更為健康快樂的人生觀。

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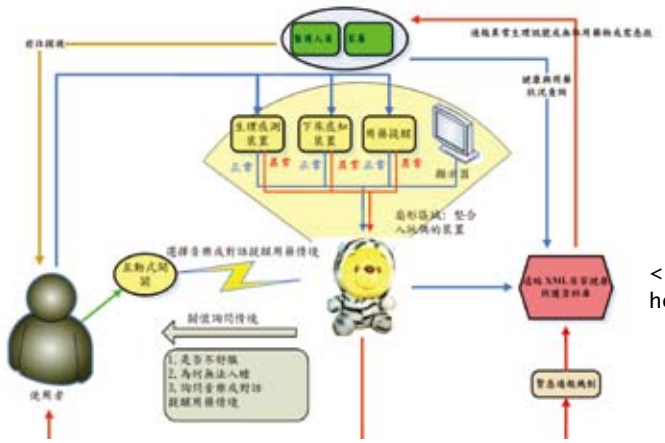
Project title: Healing Partner System for the Elderly Healthcare at Home (II)
Supported by: National Science Council
Project period: 2009/08/01-2010/07/31

The elderly often suffer from impaired memory, degenerative diseases, and multiple dysfunction in their daily living. This project proposes the practical solution for these healthcare issues for the elderly at home. These healthcare issues include the prevention of falling in night, the reminding for taking medicine correctly on time, the assistance for alleviating insomnia, the monitoring for vital signs such as blood pressure, body temperature, and blood oxygen saturation at the appropriate time , the connection & activation of the emergency alert system for immediate attention or rescue. That means a user-friendly healing partner system can help the elderly reducing these risks of emotional disturbance, inappropriate medication, sleep disorder, postural hypotension, fever, and fall after waking up, etc. This project is developing a user-friendly healing partner system to provide the following healthcare functions at home for the elderly which includes

(1) the psycho-emotional partner near the bed,
(2) the reminders for taking medicine correctly on time,
(3) the detection for sleep disorders (insomnia and sleep apnea),
(4) the monitoring for vital signs (body temperature, blood pressure, & arterial oxygen saturation).

Depending upon the severity and urgency of alert classification it will be connected to the emergency alert system for informing the medical staff and/or the family to pay attention and/or rescue the elderly if abnormal vital signs, fall, or life threatening situation detected by the system. The system can be customized for different individuals. The system also provides virtual characters with family looks and speeches to interact with the elderly. The interactions, like listening, seeing, and acting, may augment and excite the sensitiveness and alertness of the elderly. By the above-mentioned healthcare at home, this system may release the emotional disturbance such as loneliness, tension, anxiety, & depression, improve the social life, raise the life quality, and bring more benefit for the elderly, too.



<圖1> The illustrations of the healing partner system

本圖顯示為老人居家健康照護之心靈互動夥伴系統。為老人日常生活中的健康提供協助居家照護的功能。

The foregoing figures illustrate a tailored healing partner system that provides practical solution for common healthcare issues for the elderly at home.

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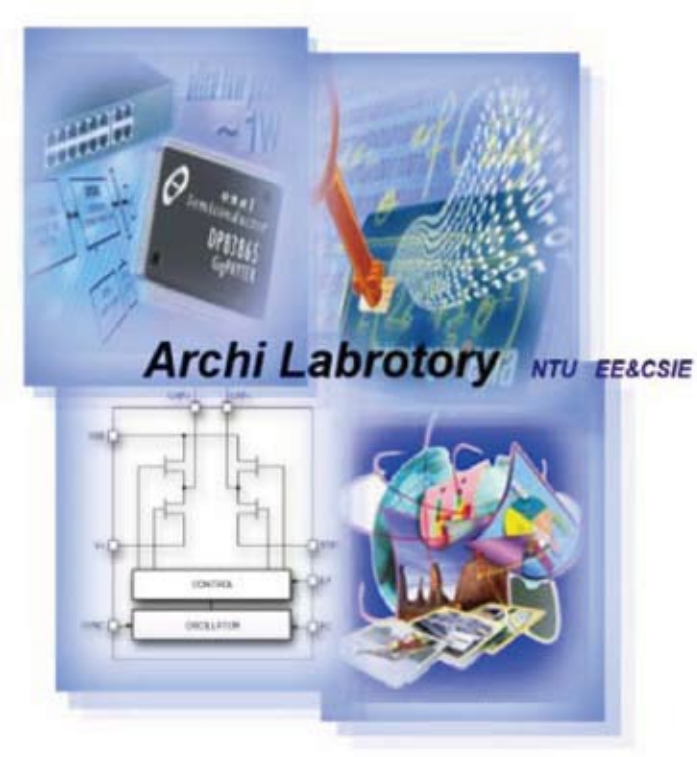
醫學資訊實驗室
Medical Informatics Lab.

本實驗室成立於1987年，由賴飛羆教授所領導的研究群組成。實驗室成員包括博士班和碩士班研究生28名。本實驗室研究領域廣泛，實驗室創立初期以研究 計算機結構，低功率系統晶片設計 為主，近年來改以 醫學資訊為主要目標，此外，目前本實驗室的成員也致力於參與臺大醫院醫療資訊系統之相關研究及開發，本實驗室的研究方向包含：

1. 低功率系統晶片設計與分析
2. 電腦與通訊網路安全機制研究
3. 醫療資訊系統

This lab. was established in 1987 and Professor Feipei Lai works together with 13 Ph.D. students and 15 master students. The major research area of the lab. includes Low Power SOC Design, Security, and Medical Information System. Our members participated in the research and development of the medical information system in Nation Taiwan University Hospital. Besides, our lab has cooperated with numerous IT companies and other overseas universities including Dortmund University in Germany, Calgary University in Canada and Mongolian University of Science and Technology.



主要研究領域 Major Research Areas

低功率系統晶片設計、資訊安全、醫療資訊系統
Low Power SOC Design, Information Security, Medical Information System

研究計畫 Research Projects

1. 自動化低功率及低漏電流 內容可定址記憶體 產生並模擬及驗證工具集(2009/08/01-2012/07/31)
   An automatic tool set for generating, simulating and verifying low power and low leakage content addressable memory
2. 開放式知識探勘平臺 (2009/08/01-2012/07/31)
   Sharable Knowledge Mining Platform
3. 醫療資訊探勘 (2009/08/01-2012/07/31)
   Data Mining on Healthcare

計畫名稱： 開放式知識探勘平臺
補助單位： 行政院國家科學委員會
計畫期間： 2009/08/01-2012/07/31

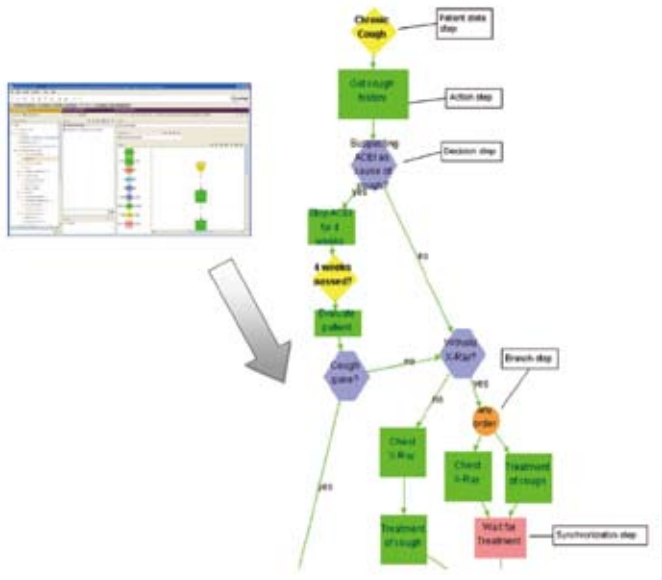
醫療資訊系統的價值在於協助醫護人員用較快速度及較少的成本處理醫療事務，可讓組織有效率的運作發揮組織最大的功能，造福更多病患；隨著資訊系統長期運作，在系統背後累積大量的電腦化數據，如能進一步進行資料探勘，則可將原始資料(Data)轉化成有用的知識(Knowledge)，產生更大的附加價值；例如分析醫令順序以及檢驗、檢查內容可以探勘出臨床路徑(Clinical pathway)及臨床指引(Clinical guideline)，如此能進一步提升醫療品質及降低醫療成本。如能採用醫療資訊相關標準進行研究平台的建立，則研究成果可分享給其他的醫療機構應用。就台大醫院而言，其醫療案例既多且廣，已具初步資料探勘所需資料，且台大醫院之醫療資訊系統遵循HL7、DICOM、ICD 等國際標準，若能以此資料庫及標準化的系統為基礎建立研究平台，並將研究成果以標準化的方式表示，則能將此成果分享給其他醫療機構。另一方面，其他醫療機構之資料也能經標準化的格式傳輸至此研究平台，使用平台上的資料探勘、知識發現等模組。

關鍵詞：醫療資訊系統、資料探勘、知識發現、臨床路徑、臨床指引

Project title: Sharable Knowledge Mining Platform
Supported by: National Science Council
Project period: 2009/08/01-2012/07/31

The basic value of health information systems is to support medical related workers to deal with their jobs more quickly and with less cost. Then, the health information systems can let organization operate more efficiently and get its best efficiency. Finally, the systems can bring a great benefit to patients. With the operation of the information system for a long time, there is a great amount of computerized data stored in the system. After doing data mining focused on these data, we can extract knowledge from these databases and bring more and more additional value. For example, if we analyze the sequence of the medical orders and the content of the laboratory and observation and we can extract the knowledge about the clinical pathway and clinical guideline. Therefore, we can improve the quality of the health care and reduce the cost. If the research platform is built based on medical related standards, then the research results can be shared to other medical related institutions. There are numerous and various cases in the NTUH (Nation Taiwan University Hospital), and the database contains the needed data used by data mining. Besides, the health information system in NTUH follows many international standards such as HL7, DICOM and ICD. If we can build the research platform based on the database and the standardized systems, then we can share the study results to other medical institutions. On the other hand, other medical institutions can upload their data to the platform through many standardized format of transmission, and then they can use the module of data mining and knowledge discovery in the platform.

Keywords: health information system, data mining, knowledge discovery, clinical pathway, clinical guideline



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統計信號處理實驗室
Statistical Signal Processing Lab.

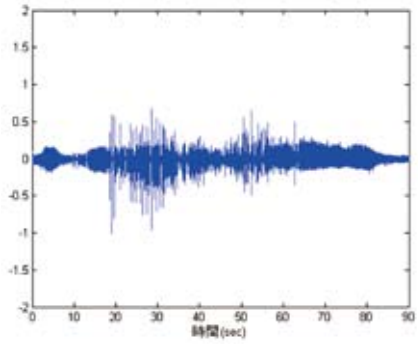
本實驗室由李枝宏教授負責成立於1986年，主要研究領域為數位信號處理之理論與技術研發，近年來也積極進行應用數位信號處理之理論與技術於生醫領域之相關研究：包含(1)由國立臺灣大學醫學院骨科部提供人體膝關節病變與運動傷害所產生之振動訊號，應用相關信號處理理論研發建立此振動訊號之數學模型的技術，以協助臨床上分析診斷人體膝關節病變與運動傷害之型態與種類，以期提供醫生進行正確且必要醫療措施所需之資訊。(2)由國立臺灣大學獸醫學系提供馬匹膝關節病變與老化所產生之振動訊號，應用相關信號處理理論研發建立此振動訊號之數學模型的技術，以協助臨床上分析診斷馬匹膝關節病變與老化之型態與種類，以期提供獸醫生進行正確且必要醫療措施所需之資訊。(3)由國立臺灣大學醫學院牙科部提供人體顳顎關節病變所產生之振動訊號，應用相關信號處理理論研發建立此振動訊號之數學模型的技術，以協助臨床上分析診斷人體顳顎關節病變之型態與種類，以期提供醫生進行正確且必要醫療措施所需之資訊。目前進行的研究希望利用此特性進而更精確的找出膝關節振動訊號的特徵，進而發展實用簡單方便的非侵襲性關節診斷系統。

I. BASIC DIGITAL SIGNAL PROCESSING：
   (1) Techniques for the Design and Implementation of 1-D and 2-D FIR and IIR Digital Filters.
   (2) Techniques for Design and Implementation of 1-D and 2-D FIR and IIR Digital Filter Banks (Multi-rate Digital Signal Processing)

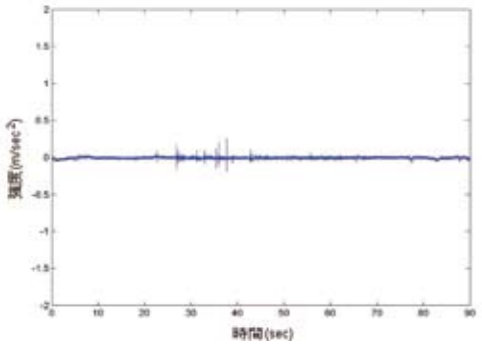
II. STATISTICAL DIGITAL SIGNAL PROCESSING：
   (1) Adaptive Signal Processing for Array Signals
   (2) Adaptive Array Beamforming Under Random Mismatches
   (3) Adaptive Array Bearing Estimation Under Random Mismatches
   (4) Adaptive Beamforming Using 2-D Circular Array for Wireless CDMA Systems
   (5) Adaptive Minimum Bit Error Rate Beamforming Assisted Receiver for Wireless Communications
   (6) Adaptive Signal Processing Techniques for Smart Antennas with Applications in Wireless and Mobile Communications

III. PROCESSING AND ANALYSIS OF BIOMEDICAL SIGNALS ：
   Analysis and Processing of Joint Vibration Signals for the Diagnosis of Cartilage Pathology
   (1) Signal Processing Techniques for Vibration Signals of Human Knee Joints
   (2) Signal Processing Techniques for Vibration Signals of Equine Knee Joints
   (3) Signal Processing Techniques for Vibration Signals of Human emporomandibular joints

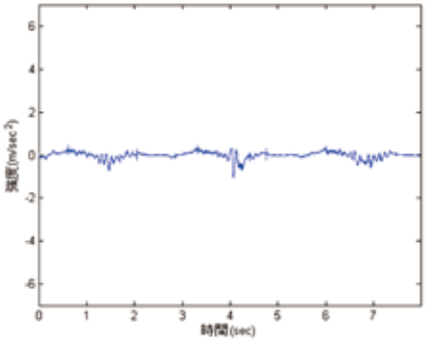
Goal of this research: To conduct research on Vibration Arthrometry (VAM) and provide the public a noninvasive, accurate tool (Expert Systems) for the diagnosis of joint disorders in clinical medicine.



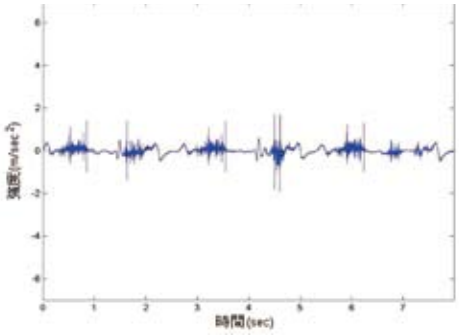
(A) 正常著膝關節在慢速擺動下所產生的振動訊號 (Physiological Patellofemoral Crepitus;PPC)



(B) 非正常著膝關節在慢速擺動下所產生的振動訊號 (Physiological Patellofemoral Crepitus;PPC)



(C) 正常著膝關節在快速擺動下所產生的振動訊號 (Vibration Arthrometry;VAM)



(D) 非正常著膝關節在快速擺動下所產生的振動訊號 (Vibration Arthrometry;VAM)

主要研究領域 Major Research Areas

數位信號處理、智慧型天線與無線通訊信號處理、生醫信號處理、數位影像處理
Digital Signal Processing, Signal Processing for Smart Antennas and Wireless Communications, Biomedical Signal Processing, Digital Image Processing

研究計畫Research Projects

1. 應用於視訊信號處理之二維副頻帶濾波器組之設計
   Design of Two-Dimensional Subband Filter Banks with Applications to Video Signal Processing
2. 應用於通訊環境下可適性陣列信號處理理論與技術之研究
   Theory and Techniques for Adaptive Array Signal Processing Under Communication Environments

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李嗣涔 教授 *Lee, Si-Chen,* Professor

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薄膜電晶體實驗室
TFT Lab.

薄膜電晶體實驗室（TFT Laboratory）由李嗣涔教授領導，是臺灣大學電子工程學研究所奈米電子組（Nano Electronics Group）的實驗室，實驗室的研究方向為：室溫窄頻電漿子紅外線發射器、雷射；多頻道量子點紅外線偵測器；窄頻紅外線照射對植物生長基因表現之研究；孔洞形狀對表面電漿子的異常穿透效應；兆赫等級之量子環偵測器及非晶矽與多晶矽薄膜電晶體的創新製程研究等。本實驗室利用表面電漿效應，首度開發出室溫、窄頻且可調變波長之紅外線發射器，且成功地應用在植物生長基因表現之研究上。在未來，我們將研究窄頻紅外光如何影響癌細胞生長和基因表現。

利用電漿子熱輻射紅外光源之窄頻寬的特性，我們可研究在不同波段下，生物持續受到紅外光照射時，其成長型態、基因表現，以及所有蛋白質的增減變化。主要使用的波段有 3、3.5、4、4.5、5 μm ，其半高寬可達0.5 μm 的窄頻寬，利於未來針對特定波段作進一步研究。

本實驗室研究發現，大腸桿菌進行24小時的紅外光照射後，能測量其菌落在不同紅外光波長下照射的變化。藉由量測菌落直徑，可統計大腸桿菌受不同波段紅外光影響的生長變化，如圖一所示。此外，利用二維電泳分析法，可測量照射紅外光後的大腸桿菌，其蛋白質表現量的變化。當特定波段紅外光促進大腸桿菌生長時，某些膜蛋白質會出現正調控的現象。在植物的研究上，我們發現當阿拉伯芥持續照射72小時紅外光，其下胚軸長度會發生差異。使用北方墨點法，能量測受不同波段紅外光影響的GASA4、CHS、RbcS之含量變化，如圖二所示。

The Thin Film Transistor lab is led by Professor Si-Chen Lee. It belongs to the Nano Electronics Group of the Graduate Institute of Electronics Engineering of National Taiwan University. The research directions of this lab are: the surface plasmonic infrared thermal emitter and laser at room temperature; the multi-color quantum-dot-infrared photodetectors; the effect of narrow band infrared illumination on the expression of the plant genes; the hole shape effect on the extraordinary transmission of the surface plasmon polariton; the quantum-ring infrared photodetectors in the THz range and the new fabrication processes of the a-Si:H and poly-Si thin film transistors.

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Our lab has developed the narrow bandwidth, tunable wavelength and room temperature-operated infrared thermal emitter. It is utilizing the surface Plasmon theory to operate. It has been applied successfully to observe gene expression during the plant growth. In the future, we plan to investigate the growth and gene expression of cancer cell after illuminated by narrow bandwidth infrared radiation.

The narrow bandwidth characteristic of plasmonic thermal emitters is used efficiently to compare growth morphology, gene expression and proteins of organism under different infrared wavelength. There are common wavelengths applied to research, such as 3, 3.5, 4, 4.5 and 5 μm. Their full width half maximum (FWHM) are about 0.5 μm.

Escherichia coli (E. coli) growth morphology is inspected by colony spot diameter and analyzed statistically as shown in Fig. 1. In order to compare proteins expression between experimental group and control group, two-dimensional gel electrophoresis is used after *E. coli* exposed by infrared radiation or just growing in dark. Recently, we found that while the specific wavelength of infrared radiation can increase *E. coli* growth rates, some membrane proteins are up-regulation obviously. *Arabidopsis* are exposed by infrared radiation for 72 hours. The hypocotyl lengths are recorded immediately, and *GASA4*、*CHS*、*RbcS* expression are measured by Northern blot method as shown in Fig.2.

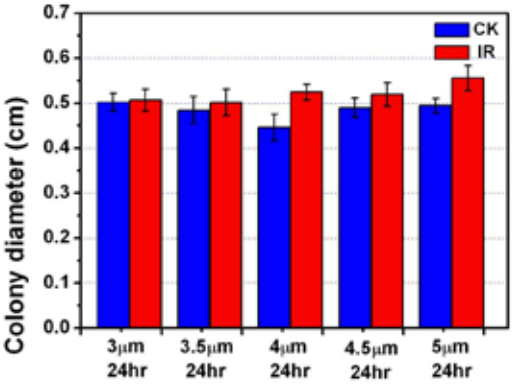

Fig.1 *E.coli* colony diameter chart after infrared exposure

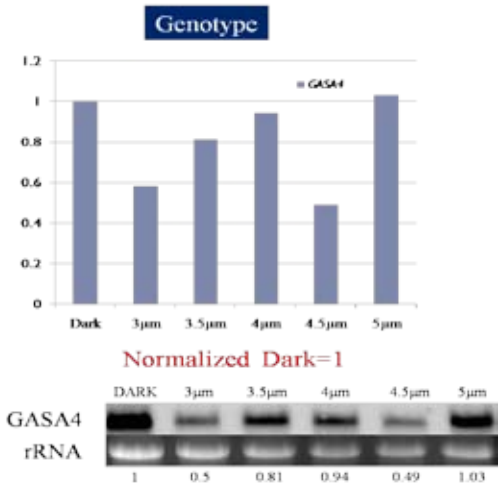

Fig.2 *Arabidopsis* gene expression after infrared exposure

主要研究領域 Major Research Areas

量子點及量子環偵測器、非晶及多晶矽薄膜電晶體、電漿子熱發射器及其在植物物生長之應用
Quantum Dot and Quantum Ring Photodetector, Amorphous and Poly-Si Thin Film Transistor, Plasmonic Thermal Emitter and Its Application on Plant Growth

1. 窄頻紅外線光源與偵測器及其在植物與神經細胞上的應用
   The narrow bandwidth infrared emitter and detector with applications in plants and neuron cells
2. 用於電子紙顯示器之軟性能量回收主動式矩陣電路
   Flexible Energy-Recycling Active Matrix Circuits for Electronic Paper Display
3. 紅外線應用在調控乳癌細胞的成長研究
   The application of infrared light in the modulation of the breast cancer cell growth

計畫名稱：窄頻紅外線光源與偵測器及其在植物與神經細胞上的應用
補助單位：行政院國家科學委員會
計畫期間：2009/08/01-2010/07/31

我們成功地製作出窄頻中紅外波段Ag/SiO2/Au熱輻射器，其樣品結構示意圖如圖1(a)及(b)所示。樣品A至D藉由改變二氧化矽層的厚度，發現當樣品厚度超過1.1μm，不謹SP模態且Cavity模態也會在反射的能量頻譜中出現。對於樣品A（SiO2厚度為0.7μm），在反射頻譜上會顯示出六個簡併態的色散關係分別為(1,0), (0, 1), (-1,1) and (1,-1) Ag/SiO2 SP模態。當SiO2厚度超過1.1μm（圖2(b)），cavity會與原本的SP模態產生混淆，並且會由原本的SP轉變為cavity模態為主。當SiO2厚度為2.6μm（圖2(c))時，反射頻譜中（約在能量為0.35eV附近）顯示一個反交叉的圖形，這主要是由於波導傳遞的模態與自己的繞射模態（藉由晶格的作用）發生藕荷反應，我們計算的結果顯示於圖2(d)中也驗證實驗的數據。

我們發展一個具備高極化特性的熱輻射元件，其主要是由波導模態結合週期性金屬光柵，結構如圖一所示。圖二顯示當光柵厚度為700奈米時，元件的熱輻射頻譜圖。此元件在操作溫度為453K時的功率為18微瓦。且半高寬為於發射波長的比例為0.058。此元件極化的程度隨著光柵的厚度增加，且發現與理論所計算的結果一致（如圖三）。這樣具備窄頻且高極化特性的紅外線光源可進一步地應用在生物醫學的領域上。

我們使用MBE成功地製做出InAs/GaAs量子環光偵測器元件。此元件的偵測範圍可達175 μm (1.7 THz)及其偵測率在80K的溫度下可達1.3×107 cmHz1/2/W。主要是藉由GaAs layer的厚度來控制In(Ga)As量子環的高度用以延伸偵測器可達之偵測範圍。十層的量子環被堆疊且埋在50 nm的GaAs barrier及在n型參雜及GaAs傳導層中形成位障，其幾何結構如圖3所示。我們使用MBE去成長InAs量子點且覆蓋上1.1nm的GaAs layer，經過適當的溫度去熱退火而形成量子環，Au/Ge/Ni合金材料被成長並經450 ℃熱退火形成歐姆接點。隨著不同的偏壓，量子環偵測器顯示不同的響應頻譜於圖4。圖5顯示在不同溫度下的電壓電流特性，從圖中可以看到BLIP可達50K，且真實操作溫度可高達80K。

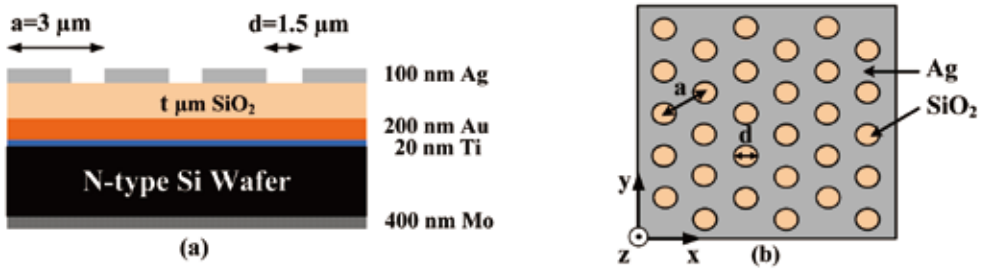

Fig.1 Schematic diagram of the (a) side and (b) top view of the Ag/SiO2/Au plasmonic thermal emitter, the top metal is perforated with hexagonal hole array.

圖一 (a)與(b)分別表示Ag/SiO2/Au電漿子熱輻射器之測試及俯視圖。

Project title: The narrow bandwidth infrared emitter and detector with applications in plants and neuron cells
Supported by: National Science Council
Project period: 2009/08/01-2010/07/31

A suitable designed trilayer Ag/SiO2/Au thermal emitter can be used as the narrow bandwidth infrared light source. The schematic diagrams showing the side and top views of the device structure are depicted in Figs.1 (a) and (b), respectively. The thicknesses of the SiO2 layer in devices A to D were 0.7, 1.1, 2.1, and 2.6 μm, respectively. The thermal radiation generated in the SiO2 layer resonates between the two metal films and results in not only the Ag/SiO2 surface plasmon polaritons but also the cavity mode in the Ag/SiO2/Au waveguide. Fig. 2 (a) to (d) shown the energy dispersion relations as a function of for devices A, D, and G with various SiO2 thicknesses, i.e., 0.7, 1.1, and 2.6 μm, respectively. For device A with SiO2 thickness of 0.7 μm, four dark lines representing the reflection minimum and the excitation of SPPs intersect with y axis at 0.32 eV (~ 3.88μm) that is composed of six degenerate modes, i.e., (1,0), (0, 1), (-1,1) and (1,-1) Ag/SiO2 modes denoted as (1,0) Ag/SiO2 mode. When the SiO2 thickness exceeded 1.1 μm as shown in Fig. 2 (b) and 2 (c), the cavity mode appeared and mixed with Ag/SiO2 mode, it could be considered as a F-P type resonance generated in SiO2 layer between two parallel metal planes. In particular, the dispersion curves shown in Fig.2 (c) displayed the anti-crossing like behavior of the two modes around 0.35 eV, which was attributed to the coupling between the propagating waves and its diffractive waves by Brillouin zone boundary in momentum space. The calculated dispersion curves (dotted red lines) are shown in Fig.2 (d), they appear in good agreement with the experimental results.

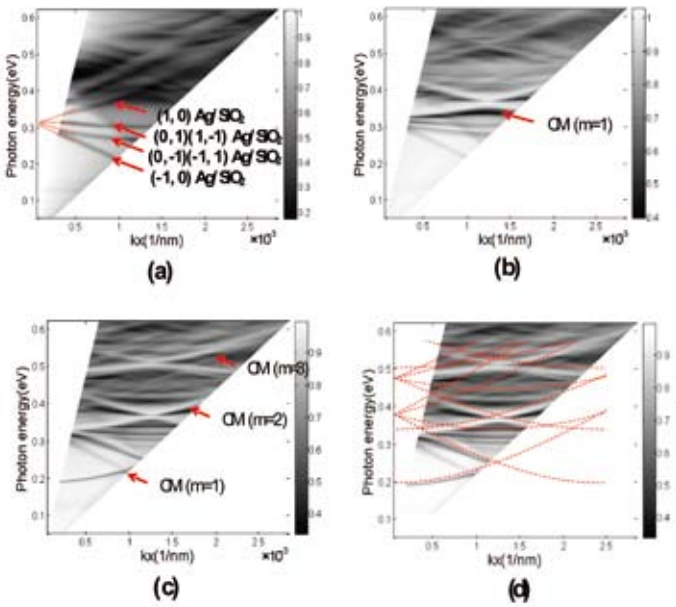

Fig.2 Measured energy dispersion relation as a function of along ΓK direction for devices A, B, and C with different SiO2 thicknesses t of (a) 0.7μm, (b) 1.1 μm, and (c) 2.6μm. The theoretical energy dispersion relation (red line) as compared with the experimental result of (d).

圖二 針對不同厚度之樣品A、B及C沿著ΓK 方向量測的反射色散關係圖，其中樣 品A、B、C厚度分別為0.7、1.1及2.6μm，理論的計算結果顯示於圖二(d)，其結果與實驗[圖二(c)]相同。

A highly polarized infrared thermal emitter was demonstrated. The structure constructed by a waveguide thermal emitter combined with silver grating as shown in Fig. 3. Fig. 4 shows the thermal radiation spectrum of device with a grating thickness of 700 nm. The output power of thermal radiation at 453 K is 18 mW. The ratio of the FWHM to the peak wavelength is 0.058. The polarized ratio increased with the grating thickness increased and the ratio up to 15 was achieved as the effective grating thickness reaching 850 nm as shown in Fig. 5. Experimental data is consistent with the theoretical calculation by equalizing the multilayer structure into an effective refractive index material. This study demonstrated that the integrated structure can be used as a narrow bandwidth and highly polarized ratio infrared light source for further biological researches.

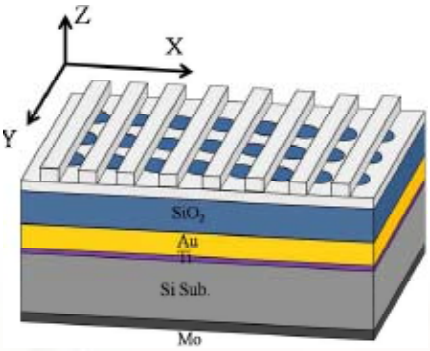

Fig. 3 Schematic diagram of devices. A 20 nm Ti film was deposited on the Si wafer followed by 200 nm gold film and 1.8μm SiO2 layer. A thickness of 100 nm silver arranged in square lattice was introduced between SiO2 layer and grating film. The period of grating and holes array is 2μm.

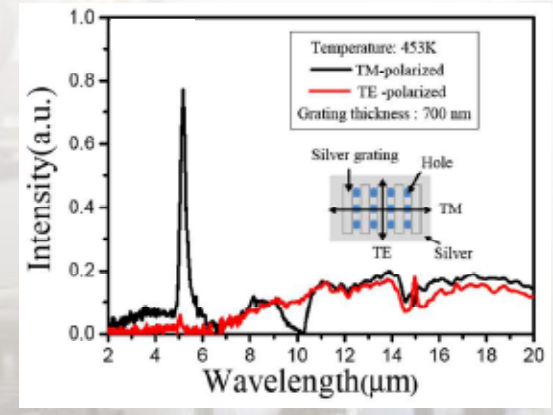

Fig. 4 The thermal radiationspectra of device with TE- and TM-polarized. The measured temperature is 453K.

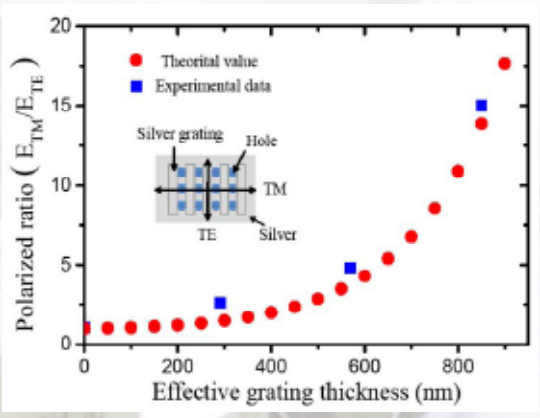

Fig. 5 The dispersion relations of reflection spectra for samples (a) A (a=2.3μm d=1.5μm), and (b) B (a=1.7μm d=1μm).

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超音波影像實驗室
Ultrasonic Imaging Lab.

本實驗室由李百祺教授成立於1997年，主要從事醫學電子與影像物理相關研究，目前以生醫超音波技術與光聲影像等領域為研究重點。本實驗室在上述領域已產出許多具體貢獻並在全世界有很高之能見度。此外，本實驗室之成員來自電子、資訊、工程、生命科學及醫學等各領域，多年來亦積極與國內外單位進行合作，合作夥伴包括產、研、學各界，領域更涵蓋基礎科學、工程技術與臨床研究。跨界整合研究資源，致力前瞻生醫科技研究，提升健康與醫療品質，是本實驗室之成立宗旨與具體目標。

Ultrasonic Imaging Laboratory was founded by Professor Pai-Chi Li in 1997, with the main research focus in biomedical electronics and imaging physics. In the past few years, we have conducted a number of research projects in biomedical ultrasound and photoacoustic imaging. We have also made several critical contributions and are now one of the most visible research laboratories in this field in the world. Members of the lab come from various backgrounds, including electronics, informatics, engineering, life sciences and medicine. We have also been actively collaborating with research labs throughout the world, covering industry, research institutes and universities, from basic sciences, engineering to clinical research. Integrating multi-disciplinary research efforts, exploring advanced biomedical technologies, and improving healthcare quality is the mission of this lab.

主要研究領域 Major Research Areas

生物醫學工程、超音波影像、生醫光聲影像
Biomedical Engineering, Ultrasound Imaging, Biomedical Photoacoustics

研究計畫 Research Projects

1. 前瞻生醫電子晶片開發與醫療系統整合
   Development of Advanced Biomedical ICs and Integration of Medical Systems
2. 血管內光聲與超音波影像技術開發及超音波輔助血栓溶解之研究
   Development of IVPA/IVUS imaging technologies and investigation on ultrasound-assisted thrombolysis
3. 使用多模式分子影像探針量化研究超音波標靶治療
   Quantitative study of US based targeted therapy: the use of US/PET and US/MRI molecular probes
4. 台灣學術里程與科技前瞻計畫之萌芽計畫(轉換科學發現為產業技術)-用於臨床前研究之多模式/多標靶顯微影像
   Multi-modality/mutli-targeting micro-imaging for preclinical research

計畫名稱：血管內光聲與超音波影像技術開發及超音波輔助血栓溶解之研究
補助單位：行政院國家科學委員會
計畫期間：2008/08/01-2011/07/31

本三年期計畫之主要目標為針對血管疾病發展先進之影像及治療科技。我們所採用的方法包括用於動脈硬化診斷之多模式影像技術，以及利用標靶穴蝕效應輔助及影像導引之血栓溶解。其中多模式影像部分，我們將結合血管內光聲影像及血管內超音波影像。光聲影像主要乃顯示與光吸收相關之性質，而超音波影像則是建立在聲學散射的基礎之上。因此，此二者之結合可以較現有之其他影像方式提供更多之診斷資訊。更進一步，這樣的影像平台亦可有效的結合超音波定量血流測量等相關影像方法。因為這二種影像方式皆以偵測到之聲波進行影像重建，故在系統端可做有效之整合，且亦有助於結合如超音波彈性影像等之相關影像技術。本計畫之另一重點為血栓溶解。我們將發展分子標靶，並結合穴蝕效應來進一步提升血栓溶解之效應。為達這些目標，我們將與台大醫院合作，以建立並使用動脈硬化之動物模型與取得血管樣本。此外，我們也將和美國新墨西哥大學合作，應用創新之微機電元件，做為光聲探頭之用。這類之元件不但有可能解決血管內影像關於元件大小限制之問題，也是一項極具前瞻性之技術。本計畫將於三年期間具體進行以下研究工作：

- 光聲探頭原型開發
- 穴蝕效應輔助之血栓溶解研究
- 血栓標靶之分子探針開發
- 穴蝕效應與分子標靶輔助之血栓溶解研究
- 光聲與超音波動脈硬化鑑別
- 光聲與超音波雙模影像系統開發
- 影像導引之血栓溶解

本計畫之成功將使本團隊於全世界，在血管內影像及血栓溶解領域，居於領先之地位。

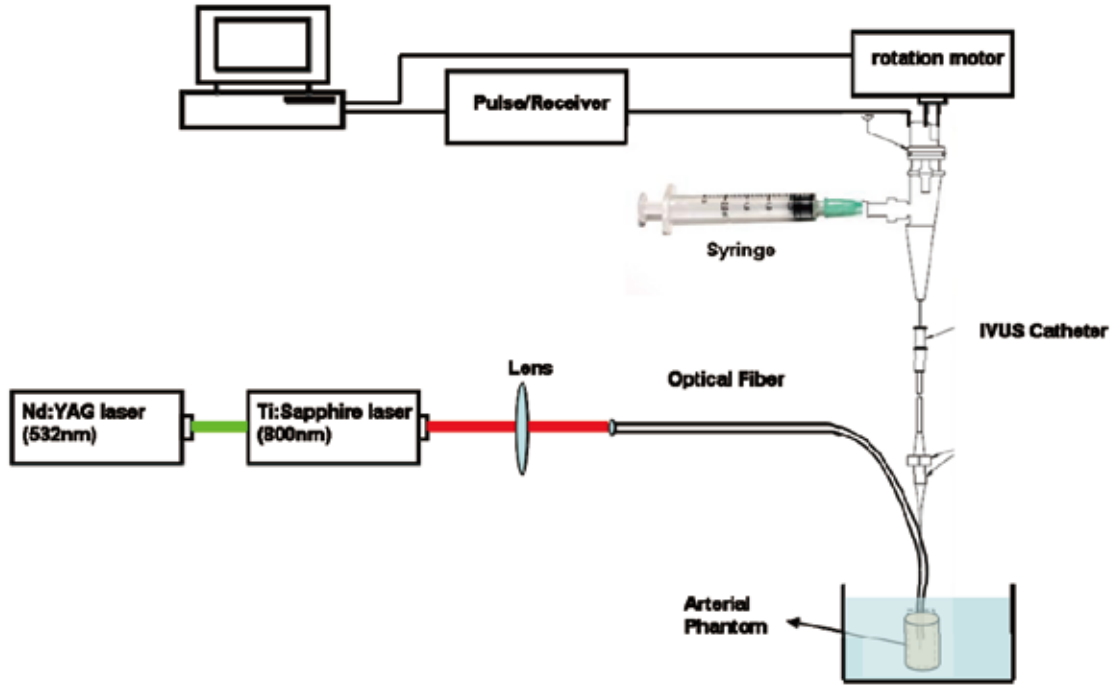

Fig.1 Laboratory prototype IVUS/IVPA imaging system setup

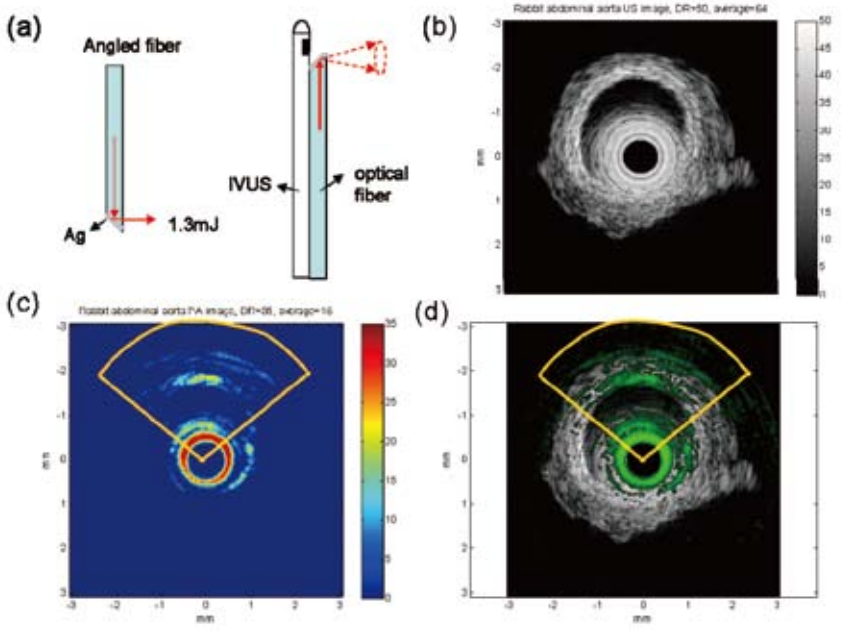

Fig.2 (a) Configuration of integrated IVUS/IVPA transducer, rabbit abdominal aorta (b) IVUS image (c) IVPA image, and (d) IVUS/IVPA fusion image

Project title: Development of IVPA/IVUS imaging technologies and investigation on ultrasound-assisted thrombolysis

Supported by: National Science Council
Project period: 2008/08/01-2011/07/31

The main goal of this three-year project is to develop advanced imaging and therapy technologies for various stages of vascular diseasess. Specifically, we will develop multi-modality imaging technologies for atherosclerotic plaque imaging and staging, and image guided thrombolysis technologies that is assisted by specific binding and acoustic cavitation effects. The multi-modality imaging will combine both intravascular photoacoustic imaging (IVPA) and intravascular ultrasonic imaging (IVUS). IVPA primarily shows information related to optical absorption, and IVUS is primarily based on acoustic scattering. Therefore, the combination can provide more clinical diagnostic information that cannot be provided by any other existing imaging technologies. In addition, correlation based ultrasonic flow estimation methods can also be incorporated in order to provide quantitative blood flow information. Because both modalities form images based on the detected acoustic waves, the multi-modality imaging system can be integrated effectively. On the other hand, other imaging methods, such as ultrasonic elasticity imaging for vessel characterization and plaque staging, can also be effectively integrated to provide additional diagnostic information in the future. The other major component of this project is on thrombolysis. In particular, ultrasound and microbubbles will be exploited in order to understand the potential of cavitation-assisted thrombolysis. Moreover, molecular probes (conjugated microbubbles) will be developed so that these probes can target thrombus, and it is expected that this can further enhance the thrombolysis effectiveness. In order to achieve these goals, we will also work with National Taiwan University Hospital on the animal models for atherosclerosis. We will work with our international collaborator at the University of New Mexico as well, on a novel CMUT based photoacoustic transducer. The development and the applications of the CMUT transducer are also a pioneering work in the field. To this end, the specific aims of this project include:

- Development of a prototype photoacoustic probe
- Investigation of cavitation assisted thrombolysis
- Development of ultrasonic molecular probes for thrombus targeting
- Investigation of targeted cavitation assisted thrombolysis
- IVPA/IVUS plaque characterization
- Development of dual mode IVPA/IVUS imaging system
- Image guided thrombolysis

Success of this project will put the research team in a leading position in the world in the area of intravascular imaging and enhanced thrombolysis.

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生醫晶片技術實驗
Bio-Electronics-System Technology Lab.

本實驗室成立於2006年，主要研究方向為奈微米生醫晶片系統相關研究，目前以生物分子檢測技術與微細胞監測技術等領域為研究重點。進一步的說明，整合現今蓬勃發展的奈微米製程科技與傳統生物科學知識，可以發展出極具應用及發展潛力之關鍵性跨領域技術，因此，本實驗室致力於開發不同之生醫電子應用晶片與系統，期能在相關領域獲得良好之成果與能見度。本實驗室之成員來自電子及工程等相關領域，以此為基礎，積極與生醫相關領域學者進行合作，合作領域及研究範疇涵蓋基礎科學、工程技術與臨床研究等。

The bio-related research activity is one of the major focuses in world wide research institutes. However, the advancement of bio-research is limited by costly instruments and time consuming analysis. To overcome this obstacle, in our research group, the nano-electronics and micro-mechanism are integrated to be a powerful tool for this emerging research field.

More specific, a series of bio-chemical molecular sensors can be developed by utilizing nano-scale electrical devices. Based on the superior fabrication facilities and skills in Complementary Metal-Oxide- Semiconductor (CMOS) and Nano/Micro Electro-Mechanical System (N/MEMS), moreover, micro protein sensor arrays technologies and living cell monitoring systems are also envisioned to be an exciting research direction. In summary, our research is aiming at developing innovative and integrated systems for nano/bio research fields.

主要研究領域 Major Research Areas

奈微米生物機電系統、生物晶片、生物分子量測技術、奈米製程技術、生物微感測器
Bio-NEMS, Bio-Chip, Nano fabrication, Biomolecular Detection Technology

研究計畫 Research Projects

1. 奈米場效生物分子感測元件
   Nano FET Biomolecular Sensor
2. 細胞監測晶片研發
   In-Vitro In-Situ Cell Monitoring Chip
3. 奈米螺旋碳管能源擷取元件
   Energy Harvesting Devices Based on Nano- Carbon-Coils
4. 無線感測器網路平台技術開發
   Wireless Sensor Network Platform Technology

計畫名稱：研製針對新衰竭患者於乙型交感神經阻斷劑藥物反應之基因檢測系統晶片
補助單位：行政院國家科學委員會
計畫期間：2009/08/01-2011/07/31

心臟冠狀動脈(Coronary Artery Disease)退化及心肌退化症，往往會使患者過勞或進行一些劇烈活動時，引起心絞痛甚至造成患者死亡，已經成為國人十大死因之第二名。雖然近幾年來醫學上對於治療心血管疾病有相當之進步，但心臟衰竭之治療仍具有相當之挑戰性及極限，因此如何提供心衰竭患者全面性的照護，是刻不容緩的議題。其中，最為重要的即為心衰竭的長期及緊急照護之用藥，然而，用藥的效果及用量，會因為心衰竭病患基因之不同而有不同的感受性，因此，如何進一步利用DNA晶片技術進行檢驗及資料篩檢即成為心臟疾病相關早期預警及輔助用藥等生醫照護科技下一步重要的發展。

本研究團隊針對此一課題發展以標準半導體製程為基礎的DNA檢測晶片系統。本研究團隊計劃將以對DNA分子及元件表面處理的了解做為為基礎，利用對奈微米電子元件的知識為工具，先以元件理論分析的方式來建構此一DNA檢測晶片的基礎模型，而後以標準半導體製程技術進行DNA檢測晶片及其相關電路之設計及製作，進一步與臨床資料進行分析比對，期能使國內生物感測元件知識與技術可以確實與臨床治療技術更進一步的整合，並可藉由國內獨步全球之半導體製程技術將此一研究成果落實於生物科學之應用層面上，以提升既有之產業價值。

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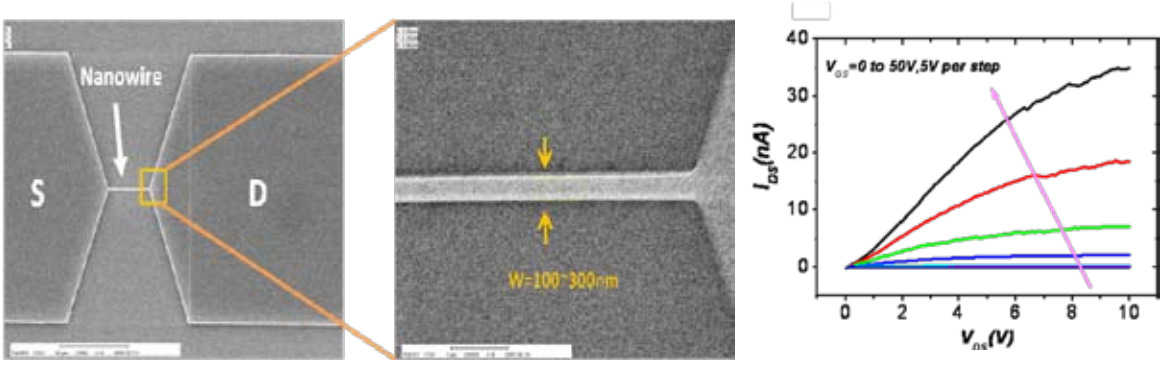
Project title: The Design and Implementation of DNA System-On-Chip for Heart-Failure Patient Response in Beta-Blocker
Supported by: National Science Fundation
Project period: 2009/08/01- 2011/07/31

With rapid advancements of System-On-Chip and MEMS/nanotechnologies, a wide variety of new chemical analysis devices and their integrated system, such as biomolecular analysis devices and micro-total-analysis systems, have been designed, implemented, and demonstrated. However, few of them integrated with clinical analysis and achieve the practical requirement of the modern biomolecular diagnosis. As the consequence, this research project will aim at the development of DNA analysis system-on-chip for the clinical heart-failure-medicine-treatment, which is one of the most important steps toward the heart failure disease treatment in both emergency and chronic recovery. In specific, this research project will be based on the basic understanding of electronic devices, biomolecular interaction, and nano/micro fabrication to design and implement the DNA chip for heart-failure medicine treatments. Furthermore, this research project will also compare with clinical data in order to bridge the electronics, bioinformatics, and clinical applications into a fully integrated system.



掃描式電子顯微鏡(SEM)拍攝多晶矽電晶體元件及通道。右圖為奈米線通道的多晶矽電晶體Ids-Vgs 電性圖（L/W = 10um/300nm，熱氧化二氧化矽=1um），右圖為奈米線通道的多晶矽電晶體Ids-Vds 電性圖（L/W =10um/300nm，熱氧化二氧化矽=1um）。

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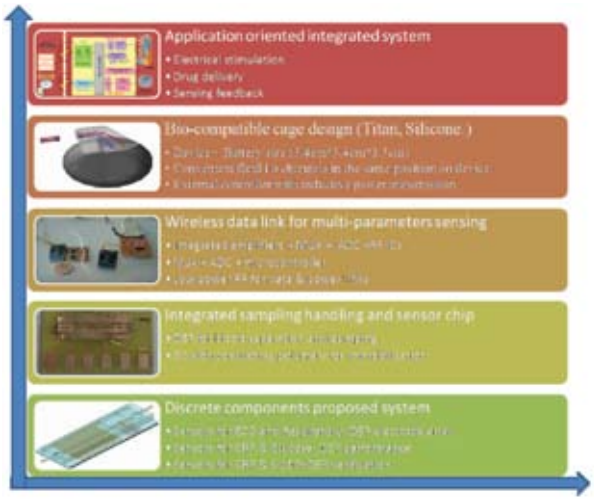
醫用微感測器暨系統實驗室
Medical Micro Sensor and System Lab.

本實驗室致力於配合醫療儀器認證與驗證法規之推動與精神體現，以微機電技術與光學感測方式進行生醫奈微米微感測器元件與系統整合之研究與應用-包括表面電漿共振(surface plasmon resonance)原理，表面電漿子感測器設計、微型系統整合、軟硬體介面溝通，主旨在於發展快速、便利、正確、與人性化醫用感測儀器，以促進個人化醫學(personalized medicine)與電子化醫療(e-health)之研究與產業發展。

We have devoted to apply microfabrication technologies and optical sensing mechanisms to develop nano/micro sensors and integrated system for the medical applications with compliance of medical device regulations and standards. Our research currently focus on the theoretical development for novel Surface Plasmon Resonance (SPR) devices, design of SPR nano/micro sensor, bioplamonics, and the heterogeneous integration of micro-system from hardware to software. The aim is to develop the fast diagnosis, easy to use, and user-friendly medical devices toward the success of personalized medicine and e-health.



主要研究領域 Major Research Areas

生物微感測器與系統、生醫晶片、生醫光電、類神經網路、醫材法規
Bioelectronics、Biomedical Micro sensors and System、Biochip、Biomedical Optics、Artificial Neural Networks, Regulatory Affairs

研究計畫 Research Projects

1. 仿生物分子交互作用統計行為之奈米陣列量子晶片設計
   Design of Quantum Nano Array Biochip for Stochastic Molecular Interactions
2. 智慧型隨身心肺音偵測與訊號分析系統
   Smart sensing material for monitoring of personal respiratory/cardiac sounds
3. Continuous Cell Culture Monitoring System
4. Efficacy studies of RF Stimulation on Lumbar DRG
5. 無線氣體監控感知系統於人體健康與環境安全之應用開發計畫
   Development of a smart wireless gas sensing SoC for health and environmental applications

計畫名稱：新型超解析度電漿子成像平臺於量測單分子奈米陣列交互作用之研究
補助單位：行政院國家科學委員會
計畫期間：2009/08/01-2012/07/31

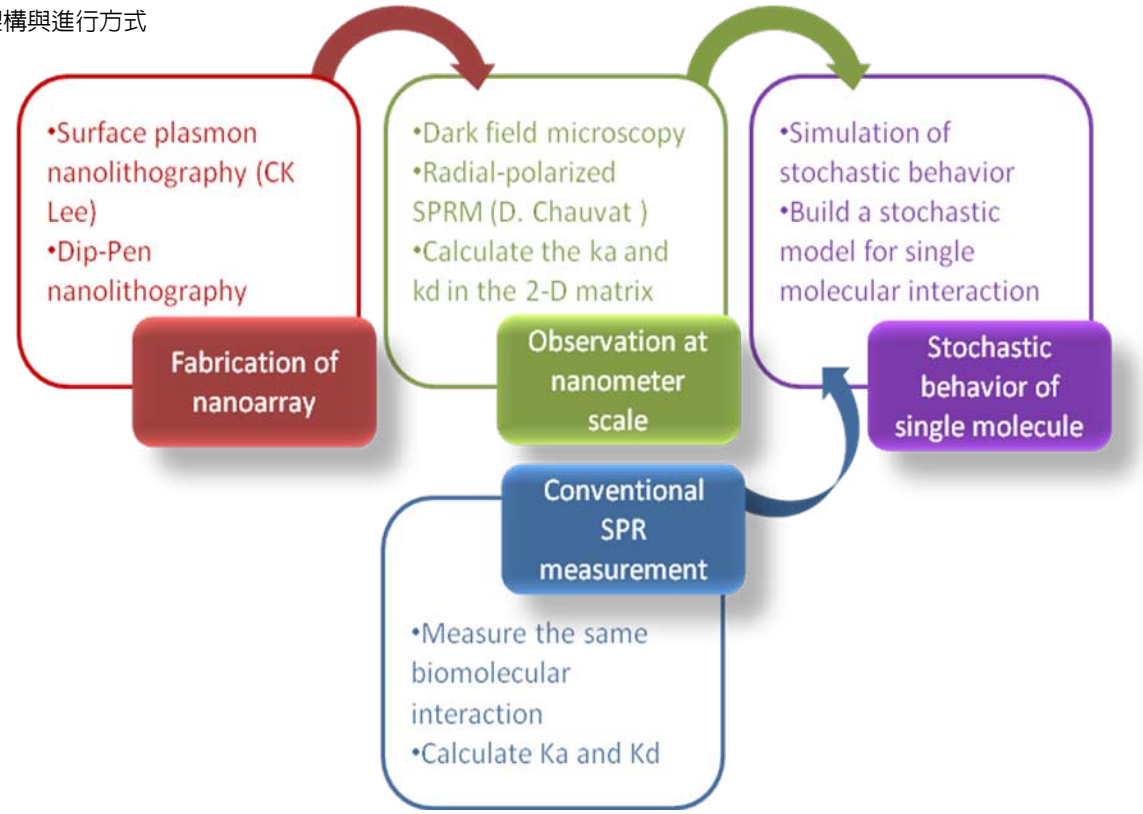
基於先前的初步研究成果與經驗，本計畫擬使用plasmonic nanolithography取代原先DPN製做生物奈米陣列樣版的方法，使用DPN於後續的多種生物分子塗佈標的優點，對奈米生物晶片進行加工。生物分子預計採用有接抗原之奈米粒子（直徑>=50奈米）與ALV病毒顆粒（約100奈米）達到在一個直徑50奈米的陣列點上因為空間限制只允許單一分子交互事件的發生。在觀測的架構部分，除了嘗試以高NA物鏡在穿透式架構下改善原先暗場顯微鏡的解析度外，達到直接觀測100奈米下的標的物目標之外，也將跟法國Ecole Normale Supérieure de Cachan, Prof. Dominique Chauvat與臺大李世光教授合作的Radially-polarized SPRM進行合作量測，以掃描或二維影像方式觀測奈米陣列上生物分子反應的動態折射率變化，達到非標識(non-labeling)的觀測。最後取得的訊號將與傳統使用表面電漿共振測量分子動態反應做比較，以驗證奈米尺度下生物分子的隨機行為模型。此一整合奈米製程與光學檢測技術之Stochastic Array研究在目前全世界的研究中尚在起步中，本團隊在長期合作努力下有希望獲得實用的突破在高度創新的生物感測器領域獲得領先地位。

Project title：Novel Super-resolution Plasmonic Imaging Platform for Measurement of Single Molecular Interactions on Nano Array
Supported by：National Science Council
Project period：2010/08/01-2012/07/31

Based on our preliminary results and experiences, this project propose to use surface plasmon (SP) nanolithography to replace the original method that is DPN to make the template for the biomolecular nanoarray. Then, this chip will be processed by DPN that has an advantage of depositing various molecules at one time. The target molecules will be the artificial

nanoparticles with a diameter of lager than 50 nm or AIV virus particle (diameter is about 100nm), which makes one site of dot (50 nm) react only with one particle. That is, there is only one event that will take place on one site due to the limitation of dot size. Regarding the observation, except to use the high NA objective lens to improve the resolution of microscopy for detecting the structure under 100 nm, we will measure these events using racially polarized surface plasmon resonance (SPRM), which is the co-work result by Prof. Zyss (Ecole Normale Supérieure de Cachan, France), Prof. Chauvat (Ecole Normale Supérieure de Cachan, Fance) and Prof. CK Lee (Institute of Applied Mechanics, NTU), to measure the reflective index change caused by biomolecular interaction with scanning or imaging the 2-D image for non-labeling observation. Finally, this experimental data will compare to that measured by conventional SPR method to identify the stochastic model of biomolecular interaction under nanometer scale. It is hopeful to obtain practical breakthrough and to obtain the leading ship in the field of biosensor based on our long-term cooperation and hard work.

計畫架構與進行方式



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人腦實驗室
Brain Imaging and Modeling Lab.

近年來，科學界逐漸了解複雜的人類行為與認知功能是藉由腦中不同階層的神經系統交互作用所表現出來，而非由單一的結構所掌控，有鑑於此，欲進一步了解人腦功能，則需要在結構與功能層面上研究以下三個問題：(1)什麼地方發生活動 (2)這些活動是何時發生以及其發生順序為何 (3)是如何藉由在大規模的神經網路中的訊息傳遞完成這些認知行為。現代非侵入性的醫學影像技術可幫助我們獲得高空間與時間解析度的神經活動資料，而定量的系統模擬將有助於解譯隱含於這些神經影像資料中協同完成感官、認知與行為歷程的動態神經活動。

本實驗室的研究方向為整合硬體研發、資料分析、與數值模擬等工程技術來幫助我們了解複雜的人腦功能。進行中的研究計畫集中於結合結構與功能性核磁共振影像，腦磁圖與腦電圖之高時間空間解析度的神經影像技術，以及系統階層的神經信號模擬，以了解神經活動與行為間的關係。

Complex behavior and cognitive functions of the human brain are suggested to be "mapped at the level of multi-focal neural systems rather than specific anatomical sites, giving rise to brain-behavior relationships that are both localized and distributed". Further understanding of these brain mechanisms requires both structural and functional knowledge to answer (i) where are the foci of activity, (ii) when are these areas activated and what is the temporal sequence of activations, and (iii) how does the information flow in the large-scale neural network during the execution of cognitive and/or behavioral tasks. Advanced noninvasive medical imaging/recording modalities are able to localize brain activities at high spatial and temporal resolution. Quantitative modeling to interpret these data is needed to understand how large-scale distributed neuronal interactions underlying perceptual / cognitive / behavioral functions emerge and change over time.

Our research interests include the integration of hardware development, data analysis, and mathematical modeling to facilitate our understanding of brain cognition. Current research projects try to explore challenges of spatiotemporal brain imaging and modeling by using a combination of hardware and analytical approaches to enhance the spatiotemporal resolution of single (MRI) or combined (MRI/fMRI and MEG/EEG) modalities. In addition, mathematical approaches for identifying large-scale neural networks and their correlation to behavioral measurements are investigated.

主要研究領域 Major Research Areas

神經影像、核磁共振影像、腦磁圖、腦電圖、神經系統模擬
Neural imaging, Magnetic resonance imaging, Magnetoencephalography (MEG), Electroencephalography (EEG), Neuronal modeling

研究計畫 Research Projects

1. 超快速人腦功能性核磁共振逆影
   Ultra-fast functional magmetic resonance inverse imaging of the human brain
2. 利用多種神經影像進行人腦視覺系統之時空映象與系統模擬
   Multimodal
3. 高時間高空間解析度之正規化平行核磁共振影像擷取與重建
   Regularized parallel MRI acquisitions and reconstructions for high spatiotemporal resolution
4. 使用三維核磁共振逆影像技術抑制高場腦功能性核磁共振影像之生理雜訊
   Physiological Noise Reduction Using Volumetric Functional Magnetic Resonance Inverse Imaging

計畫名稱：利用多種神經影像進行人腦視覺系統之時空映像與系統模擬
補助單位： 行政院國家科學委員會
計畫期間：98/08/01-101/07/31

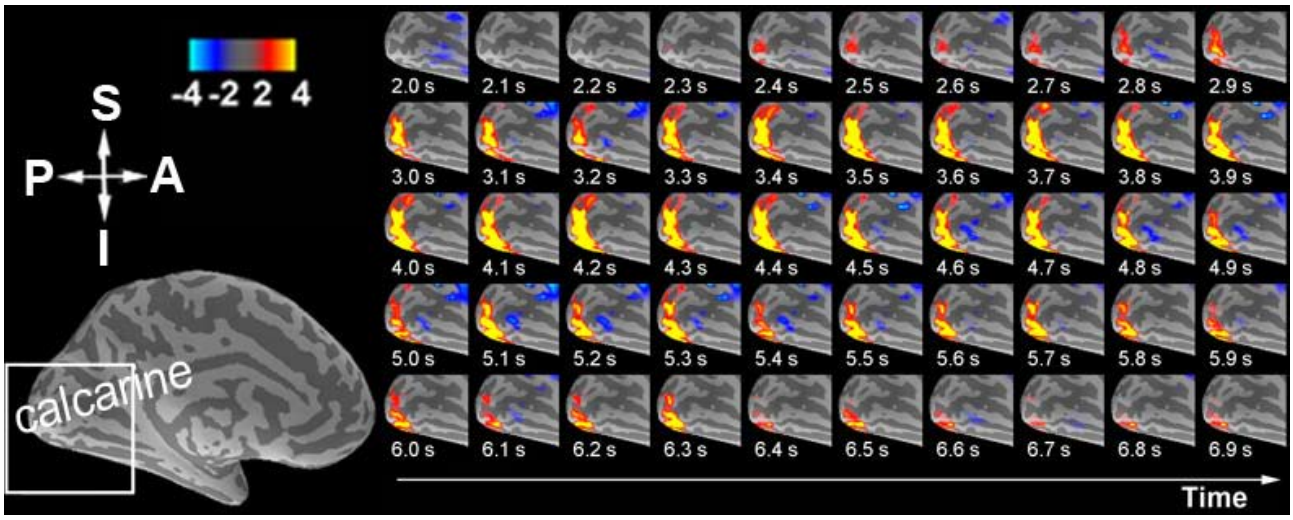
本計畫旨在發展一完整的時空映像與系統模擬實驗與分析架構，以應用於人腦感覺、認知與行為的研究。我們認為人類複雜的行為是由於腦內空間不同的區域在時間與空間上相互協調才能產生，而非單一解剖學上的位置所能獨力完成。近幾年來，我們已經發產了一系列時空映像的工具幫助我們達成以非侵入性的方式了解人腦視覺系統的目的。我們將持續這些技術以提高它們的時間和空間解析度，同時也將研究腦內是如何使用遠距同步(long range synchronization)的方式來傳遞和整合訊息。最終希望能了解人腦內在處理感覺與運動的過程中各區域間的因果關係(causality)。

為了達成上述目標，我們發展結合功能性核磁共振影像(functional magnetic resonance imaging, fMRI)與腦電波／腦磁波圖(EEG/MEG)的方式來取得空間上達釐米精準度與時間上達毫秒精準度的神經影像。我們將進一步整合功能性核磁共振影像與腦電波/腦磁波圖的資料擷取，改進新發展之核磁共振逆影像技術(magnetic resonance inverse imaging)。並利用相位同步的概念探討腦內電訊號如何傳地震盪訊號，進一步在時域以及頻域上量化腦部各區域間的葛氏因果關係(Granger causality) 。最後應用這些技術來研究注意特徵(feature-based attention)在人腦高階視覺中的神經基礎。本計畫所發的各項神經影像工具與視覺研究希望能對臨床科學與神經科學能有所助益。

Project title: Multimodal spatiotemporal brain mapping and modeling of human visual system
Supported by: National Science Council
Project period: 2009/08/01-2012/07/31

The overall goal of our research program is the development of a comprehensive experimental and analytical framework for spatiotemporal imaging and modeling of the neural basis of perception, cognition and action. According to our general model, complex behavior results from the coordinated activity of spatially distributed neural systems rather than specific anatomical sites, giving rise to brain-behavior relationships that are distributed in space and time. To date, we have developed a range of spatiotemporal imaging methods that have enabled innovative, non-invasive studies of the human visual system at higher resolution spatial and temporal resolutions than previously achieved. We now propose to carry forward the development of our spatiotemporal imaging approach by exploring methods for acquiring functional brain imaging data at ever higher rates, probing the brain mechanisms for long-range spatial synchronization and achieving a better understanding of information flow during perceptual and sensorimotor processing by establishing a robust framework for causal modeling.

To these ends we have developed novel methods combining functional MRI (fMRI) and magnetoencephalography / electroencephalography (MEG/EEG) data to obtain noninvasive spatiotemporal maps of cerebral activity with both high temporal (millisecond) and spatial (millimeter) resolution. We propose to continue and extend this technical development. Specifically, we will further improve fMRI and MEG/EEG data acquisition and analysis methods, develop new methods to explore mechanisms of oscillatory brain activity combining fMRI, MEG and EEG data, thereby increasing the accuracy and sensitivity of the spatiotemporal brain imaging approach. Further, we will continue development of causal modeling approaches, allowing study of how large-scale distributed neuronal interactions give rise to perception and cognition. Finally, we will apply these technical advances to studies of human higher visual processing in healthy individuals to study the neural mechanisms of feature-based attention. Given the increasing availability of both MRI and EEG/MEG, our combined approach should have significant impact on understanding the neural basis of behavior.



單一受試者對於視覺刺激以100毫秒解析度INI重建之功能性核磁共振影像(fMRI)時間序列 (TR/TE = 100/30毫秒，Flip angle = 20度，視野 = 200微米)。本實驗使用32通道頭部線圈陣列，資料從128次隨機呈現的刺激中取得，每此測試包含了6秒的baseline，跟接下來的0.5秒8Hz閃爍棋盤格刺激，以及接下來的23.5秒後刺激期 (每次總共30秒)。圖上的時間標記指的是閃爍棋盤格刺激開始後的時間。

A single-subject 100-ms resolution INI fMRI time series of activations to visual stimulation (TR/TE=100/30 ms, flip angle 20º, FOV=200 mm), co-registered to a flattened region of the left occipital cortex. The data were obtained using a 32-channel head coil array in 128 randomized trials, each of which consisted of 6 seconds pre-stimulus baseline, followed by 8-Hz flashing checkerboard flashing for 0.5 sec and subsequently 23.5 s post-stimulus (30 sec in total for each trial). The time stamps labeled in the figure indicate time after onset of the flashing checkerboard.

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整合神經生理學實驗室
Integrative Neurophysiology Lab.

本實驗室成立於1999年，主要從事整合性之電氣生理學相關議題研究，目前以脊髓神經反射塑性等領域為研究重點。在該領域本實驗室已發表相關著作。

Integrative Neurophysiology lab was founded in 1999, with the main research focus on systemic neurophysiology. In the past few years, we have conducted a number of research projects and published several articles in spinal reflex potentiation.

主要研究領域 Major Research Areas

神經生理學、感覺神經生理學
Neurophysiology, Sensory physiology

研究計畫 Research Projects

計畫名稱： 一氧化氮媒介之電針刺激-引發尿道反射增益現象及參與之細胞內訊息傳遞路徑
補助單位：行政院國家科學委員會
計畫期間： 2007/08/01-2010/07/31

臨床已廣泛應用針刺(Acupuncture) 引發體-臟器反射(somato-visceral reflex) 的機制來改善各種臟器功能，例如針刺或電刺激特定穴位（如八穴、關元、中極、子宮、太谿及三陰交等），可以透過腰、薦髓層次體傳入神經之興奮，而達到改善骨盆底生殖泌尿功能異常的效果，但目前對相關反射傳導路徑的細胞機制所知有限。近年本實驗室發現，以1Hz 頻率重複通電刺激大白鼠子宮穴位深處腹肌，發現尿道外括約肌的肌活動性不斷增加，推測此種神經突觸活性增強的現象（尿道反射增益現象；urethral reflexpotentiation, URP），是膀胱儲尿期關緊尿道使尿液禁制(contience) 的重要機制。本研究計劃預計以麻醉大白鼠為實驗動物，利用電針刺激來建立URP 的實驗模式，並探討相關細胞內訊息傳遞路徑及應用價值。

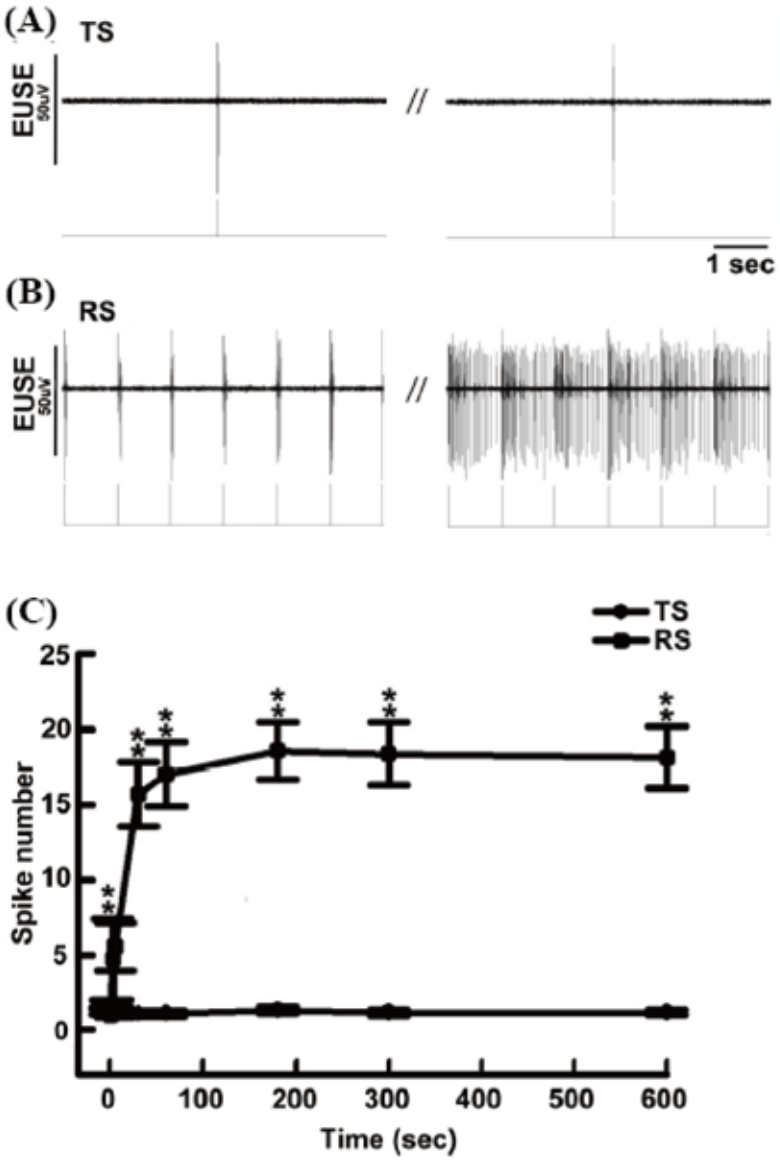
第一年：以1Hz 頻率重複通電刺激大白鼠子宮穴深處腹肌，誘導URP 形成後，經由椎管內分別注射麩胺酸接受器的拮抗劑（NBQX 及APV）；或在基本反射活性（1/30Hz 頻率不會引發URP）時，由椎管內分

別注射麩胺酸接受器的致效劑（Glutamate 及NMDA），觀察外尿道括約肌產生動作電位數之變化；同時比較兩種頻率的電針刺激下，L6~S2 脊髓組織中一氧化氮合成酶（已知與中樞神經突觸塑性的形成有關）表現量的變化。預期第一年的實驗可建立“重複性電針刺激誘導麩胺酸-依賴型URP”的實驗模式，而且與NO 的生成有關。第二年：沿用第一年的實驗模式進一步證實“麩胺酸-依賴型URP”的建立，與胞內CaMK / NO / sGC / PKG（Calmodulin kinase / nitric oxide / soluble guanylyl cyclase / protein kinase G）訊息傳遞路徑的活化有關，阻斷路徑中任何物質的活化，將會抑制麩胺酸-依賴型URP 的形成。希望藉由第一、二年的實驗結果，不但能釐清誘導URP的胞內訊息傳導路徑，亦可應用於臨床閉鎖尿道的訓練，應該有助於應力性尿失禁症狀的改善。第三年我們將利用環磷胺(Cyclophosphamide; CP) 灌注大鼠膀胱，誘發膀胱發炎的實驗動物模式後，觀察上述NO 媒介之URP 的變化，預期CP長時間擴張膀胱，造成NO 過度生成，將使增益現象的程度顯著增大。我們推測臨床長期使用CP 來抗癌或當免疫抑制劑的病人，若能配合適當降低NO 作用的處理，應可降低得到CP-誘發出血性膀胱炎副作用的機會。

Project title: NO-mediated electroacupuncture-induced urethral reflex potentiation and the intracellular messenger pathways involved.
Supported by: National Science Council
Project period: 2007/08/01-2010/07/31

The acupuncture has been widely used to treat various diseases. The mechanism involved in the therapeutic effect elicited by the acupuncture maybe the activation of nerve activities influencing visceral functions via somato-visceral reflexes. Many acupoints (i.e. UB31, UB32, UB33, UB34, CV3, CV4, SP 6, KI3, and Uterus) with therapeutic efficacy for pelvic floor or lower urinary tract dysfunction via the lumbar-sacral spinal afferent inputs have been reported. However, the intracellular signal pathways involved in the effectiveness of acupuncture is still unclear. Recent studies in our laboratory found that the urethral reflex potentiation (URP), which was elicited by repetitive electroacupuncture (Ea) stimulation at abdominal muscle below the Uterus acupoint is essential for urine continence. In the present study we designed to apply 1 Hz Ea at Uterus acupoint for 30 min to establish a URP (long term potentiation-like reflex in the external urethral sphincter electromyogram activity) in anesthetized rats. To evaluate whether glutamate involves in Ea-elicited URP, intrathecal glutamergic agonists/ antagonists are administered during Ea test stimulation (TS, 1/30 Hz) / repetitive stimulation (RS, 1 Hz). In addition, the role of nitric oxide (NO) related in the Ea-elicited URP is also determined in the study. For this assay, spinal nNOS protein levels are measured 1 hour after TS/RS byWestern blot assay.

NO and the downstream intracellular messenger cGMP, which is activated by soluble guanylate cyclase (sGC), are believed to induce long-term changes in efficacy at glutamatergic synapses through activation of protein kinase G (PKG). The aim of 2nd year is to study the involvement of the NO/sGC/PKG pathway in a novel form of Ea-elicited glutamate-dependent URP. To determine the participation of nitrergic neurotransmission in the cyclophosphamide (CP)-elicited facilitation on the distension-induced URP is another specific aim of this study at the 3th year. We infer that the increased production of nitric oxide in spinal levels appears to be involved in the hypergesia and/or hypereflexia induced by CP. To decrease nitrergic neurotransmission is proposed to prevent the side effect that CP administration to patients causes hemorrhagic cystitis.



本圖分別以測試性電刺激 (TS)，及反覆性電刺激 (RS) 刺激腹直肌引發外尿道括約肌的活動性。
Illustration of test stimulation (TS) and repetitive stimulation (RS) induced pelvic-urethral reflex activity.
EUSE: external urethral sphincter electromyogram（尿道外括約肌肌電圖）
TS: Test stimulation（測試性刺激, 1/30 Hz）
RS: Repetitive stimulation（重複性刺激, 1 Hz）

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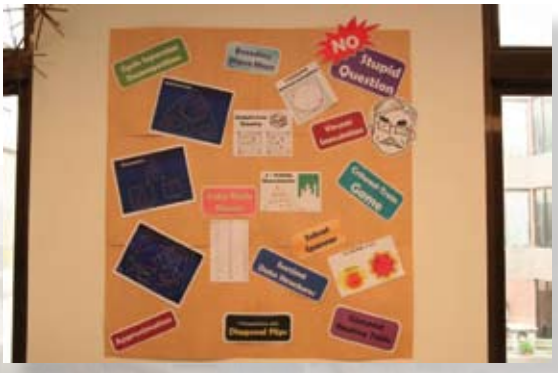
Algorithmic Research Lab.

演算法實驗室於2005年成立，目前我們有八位博士班學生與十九位碩士班學生。本實驗室的研究專注於基礎演算法的設計、分析以及應用。

The Lab of Algorithmic Research was established in 2005. We currently have 8 Ph.D. students and 19 master students. Our research focuses on fundamental algorithms and their applications.

主要研究領域 Major Research Areas

演算法、圖論、生物資訊
Algorithms, Graph Theory, Bioinformatics



研究計畫 Research Projects

1. 平面圖之「簡潔編碼」與「簡潔呈現」演算法
   algorithms for succinct encodings and compact drawings of planar graphs
2. 動態簡潔資料結構
   Succinct dynamic data structures

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計畫名稱： 動態簡潔資料結構
補助單位： 行政院國家科學委員會
計畫期間： 2009/08/01-2012/07/31

我們希望在動態簡潔資料結構的研究上，探討如何設計有序根樹的動態編碼。有序根樹(ordinal tree)是一種有根樹，每個樹節點的所有子節點都有固定的順序排列。我們希望能對有序根樹設計出一套動態編碼，達成下列兩個目標：
1. 希望編碼所需的儲存空間，在最高項達到資訊理論上的最佳解。
2. 希望編碼能夠有效率地回答一些對有序根樹的查詢，和支援樹上節點的動態更新。

在靜態簡潔資料結構的研究領域，針對有序根樹的文獻已有廣泛的探討，但在允許快速更新樹節點（新增和刪除）的動態簡潔編碼研究上，迄今相對少見。目前已知最好的結果是由 Chan、Hon、Lam、和 Sadakane 在 2005 (2007)年，以及 Arroyuelo 在 2008年所提出的編碼。基於一棵有 n 個節點的樹和 2n 個括號的平衡字串的關係，Chan 等學者針對動態平衡字串，提出第一套使用線性空間的動態編碼方案。他們的結果包含兩種動態編碼，針對不同的查詢，達到O(lg n) 時間和 O(lglg n) 時間的回答和更新效率。學者 Arroyuelo 則進一步將儲存空間降低到 2n + o(n) 個位元，其最高項已達到資訊理論上的最佳解，他們的編碼能在 O(lg n) 時間內支援節點的更新，以及更多種查詢。我們盼望能在有序根樹的簡潔動態編碼設計上，進一步改良現有的方案，研究如何開發新的輔助資料結構，有效率地同時支援樹節點的更新，以及更豐富的查詢。

Project title: Dynamic Succinct data structures
Supported by: National Science Council
Project period: 2009/08/01-2012/07/31

We study the problem of designing succinct dynamic data structures and focus on representing dynamic ordinal trees succinctly. An ordinal tree is a rooted tree where the children of each node are ordered. On the unit-cost RAM model with (lg n)-bit words, we would like to develop a succinct dynamic encoding for an ordinal tree to achieve the following objectives:

1. minimizing the space usage of the encoding to match its information- theoretical lower bound in the first-order term.
2. supporting efficient queries and updates in the worst-case time complexity.

While succinct representations for static trees have been extensively studied, the literature is limited on dynamic cases which permit efficient updates (insertion and deletion of arbitrary nodes). The best currently known dynamic encoding for trees are due to Chan, Hon, Lam, and Sadakane in 2005 and 2007, and Arroyuelo in 2008. Based on the natural association between an n-node tree and a sequence of 2n balanced parentheses, Chan et al. gave the first linear space solutions for the dynamic parentheses maintenance problem. They proposed two different O(n)-bit encodings with time efficiency of O(lg n) and O(lg n/ lg lg n) respectively, supporting updates and few queris. Arroyueloe reduced the space to 2n + o(n) bits, whose first-order term is information-theoretically optimal, and supported more queries in O(lg n) time. We propose to improve the results of of Arroyuelo and Chan et al. to achieve a 2n + o(n)-bit encoding for an n-node ordinal tree. We would like to obtain new o(n)-bit auxiliaries that enrich the set of supported queries, and achieve better performance as well for updates in the worst-case poly-logarithmic time.

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Molecular Biomedical Informatics Lab.

分子生醫資訊實驗室專注於設計先進的機器學習演算法以應用於系統生物學的研究上。在過去幾年中，實驗室團隊提出三個創新的機器學習演算法並運用這些演算法以發展以下幾項生物資訊軟體工具：

1. HomoClust—以蛋白質序列比對為基礎建構蛋白質家族的階層架構
2. iPDA—蛋白質非穩定結構區段之預測
3. Proteminer and Protemot—以局部蛋白質結構比對為基礎預測蛋白質功能
4. MEDOCK—模擬蛋白質與配體嵌合
5. Prote2S—預測蛋白質二級結構
6. ProteDNA—預測轉錄因子上與DNA鍵結殘基

The Molecular Biomedical Informatics (MBI) laboratory focuses on design of advanced machine learning algorithms for systems biology research. During the past few years, the MBI team has proposed three innovative machine learning algorithms and has exploited these algorithms to develop various bioinformatics software tools including:

1. HomoClust — construction of protein family hierarchy based on sequence alignment;iPDA — prediction of disorder regions in protein sequences
2. Proteminer and Protemot — prediction of protein functional sites based on local structural alignment
3. MEDOCK — emulation of protein-ligand docking
4. Prote2S — prediction of protein secondary structures based on the polypeptide sequence
5. Prote2S — prediction of protein secondary structures based on the polypeptide sequence
6. ProteDNA — prediction of sequence specific DNA binding residues in transcription factors

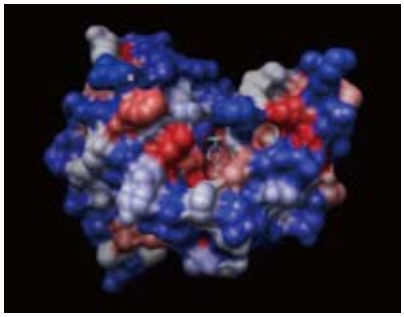
主要研究領域 Major Research Areas

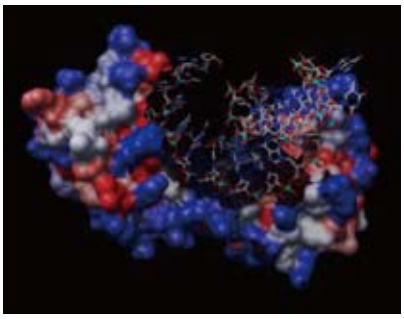
生物資訊學、資料檢索／機器學習
Bioinformatics, Machine Learning

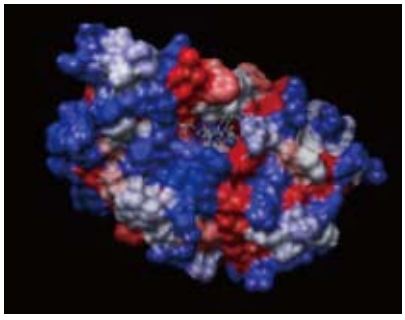
研究計畫 Research Projects

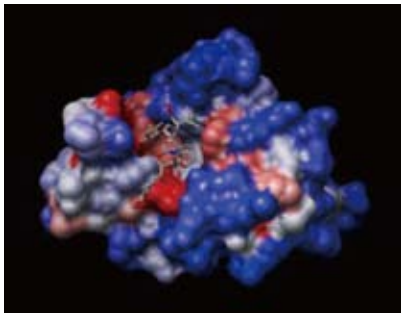
以自動知識擷取為基礎之計算功能性蛋白質體學
Computational functional proteomics based on automated knowledge extraction

計畫名稱：以自動知識擷取為基礎之計算功能性蛋白質體學
補助單位：行政院國家科學委員會
計畫期間：2009/08/01 – 2012/07/31









本整合計畫的終極目標，是設計以精確的能量評估函數為核心的生物資訊預測軟體，以期能精確地分析蛋白質/蛋白質交互作用（protein-protein interactions簡稱PPI）、蛋白質/DNA交互作用（protein-DNA interactions）、以及蛋白質/配體交互作用（protein-ligand interactions）的細節。由於本團隊將建構下列3項獨特的基礎，預期本計畫中所提出的能量評估函數將具有突破性的精確度：

1. 運用資訊擷取(information extraction)技術，以自動化的方式由文獻中擷取蛋白質結合強度的資訊，以建立最完整的蛋白質結合強度資料庫；
2. 確認影響結合自由能的關鍵因子並設計創新且高效率的評估演算法；
3. 設計創新性的非線性迴歸演算法以及多變量分析演算法。

以本計畫所提出的精確能量評估函數為核心，本團隊將設計最先進的分子嵌合模擬軟體、蛋白質功能預測軟體、蛋白質結合區預測軟體、DNA上轉錄因子結合區預測軟體等。由於蛋白質在所有的生化反應與生理作用中均扮演了最基礎的角色，因此本計劃所研發的生物資訊預測軟體，不僅能夠被有效地運用於許多生命科學的基礎研究上，同時亦可以提供分子診斷與醫療(molecular diagnosis and therapy)研究上創新性的分析工具。

Project title: Computational functional proteomics based on automated knowledge extraction
Supported by: National Science Council
Project period: 2009/08/01-2012/07/31

The ultimate objective of this integrated project is to design advanced bioinformatics software for analyzing the details of protein-protein interactions, protein-DNA interactions, and protein-ligand interactions based on the accurate energy scoring functions proposed by this integrated project. It is anticipated that with the following distinctive frameworks, the energy scoring functions developed by this integrated project will feature superior accuracy in comparison with the existing ones:

1. construct comprehensive binding affinity databases of protein-protein, protein-DNA, and protein- ligand interactions with automatic information extraction technology;
2. dentify critical energetic terms and design innovative and efficient evaluation algorithms;
3. design advanced non-linear regression algorithms as well as novel multivariate analysis algorithms.

With the advanced energy scoring functions, we will then move to design innovative computational methods and algorithms for implementations of molecular docking and predictors of protein functions, protein binding sites, and TFBS (transcription factor binding sites). As proteins play the fundamental roles at the molecular level in essentially all physiological processes, the advanced bioinformatics software designed in this integrated project will not only facilitate the investigations on many important physiological processes but also provide innovative analytical mechanisms for studies on molecular diagnosis and therapy.

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臨床-生物醫學工程-產業融合實驗室
Merger Laboratory for Clinical Sciences, Biomedical Engineering and Industry

本融合實驗室由孫維仁教授成立於1992年，主要工作是從臨床服務的病患需求觀點，來提供醫療儀器與資訊處理之相關整合研究和產品研發。九〇年代開始，是以病患自控式鎮痛儀(Patient-Controlled Analgesia, PCA)導入數位化和無線化技術為主軸的急性疼痛服務提升，開發出 i-Pain®整合平台，並已和領先全球品牌進行緊密的結合。〇三年經歷SARS氣管插管爆發群聚感染的致命性災難時，本融合實驗室針對非感染性醫材的迫切市場需求，研發出可拋式內視鏡Sunscope®，獲得經濟部學界科專和產業的贊助，朝向全球商業市場邁進。三位一體的融合實驗室成立的宗旨就是要：敞開各專業的藩籬，主動並積極的邀集跨領域人才進行多元腦力激盪，讓一切研發終極目標導向臨床應用，通過醫師嚴格的臨床驗證，確保病患實際需求獲得超值滿足，以吸引產業關注和早期資本投入。

In 1992, Professor Wei-Zen Sun founded the merger laboratory in National Taiwan University Hospital. Based on the unmet demand from patient’ s perspective, we have successfully provided innovative development of medical devices and informatics through synergistic interaction among clinician, and biomedical engineer, and entrepreneur. We started by integrating the digital and wireless technology with conventional PCA pump (patient-controlled analgesia) to transform into an update web-based platform, i-Pain®. This product is currently adopted by a global leader brand and served as the major service module in Asia. In 2003, as SARS outbreak through non-protected endotracheal intubation, we developed the most advanced intubation device with disposable visual tube. This design totally eliminates the risk of air-borne lethal infection by avoiding close contact with patient’ s airway. This innovative product, Sunscope®, has won a first prized award and is currently supported by government grant and industry investment. Collectively, we establish this merger laboratory to trigger brainstorming among multidisciplinary specialties and to make sure that the cross-reaction of respective domain knowledge is taken place under the goal: to put forth any helpful effort and technology in synergy, to assess the product under critical assessment of clinicians, to bring in industry investment and commercial distribution for patient welfare.

主要研究領域 Major Research Areas

臨床與生物醫學工程與產業整合、疼痛醫學、麻醉醫學、緊急醫療
Integration of Clinical Science, Biomedical Engineering and Industry, Pain Medicine, Anesthesiology, Emergent Medical Service

研究計畫 Research Projects

1. *i*-Pain®（美商赫士睿公司技術轉移, Hospira, USA）
2. Sunscope®（經濟部學界科專委託計畫）
3. Lidopat® / Lidocap®（美時製藥合作）
4. 健保資料庫分析（歐陽彥正教授合作）
5. 遠距緊急救護監測－同步互聯醫療網：開發以緊急救護技術員為中心的移動式整合播放站（新北市消防局中長程計畫，送審中）

計畫名稱：遠距緊急救護監測－同步互聯醫療網：開發以緊急救護技術員為中心的移動式整合播放站
Interactive Telemedicine in Emergent Medical System: Emergent Medical Technician-Based Mobile Broadcasting Station
補助單位：新北市消防局中長程計畫（送審中）
計畫期間：2011 – 2013

本研究計畫將發展以緊急救護技術員（Emergency Medical Technician -EMT）為中心的無線救護通訊系統，有別於一般以救護車為資訊中心的方式。本計畫預計研發兩個模組以及一套軟體整合系統，兩模組分別為擁有3.5G無線發射功能之遠距離通訊裝置模組，另一模組為包含低耗電的藍牙（Bluetooth）4.0版本之近距離通訊裝置模組，整合系統則包括了患者影音資料庫的緊急救護資源整合平台，三部分所運用之技術如下所述：

1.遠距離通訊裝置模組（Long Range Transmission Module- LRTM）

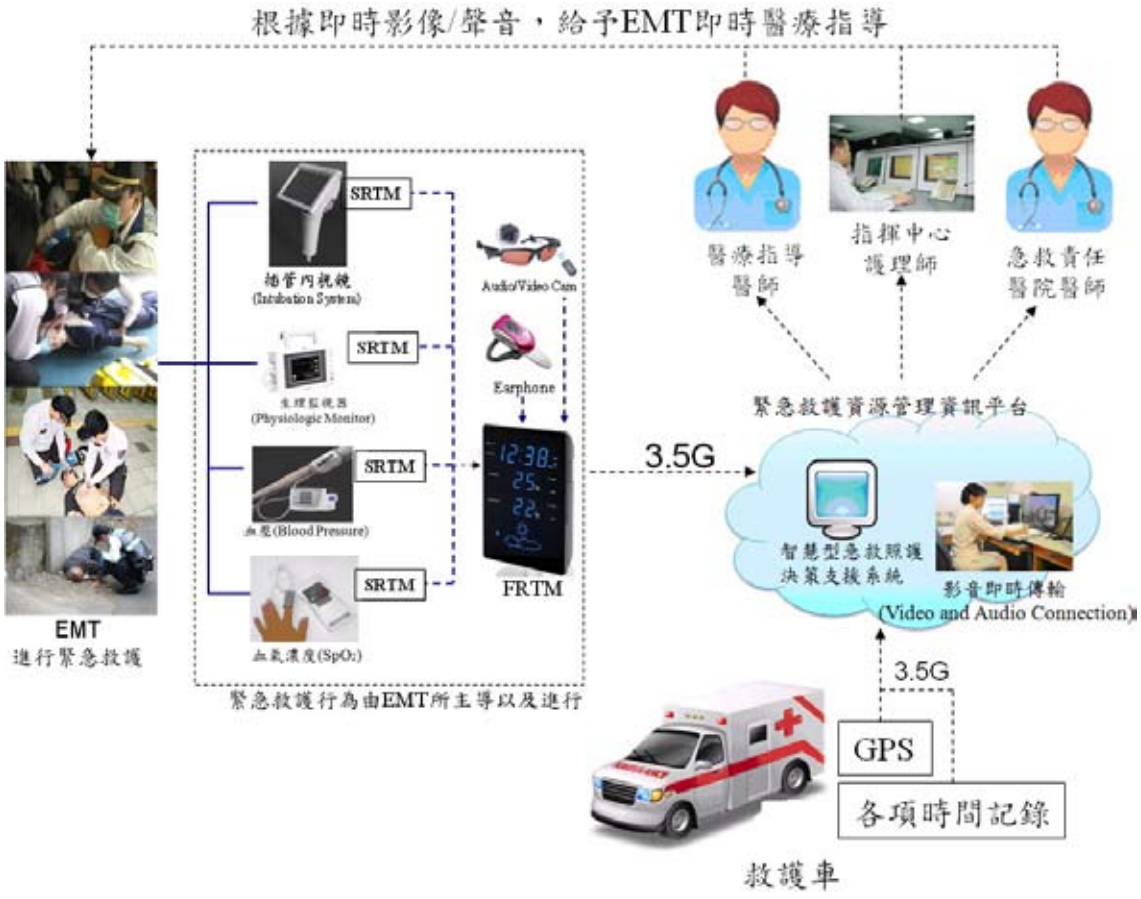
本模組預計採用ARM Cortex A9 1.2GHZ處理器，內含3.5G及Bluetooth Module並且提供2組Audio/Video接點以及一組數位接點給予微型攝影機以及微型麥克風使用，生理量測儀器間的通訊方式將依ISO/IEEE 11073（X73）所訂定的規格標準來實作，傳輸介面則採用藍牙無線傳輸；遠距離通訊裝置模組將所收到的影音訊號壓縮後，以3.5G無線網路發送至緊急救護資源整合平台進行後續處理。

2.近距離通訊裝置模組（Short Range Transmission Module- SRTM）

本模組主要以低功率藍牙通訊協定作為各項儀器與遠距離通訊裝置模組溝通之橋樑，此模組主要將急救相關設備如攜帶式生理監視器、血氧濃度劑、插管型內視鏡、搜救型內視鏡等不具有無線傳輸功能的醫療裝置無線橋接至遠距離通訊裝置模組。

3. 緊急救護資源整合平台

救護資源整合平台則為遠距資訊的匯集站，此整合平台接受由各遠距離通訊裝置模組所發送出的IP Based訊號後，開始進行資料儲存以及發送，生理相關儀器資料依照IEEE 11073規範進行儲存，影音則儲存由遠距離通訊模組發送之H264之串流資訊，不另外進行壓縮；整合資訊的發送則透過網頁進行，僅持有相關權限者，如指揮中心護理師、醫療指導醫師、相關醫療人員等，可進入觀看、交互對談模式。



本系統以ARM架構的處理器為中心，使用3.5G行動通訊網路連結相關醫療設備，如帽沿攝影機、隱藏式麥克風、藍牙耳機、氣管插管內視鏡、血氧濃度器、攜帶型生理監視器等急救器材，即時將病患的生命徵象數值(vital sign)傳遞至緊急救護資源整合平台，使得相關醫療專業人員，如救護指揮中心的護理師以及地方急救責任醫院的醫師均可即時得知病患的狀況，並及對EMT給予即時的醫療指導，有效的促進EMT、救護指揮中心之派遣員、護理師及醫療指導醫師、地方急救責任醫院的溝通與資源整合，即時的經由EMT進行最恰當的處置，給予病患必要且適當的照護，提高救護的品質與病患的存活率，以EMT為資訊中心的資訊連結架構圖如圖所示。

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Assistant Professor, Graduate Institute of Biomedical Electronics and Bioinformatics /Department of Electrical Engineering, National Taiwan University

生醫光譜與影像實驗室
Biomedical Optical Spectroscopy and Imaging Lab.

我們實驗室的研究方向是以光學方法來觀察生物組織、細胞與分子，主要分為各種光譜的分析以及光學影像系統的應用，以期對生物醫學領域的研究有所助益，並開發新的輔助醫學診斷的工具。長期的目標是針對疾病（特別是癌症）的早期徵兆，發展低侵入性的診斷儀器系統。

The research focus in our laboratory is to push forward the technologies of sensitive optical detection and imaging systems and utilize these systems to aid biomedical research and develop new diagnostic tools. The long-term objective is to develop minimally invasive diagnostic tools for early detection of disease such as cancer.

主要研究領域 Major Research Areas

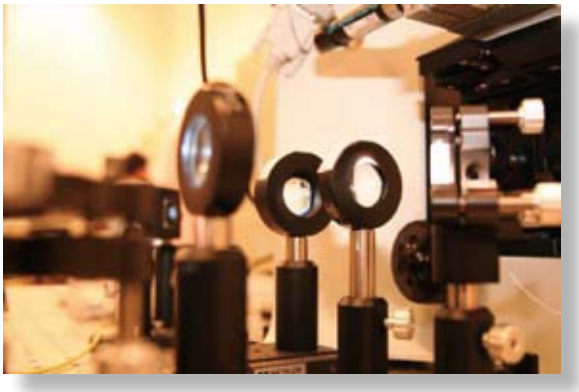
生醫工程、生醫光電
Biomedical engineering, Biophotonics

研究計畫 Research Projects

1. 乳癌治療抗療性之整合研究－乳癌經放射治療、化學治療或合併治療後分子特徵之比較（子計畫二）
   Integrated approach to dissecting resistance of anti-cancer treatment in breast cancer – comparison of molecular signatures in breast cancer following chemo- and/or radiotherapies (subproject 2)
2. 上皮細胞之結構與其散射光譜之關連性研究
   Study of the relationships between structure of epithelial cells and scattering spectra
3. 以結合光纖之高光譜影像術進行非侵入性癌前病變與癌症早期診斷
   Noninvasive early diagnosis of precancer and cancer using fiber-optic-based hyperspectral imaging

計畫名稱：以結合光纖之高光譜影像術進行非侵入性癌前病變與癌症早期診斷
補助單位：行政院國家科學委員會
計畫期間：2010/08/01-2013/07/31

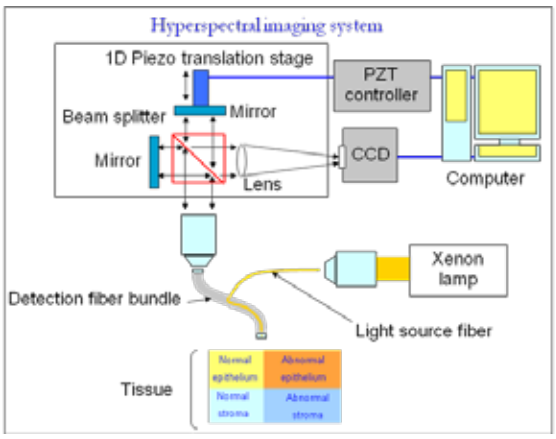
本三年期研究計畫之目的是運用反射光譜與螢光光譜的技術，發展新穎的非侵入式癌(前)病變的早期診斷工具。現有的應用光譜進行非侵入式診斷主要有兩種方式，使用單點的光纖探頭測量組織局部區域的平均光譜，以及使用少數幾個特定波長的濾片來擷取大範圍的組織影像。本研究方法的優點在於結合光纖束與高光譜影像系統，可快速擷取組織上較大範圍內不同位置的光譜信號，因此同時具有兩種現有技術的優點，再利用蒙地卡羅數值模擬開發資料分析工具，將組織內不同深度的光學特性如散射、吸收與螢光強度定量，以輔助早期病灶之診斷。本計畫選定口腔與皮膚的癌（前）病變作為測試標的，由於組織的影像資訊是經由光纖束傳導到高光譜影像系統，不需要使用複雜且昂貴的微小化掃描機制造影，因此未來若使用與內視鏡的工作通道相容的光纖探頭，便可進一步將此技術廣泛應用在消化道黏膜上的早期癌病變檢查。我們首先將建構可移動的高光譜影像系統，並使用具有跟組織的散射與吸收係數相近的仿體，驗證此系統測量到的光譜資料與組織光學參數的關係。然後將進行動物實驗，以致癌物誘發小鼠皮膚癌以及倉鼠口腔癌的動物模式，在致癌的不同階段收集光譜影像資料，並在測量的位置做組織切片以提供組織分層結構與上皮細胞型態等資訊，協助開發與驗證用以分析組織深度與光學參數的工具。最後將進行先導性人體實驗，以評估此新穎儀器與資料分析方法作為輔助診斷工具之可行性，並與現有方法比較效能。

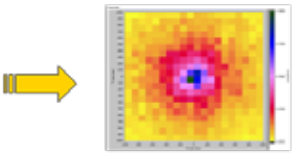


Project title: An integrated system Project title: Noninvasive early diagnosis of precancer and cancer using fiber-optic-based hyperspectral imaging

Supported by: National Science Council
Project period: 2010/08/01-2013/07/31

The objective of this proposed three-year project is to develop a novel non-invasive system based on reflectance and fluorescence spectroscopy for early detection of precancerous and cancer lesions. The major novelty of our approach is the hyperspectral imaging capability that enables simultaneous acquisition of spectra from hundreds to thousands of separated locations on tissue surface through an imaging fiber-optic bundle. Compared with existing point-probe optical spectroscopy systems, the proposed method covers a larger area of tissue and has the ability to obtain depth-resolved tissue optical properties and fluorophore concentration for more accurate diagnosis. Compared with multispectral imaging systems developed for in vivo diagnosis, our approach has higher spectral resolution which facilitates extraction of tissue optical properties. We will build a movable hyperspectral imaging system incorporating an imaging fiber-optic bundle to relay the spatial information from tissue to the rest of the instrument, which eliminates the need to miniaturize the scanning mechanism so the probe can be made to be compatible with endoscopes. Reflectance and fluorescence spectra will be measured from tissue mimicking phantoms with known optical properties and geometry and validated with theoretical predictions obtained by Monte Carlo simulations. To investigate the feasibility of the proposed method to obtain diagnostically relevant tissue information in vivo, we will use animal models of oral and skin cancers to investigate the relation between dysplastic changes in tissue and the measured spectra. Monte Carlo-based data analysis methods will be developed to solve the inverse problem of obtaining tissue optical properties from measured spectra. Histopathologic information of the measured tissue sites will be provided as the gold standard for diagnosis. Finally, we will conduct pilot in vivo studies on the skin and the oral mucosa to determine whether the unprecedented spatial-spectral information can improve the discrimination between normal tissue, benign lesion, various degrees of dysplasia and cancer. We believe that successful completion of the research could lead to future development of a clinical tool which can detect the presence of epithelial precancer and provide information about the stage and the extension of the lesion.





Spatially resolved reflectance spectroscopy

1. Extracting tissue optical properties
2. Detecting tissue neoplasia for in vivo diagnosis

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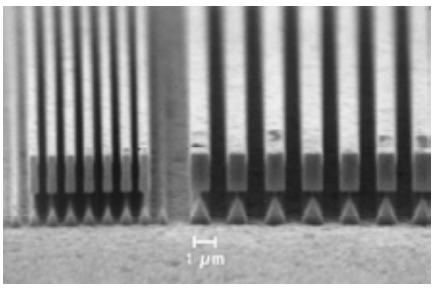
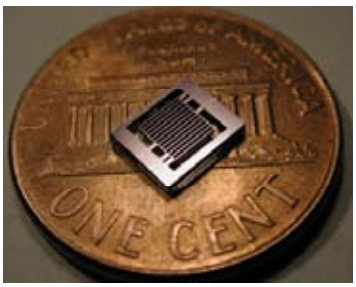
微奈米分析技術及系統實驗室
Micro/Nano Analytical Technologies & Systems Lab.

本實驗室由田維誠教授成立於2009年。本實驗室的研究方向為微奈米分析技術及系統在生醫檢測，醫療技術，及生物化學應用之研究。本實驗室的研究重心在微奈米機電、微奈米流體力學及有關元件系統整合、封裝及可靠性之研究，並希望與CMOS製程相結合。

未來將以微奈米分析技術及系統儀器出發，希望能大幅改進臨床前、臨床及體外診斷之準確性、速度、成本及使用方便性。

My research interests are on biological, chemical, and medical applications of micro & nano technologies with the focus on the CMOS compatible integration, packaging, and reliability of the micro/nano devices and systems. The future goal is to improve the accuracy, speed, cost, and ease-of-use of pre-clinical, clinical, and in vitro diagnostics by using micro/nano-enabled systems or instrumentations.





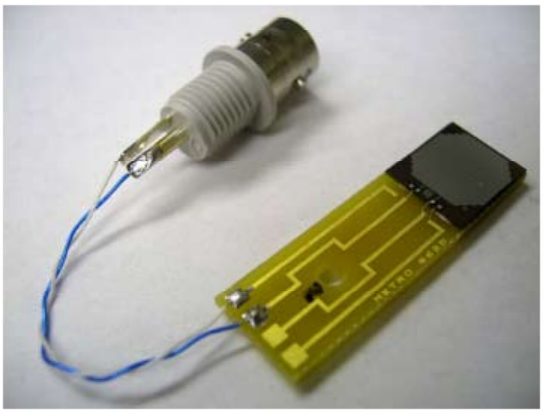
主要研究領域 Major Research Areas

微奈米分析及流體集成技術、微奈米機電系統儀器在生化醫療之應用

Micro and nano analytical & fluidic integrated technologies, MEMS/NEMS enabled instrumentation for biological, chemical and medical applications.

研究計畫 Research Projects

1. 人體呼吸氣體分析儀關鍵元件之研製與開發
   Research and Development of Key Components for Human Breath Analyzer
2. 混合式CMOS相容壓力微感測器陣列在非侵入血流監控之應用
   Mixed Mode CMOS-based Pressure Microsensor Arrays for Non-Invasive Hemodynamic Monitoring



計畫名稱：人體呼吸氣體分析儀關鍵元件之研製與開發
補助單位：行政院國家科學委員會
計畫期間：2010/01/01-2010/12/31

現有之非入侵式癌症醫療診斷儀器，通常癌症早期小於0.5 cm之腫瘤不易被偵測出，因而延誤病患就診最佳時機。然而，磁振造影需要較長時間之掃描，或胸腔X光檢測病患需暴露於放射線，這些都會使病患感到不適或產生健康上的疑慮。此外，此類儀器通常體積龐大且售價昂貴。

可攜式人體呼吸氣體分析儀可用來對疑似癌症病患作其呼出氣體之分析，例如病患呼出之某些揮發性有機化合物即將被美國FDA認定為肺癌及乳癌之生物標記。藉由適當設計微型化氣體分析關鍵元件(包含前端之前濃縮管、高效能微米分離管、高感度奈米感測器)，癌症之生物標記可以被偵測出，且其濃度有可能被放大數千至數萬倍，因此初期癌症極微量的生物標記也能被偵測到。

本計劃依研究內容性質分成三個領域：微型化氣體分析關鍵元件設計製造、效能測試及理論研究，關鍵元件間之整合，及系統原型研製與人體呼吸實測。計畫期程規劃為三期：第一期(1)高感度奈米感測器之研製與模型研究(2)微型化氣體分析關鍵元件及系統測試平台之建立。第二期(1)高效能微米分離管之最佳化設計及製程研究(2)微濃縮管及其高容積奈米吸附表面之研究(3)微型化氣體分析元件及系統整合。第三期(1)微型化氣體分析系統原型研製(2)人體呼吸實測。

Project title: Research and Development of Key Components for Human Breath Analyzer
Supported by: National Science Council
Project period: 2010/01/01-2010/12/31

With the existing non-invasive cancer diagnostic equipments, it is very difficult to detect the abnormal tissue or tumor size smaller than 0.5 cm at the early stage of the cancer. This poor diagnostics on early cancer detection will delay the best time for patient to be treated. For example, diagnostic technology such as magnetic resonance imaging or Chest X Ray can be used for cancer diagnostics. However, it either took a relatively long time to scan patients or the patients need to be exposed to radiation, both of these attributes may result the un-comfortableness of the patients. In addition, the equipments are typically large in size and the cost is expensive.

A portable human breathe gas analyzer can be used to diagnose the patients who may suffer from cancer. Some volatile organic compounds from human breath gases are going to be approved by USA FDA as bio markers for human diseases, e.g. lung cancer or breast cancer. By properly designing the micro gas analyzer, or called MGA, (including front-end micropreconcentrator and high surface area adsorbents, high resolution micromachined separation columns, and highly sensitive nano detectors), some key bio markers should be able to be identified and the concentrations of these bio markers can be amplified up to 103 to 104 times. Thus, we should be able to detect the trace concentration of bio markers from patient's breath gases even in the early stage of cancer.

The advantages to use a MGA is the following: high sensitivity, low power, rapid detection, small in size, lower cost compare to conventional equipments, multiple gas detection capability. More importantly, our MGA will decrease the pain and un-convenience significantly compare to conventional diagnostic methods. The same MGA system can also be used to track the efficacy of cancer therapies.

Three main areas are proposed for this project: MGA key component design, MGA key component fabrication and integration, and MGA key component test and model. A 3-phase program is proposed for this project: Phase I (1) Highly sensitive nano detector design, fabrication, package, testing, and modeling, (2) MGA key component and subsystem testing platform development; Phase II (1) Optimal design and fabrication for high resolution micromachined separation columns, (2) Front end sampling device development, (3) MGA key component integration and packaging; Phase III (1) MGA breadboard prototype development, (2) MGA field testing on human breath analysis.

Proposed 3-phase portable breath analyzer key components development plan and conceptual system diagram. This portable breath analyzer consists of preconcentrators, high performance separation columns, and highly sensitive nano detector.

可攜式人體呼吸氣體分析儀其關鍵元件設計製造、效能測試及理論研究、系統原型研製及人體呼吸實測將於分三期完成。可攜式人體呼吸氣體分析儀包含微濃縮管、高效能微米分離管及高感度奈米感測器。

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Digital Signal Processing Lab.

一、生醫訊號處理

1. 超音波：對比劑的研究和利用，計算經由對比劑回波訊號中的諧波成分來估測理論中組織的衰減係數，其中必須利用周期譜的方式求得訊號的功率頻譜密度。設計一個可用在體內實驗的適應性演算法，用以估測體內組織的衰減係數。並且，對此法做誤差分析以得知應用此方法估測衰減係數與理論值的差距。利用動物實驗，將不同程度的肝臟疾病應用超音波對比劑在肝組織的分佈情形藉以判斷肝病。
2. 胎兒心電圖：胎兒心電圖的觀察有實際上的困難，因為胎兒位於母體之內，皮膚上的電極所紀錄的信號中，同時存在兩個本質上相同的來源，為母親和胎兒的心臟。尤其母親心電圖的信號強度遠大於胎兒心電圖，更增加了處理上的困難。另外，因為胎兒心電圖十分微弱，其他生理現象所產生的干擾或是量測上造成的雜訊，相對於胎兒心電圖的影響也會十分顯著。本研究著力於胎兒心電圖的信號取得。
3. 腦波

二、水下通訊

水聲通訊和無線電通訊主要有二個最大的差異點，一是水聲通道有非常長的多重路徑延遲，範圍可涵蓋十到一百多個符號(symbols)，另一個是通道時變的速度。對於基於通道估測的等化器來說，通道估測是決定其效能的表現的最重要因素。

主要研究領域 Major Research Areas

- Diagnostic Medical Ultrasound: Ultrasound Contrast Imaging, Ultrasonic Liver Imaging
- Bio-signal Processing : Fetal ECG extraction,EEG Signal Analysis
- Underwater Acoustic Communication: UWA Channel Estimation, Tracking and Equalization

1. 超音波對比劑於組織參數估測之應用(1)
2. 超音波對比劑於組織參數估測之應用(2)
3. 一個用於二次諧波脈衝壓縮成像之多頻合成技術

計畫名稱：超音波對比劑於組織參數估測之運用
補助單位：行政院國家科學委員會
計畫期間：2007-2009

對於生物組織的超音波反應特性而言，衰減係數是個重要的參數。一般估測組織的衰減係數大略可分為利用背散射訊號估測以及穿透訊號估測兩種。其中，背散射訊號的估測方式可適合於大部分的應用。但是卻有散射成份干擾的困難。應用穿透訊號的方式是較為適合於估測衰減係數，但是由於必須在組織兩端皆放上探頭，因此只適合體外實驗用。近年來由於超音波對比劑的的技術成熟，使得我們可以發展一個新方法，使用對比劑來估測體內組織的衰減係數。由於對比劑有高度非線性的特性，因此我們藉由使用多組頻率激發組織之後的對比劑，我們可應用其所產生的諧波訊號達到應用穿透訊號估測組織衰減係數的目的。除此之外，我們也應用對比劑在肝組織當中的分佈比率估測肝組織整體的健康程度。

在本計劃中，我們將研究分成三個部份來進行研究：（一）我們計算經由對比劑回波訊號中的諧波成分來估測理論中組織的衰減係數，其中必須利用周期譜的方式求得訊號的功率頻譜密度。（二）設計一個可用在體內實驗的適應性演算法，用以估測體內組織的衰減係數。並且，對此法做誤差分析以得知應用此方法估測衰減係數與理論值的差距。（三）利用動物實驗，將不同程度的肝臟疾病應用超音波對比劑在肝組織的分佈情形藉以判斷肝病。

Attenuation Coefficient (Att. Coef.) is an acoustic parameter for tissue characterization. Two major techniques for Att. Coef. Estimation are the backscattering and transmission methods. Backscattering method is suitable for general applications, but the speckle interference makes it inaccurate. Transmission method is more reliable, but it is suitable for peripheral organs only, due to the need of a separate transmitter. With the aid of contrast agent (microbubble), a new way to estimate the Att. Coef. of soft tissues is proposed, which is suitable for general applications . Since microbubble is a highly nonlinear object, Using the multiple frequencies generated by microbubbles behind the tissue, the Att. Coef. Can be estimated in transmission mode. Since the harmonics are generated by common microbubbles, their relative strengths can be predicted by theory and measured for Att. Coef. Estimation.

The research is divided into three parts. First, we use periodogram to estimate the power spectrum of echo signals and using the second harmonic component to estimate the theoretical Att. Coef. Secondly, we will develop an adaptive algorithm to estimate Att. Coef. Which is suitable for general application. Finally, we use agent distributed in different rates to estimate liver diseases.

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計算分子之設計與偵測實驗室
Computational Molecular Design & Detection Lab.

本實驗室是一個跨領域的實驗室，研究的方向有兩個主軸，一是以分子結構為中心探討分子結構與活體、活性、毒性之關係，包括計算化學用在藥物設計、計算毒理學、化學資訊、生物資訊及代謝體學等，本實驗室應用物理化學、數值分析及資訊統計的技術來解決各種生物、化學及醫學方面的問題。目前主要的研究包括 1. 發展新的計算化學方法做為臨床前藥物吸收、分佈、代謝及毒性之分析及新藥設計 2. 以化合物三維結構分析用在化學資料庫做虛擬藥物篩選與化學結構資訊比對 3. 應用代謝體之化學結構光譜找尋臨床上用來做為診斷、病程及癒後生物指標之結構及新藥設計。

另一主軸則是運用台灣特有之健保資料庫來分析台灣藥物使用之各種問題及行為模式等。此外，本實驗室亦與其他相關藥物設計、分析、合成團隊共同執行國內外各項藥物開發之研究計畫。

Bioinformatics and Cheminformatics Laboratory is a multidisciplinary lab. There are two main research themes in this lab. First and the major one is to analyze molecular structures such as drugs, endogenous molecules, proteins, and relate the structure for their pattern with biological activities, toxicities, and biological systems in the field of computational chemistry, computational toxicology, bioinformatics, cheminformatics, and metabonomics.

The other major theme is to use National Health Insurance Research database to perform analysis in prescription usage, prescribing pattern of medical personal, related policy impact and health behavior. We collaborate closely with pharmaceutical companies, drug synthesis groups, and drug analytical groups to conduct drug discovery research.

主要研究領域 Major Research Areas

計算化學及計算毒理學、生物資訊學、化學資訊學、醫學資訊學
Computational Chemistry and Computational Toxicology, Cheminformatics, Bioinformatics, and Medical Informatics

研究計畫 Research Projects

1. 三維結構模式生物資料庫的快速檢索
   3D conformational structure patterns for fast bioinformatics database searching
2. 乳癌治療抗療性之整合研究--以aptamer之電腦模擬篩選(In silico)平台發展抑制血管新生抗乳癌藥物（子計畫一）
   In Slico aptamer platform for anti-angiogenesis on breast cancer (subproject 1 of Integrated approach to dissecting resistance of anti-cancer treatment in breast cancer)
3. 結構最佳化計算暨臨床前結構安全性篩選
   In Silico Lead Optimization and Preclinical Safety Screening

計畫名稱： 乳癌治療抗療性之整合研究-以aptamer 之電腦模擬篩選(In silico)平台發展抑制血管新生抗乳癌藥物（子計畫一）
補助單位： 行政院國家科學委員
計畫期間： 2007/08/01-2008/07/31

在這個子計畫中，我們透過電腦平台來發展TW01系列(replace aptamers)的化合物，以期對於小分子在抗血管新生的藥物開發能有所貢獻。對於與receptor independent的QSAR分析，我們藉由一系列抑制劑的結構、比對和基團等資訊，藉由4D-QSAR的方法建立抑制酵素的相關結構活性定量模型。根據4D-QSAR對於BCM-TW這一系列激酶抑制劑中分析的結果，結構上的修正可用來做結構的最佳化。

QSAR模型是由TW01類似物對人類腫瘤細胞株MDA-MB-231（乳房）和PC-3（攝護腺）之IC50數值建構而來的基團模型。對於二個資料集中較佳的模型皆展現相關係數R2大於0.8與交叉驗證相關係數Q2大於0.7。從MDA-MB-231建構出之較佳模型的基團來看，IC50是與籠罩化合物的非極性或任意型態的描述子相關，即使是由PC-3所建構出的模型來看，亦有一個類似的基團之描述子比其他在同一模型中之描述子有較高的權重，此外其他出自PC-3模型之基團為負極性與氫鍵受體。

先前在激酶與ATP主要結合區域的基團研究中，結合模式高度地與散佈在蛋白質基酶ATP結合區域的疏水和芳香族基團有關，從4D-QSAR的基團模型與文獻推論，我們判斷ATP結合區域是TW01類似物最有可能的標的。

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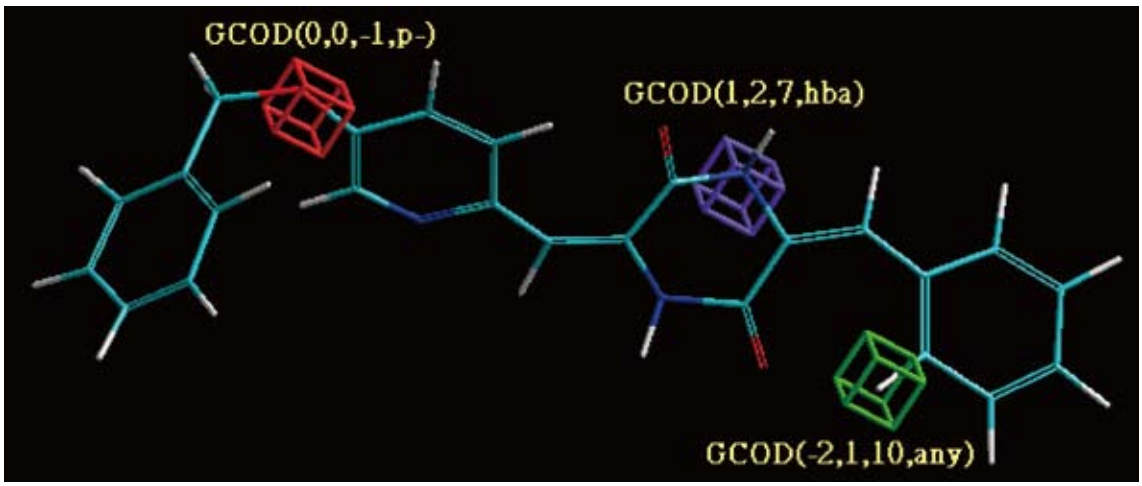
Project title: In silico platform for anti-angiogenesis screening
Supported by: National Science Council
Project period: 2007/08/01-2008/07/31

We developed an in silico platform for a series compounds as guides for anti-angiogenesis. We performed receptor independent 4D-QSAR analysis to construct quantitative models of enzyme inhibition as a function of the conformation, alignments, and putative binding pharmacophore of the series inhibitors from ligand structure and conformation profiles. The QSAR analysis result indicated possible structural modifications of the BCM-TW series class of protein kinase inhibitors with the goal of expanding the pool of TW01 series derived inhibitors of protein kinase.

QSAR models were constructed and structure pharmacophore models with IC50 value of TW01 analogues against human tumor cell lines of MDA-MB-231 (breast) and PC-3 (prostate) were proposed. The preferred models for both two data sets contained correlation coefficients, R2, larger than 0.8 and cross-validation correlation coefficients, Q2, larger than 0.7. For MDA-MB-231, the pharmacophores of the preferred models indicated that the IC50 was related to the descriptors to specific special arrangement with the pharmacophore type non-polar. For PC-3 cell line assay, similar special arrangement descriptors with the similar pharmacophore type displayed the highest weight and much larger than the other descriptors in the same model. Moreover, the other pharmacophores in the model for PC-3 are either of polar negative or hydrogen-bonding acceptor type.

In the previous kinase pharamacophore studies on the main binding site with ATP, the binding mode highly depended on hydrophobic and aromatic pharmacophores around the ATP binding site of protein kinases. From the 4DQSAR pharmacophore model and the literature, we concluded that the ATP binding site was the most possible target for TW01 analogues.



本圖顯示利用從演算法取得的單一模型預測化合物BCM-TW-026具有活性的構形，圖中的方格邊長皆為1Å，並分別以綠色、紅色及紫色分別表示「任何基團」、「具負極性」及「氫鍵的受體」等IPE的形式。

Predicted Active Conformation for Compound BCM-TW-026 Using The Unique Models from Alignment. The grid cells from the model are the colored 1Å cubes. IPE type “any”, “polar” or “H-bond accepter” was represented by the color of cube with green, red or violet respectively.

王水深 教授 *Wang, Shoei-Shen,* Professor

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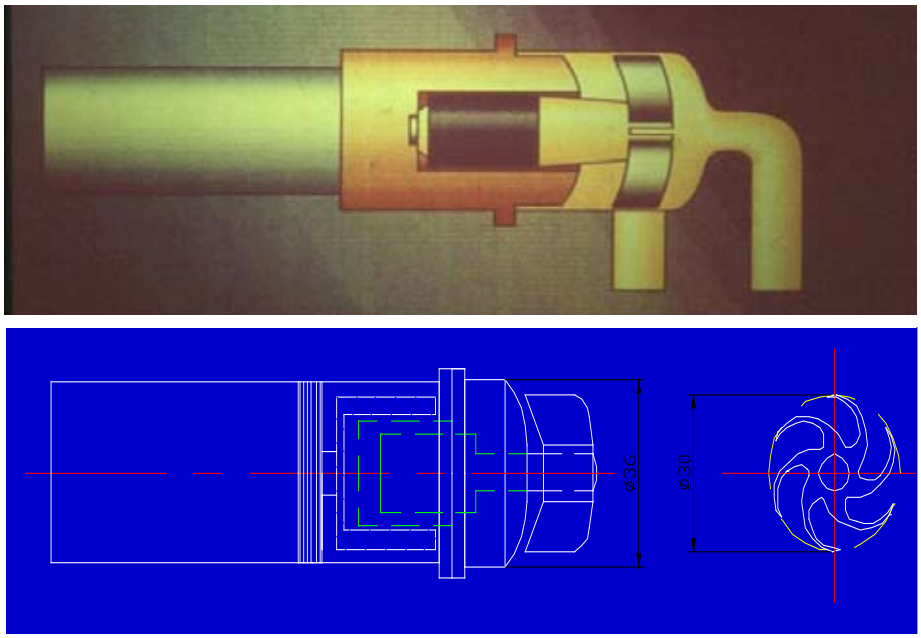
心臟輔助器實驗室
Ventricular Assist Device Lab.

自1993年我們就積極研究流線型離心幫浦做為心臟衰竭的輔助循環，可在100mmHg阻力下提供8 L/min的輔助。而利用電壓的改變而改變葉輪的轉速造成博動流。包含馬達的總重量只有110g，總長度只有7 cm，溶血系數只有0.020。此心臟輔助器擁有經濟部智慧財產局新型第一五四一O五號及新型第M323290號專利。目前我們持續研究小而美的心臟輔助器以供幼兒使用。

We started to develop our own centrifugal pump with streamlined design in impeller type in 1993. It can produce 8L/min output at a resistance of 100 mmHg. It can provide pulsatile flow by changing the rotating speed of the impeller periodically via introducing a square wave form voltage into the driving motor coil of the pump. Together with the generator, it weighs only 110 gm with a total length of 7 cm, and index of hemolysis of only 0.020. Now we keep on developing a smaller pump to treat the intractable heart failure for infants.



臺大一號心室輔助器

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主要研究領域 Major Research Areas

- 心臟外科包括冠狀動脈繞道手術、瓣膜手術、主動脈手術、心律不整手術、心臟衰竭手術等
- 血管外科包括胸主動脈瘤支架或手術、腹主動脈瘤支架或手術、周邊動脈阻塞重建手術、靜脈曲張手術、尿毒症血液透析之廔管手術等
- 心臟輔助循環包括葉克膜體外維生系統、心室輔助器等
- 移植手術包括心臟移植、心肺移植

研究計畫Research Projects

1. 台大心室輔助器導管組織化之研發：Poly(ε -caprolactone)(PCL)- Chitosan表面奈米化對細胞成長之效應
   Taita left ventricular assist device application for tissue-engineering :
   surfaces technique could enhance the growth of cells and application for tissue engineering.
2. 一項為期6個月、多中心、隨機化 、開放性的研究，其目的在評估Certican加類固醇並加上二種劑量的Neoral在新的心臟移植患者的安全性、耐受性及有效性
   A six-month, multicenter, randomized, open-label study of the safety,tolerability and efficacy of two Neoral doses in addition to Certican and steroids in de novo heart transplant recipients.
3. 骨髓間葉幹細胞於心肌再生的研究：組織工程支架與骨髓間葉幹細胞的分化 一、材料的修飾 二、不同的生長與分化環境
   Regenerating myocardial cells by using mesenchymal stem cell(MSC)-the effect of a.different scaffold surface material, b.different growth and differentiation environment on the differentiat of MSC within tissue engineering scaffold.
4. 正位心臟移植手術其術後身體活動度與心率變異度相關性之探討
   heart rate variability in orthoropic heart transplant recipient.
5. 人體心肺移植/ Heart-lung transplantation.
6. 一項為期24個月、多中心隨機分配、開放性、非劣性的研究，比較在兩個濃度控制的Certican併用降低劑量的Neoral對照3克的MMF併用標準劑量的Neoral於新接受心臟移植病患者的療效與安全性
   A 24-month, multicenter, randomized, open-label non-inferiority study of efficacy and safety comparing two exposures of concertration-controlled Certican with reduced Neoral versus 3.0g MMF with standard dose Neoral in de novo heart transplant recipients.
7. 人類心臟幹細胞之分離與鑑定
   Identification and characterization of human cardiac stem cells.
8. 不同製備方式評估蠶絲支架(scaffold)及不同的表面修飾對骨髓間葉幹細胞的體外心肌細胞分化與動物植入心肌再生實驗
   Effect of different surface modifications and fabrication techniques of silk fibrion-based scaffolds on differentiation of MSC into myocardiocytes in vitro, and on regenerating myocadiacytes in myocardial infarction(MI) rats.
9. 骨髓間葉幹細胞於心肌再生的研究：評估不同製備方式評估蠶絲移植物對骨髓間葉幹細胞分化影響與動物實驗(1,2,3)
   Regenerating myocardial cells by using mesenchymal stem cell(MSC)- effect of different fabrication techniques of silk fibrion-based scaffolds on differentiation of MSC into myocardiocytes in vitro, and aminal study(1,2,3).
10. 幹細胞於心肌再生的研究：評估蠶絲移植物對幹細胞分化影響與動物實驗
    Regenerating myocardial cells by using stem cell-silk fibrion-based thin film on differentiation of stem cell into cardiomyocytes in vitro, and animal study.

王唯工 教授 *Wang, Wei-Kung,* Adjunct Professor

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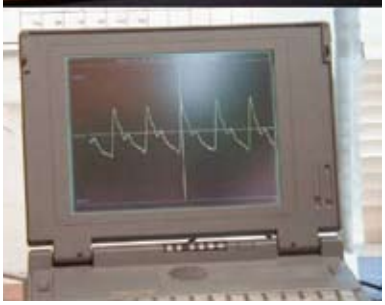
非侵入式生理量測實驗室
Non-Invasive Physiological Measurements Lab.



非侵入式生理量測實驗室，其主要乃以科學之方法來進行中醫在疾病診斷、治療以及保健等原理與其可行部份之驗證研究；以及利用非侵入方式量測生理參數如血糖、血氧等。

近幾年來，實驗室在王唯工老師的帶領下，所進行的研究如下：

1. 脈診分析理論在臨床診斷之應用：
   在此項中，早於民國81年即已完成脈診儀的原型儀器(Prototype)，進行以脈診儀協助中醫診斷的可行性研究；進而將之應用於中藥的方劑作用分析；再進一步針對血壓波及微循環血流波頻譜的交互關聯做更深入地探討。將其用之於臨床疾病診斷的評估及應用。
2. 非侵入式生理參數量測：
   近年來，實驗室研究以非侵入方式量測血液中成份，包括血糖、血氧。

Non-invasive physiological Laboratory was founded by Professor Wang Wei-Kung with the main research focus in Pulse-feeling and foundation of Chinese medicine and non-invasive means to study blood ingredients, such as Glucose, Oxygen. In the past few years, we have conducted a number of research projects in the following:

1. Applications of Pulse-feeling in clinic diagnosis
   We had finished the prototype of pulse diagnosis system in 1992. We used the pulse diagnosis system to assist diagnosis of Chinese medicine and analyze the mechanism of Chinese herbs. And research focus in the relationship between pressure pulse and spectrum of microcirculation and applications of Pulse-feeling in clinic diagnosis.
2. Non-invasive means to study blood ingredients
   In the past few years, we used the non-invasive means to study blood ingredients, such as Glucose, Oxygen.

主要研究領域 Major Research Areas

非侵入性式生理量測

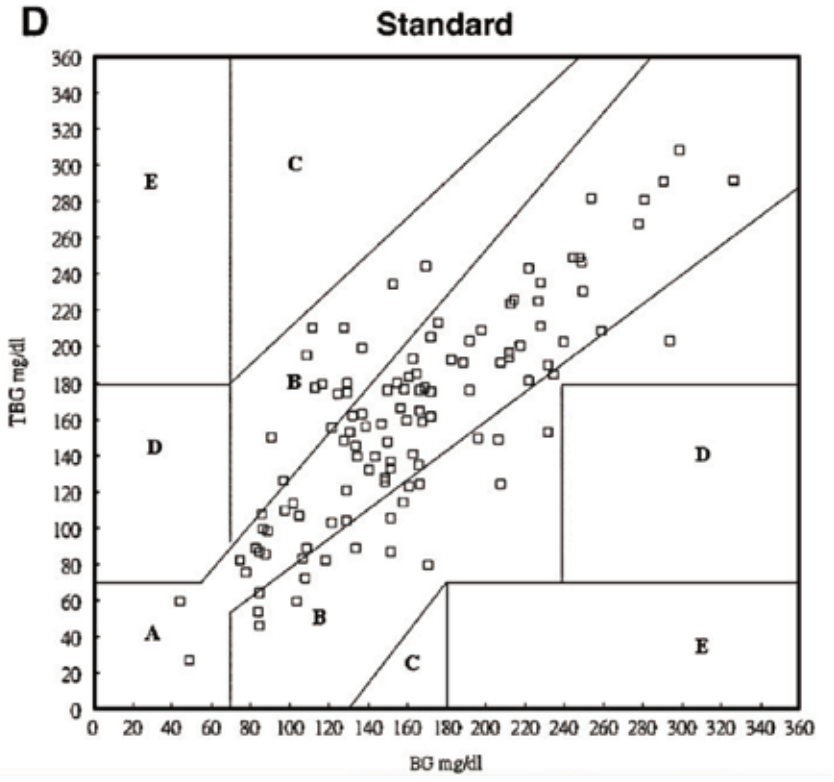
Major Research Areas: Non-invasive physiological measurement

研究計畫 Research Projects

1. 非侵入性生理量測血液成份如血糖、血氧
   Non-invasive means to study blood ingrediences. Such as Glucose, Oxygen
2. 中醫基礎與脈診研究
   Pulse-feeling and fundation of Chinese medicine
3. 減少二氧化碳產生之食品與塑身研究
   Food to reduce CO2 production and body Casting
4. 遠距醫療服務之研究
   How to provide these services through Web

計畫名稱：非侵入式血糖監視儀
補助單位：Tangtest股份有限公司
計畫期間：2003-2010

研究並改進Tangtest非侵入式血糖監測儀，包括其軟硬體的修改與臨床試驗的程序。相關成果論文發表於Journal of Diabetes and Its Complications doi:10.1016/j.jdiacomp.2007.03.011



Y軸為非侵入血糖監測儀所量測數值，X軸為一般採血血糖值。113資料點全落於Clarke error grid中A、B區。其線性關係(r=.81; slope=0.82; intercept=28.0)

The y-axis represents measurements from the TG (TBG), and the x-axis represents measurements from the fingerstick blood glucose meter (BG).The 113 data points with correction of both the position and P criterion, of which 100% fell within Zones A and B in the Clarke error grid. Data in Zones A and B exhibit a linear relationship (r=.81; slope=0.82; intercept=28.0) between noninvasive and fingerstick measurements.

Project title: Non-invasive blood glucose monitoring
Supported by: Tangtest Co. USA
Project period: 2003-2010

The objective of this study was to determine the conditions for optimizing measurements obtained with a noninvasive blood glucose monitor using the optical signal of pulsatile microcirculation (OSPM) in both prediabetic and diabetic subjects receiving medication. Research design and methods: Eighteen subjects (3 prediabetic, 15 diabetic) aged 61.8 [15.9] years (mean [S.D.]) were studied. OSPM was the pulsatile component (P) of the signal obtained and analyzed by a blood glucose monitor. The measurement was calibrated to the fingerstick meter for each subject for personal calibration. Data were obtained from all subjects using both meters. Results: A total of 179 data pairs were measured and analyzed. The validity of the position of the tested finger was assessed using the position criterion, which

resulted in the removal of 38 data pairs. The criterion for the intensity of the P signal was satisfied by 141 data pairs, with nonconforming data (with a much lower P signal) mainly occurring below 26℃. A total of 113 data points passed both criteria, and 100% of them fell within Zones A and B of the Clarke error grid. Data in Zones A and B exhibited a linear relationship (r=.81; slope=0.82; intercept=28.0) between noninvasive and fingerstick measurements. Conclusions: Environmental temperature has the greatest influence on the capability of the OSPM technique to monitoring blood glucose concentration, which is subject dependent. The position of the tested finger is the second major factor, hence a carefully designed finger adaptor is essential.

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吳文超 助理教授 *Wu, Wen-Chau,* Assistant Professor

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國立臺灣大學生醫電子與資訊學研究所 合聘助理教授
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Adjunct Assistant Professor, Department of Medical Imaging, College of Medicine, National Taiwan University

臨床磁振影像實驗室
Clinical Magnetic Resonance Imaging Lab.

本實驗室由吳文超教授成立於2010年，主要從事磁共振影像技術開發與臨床應用之相關研究，目前以微灌流影像與功能性影像為研究重點，並與台大醫院影像醫學部、核子醫學部合作，建立多模技術平台，提高於臨床診斷及預後的準確性。

Professor Wen-Chau Wu founded the Laboratory of Clinical Magnetic Resonance Imaging in the summer of 2010. The main research focus has been placed on the technical development and clinical applications of magnetic resonance imaging (MRI). Currently, we are conducting three NSC funded projects using advanced MRI techniques, including multi-modal functional MRI, perfusion MRI (arterial spin labeling, dynamic susceptibility contrast enhanced imaging, and dynamic contrast enhanced imaging), and diffusion-weighted MRI. We closely collaborate with the Departments of Medical Imaging and Nuclear Medicine in National Taiwan University Hospital to build up a multi-modal framework to improve the accuracy of diagnosis and prognosis in various diseases.

主要研究領域 Major Research Areas

微灌流磁共振影像、功能性磁共振影像、醫學影像處理、生醫信號分析
Perfusion Magnetic Resonance Imaging (Arterial Spin Labeling and Bolus Tracking), Functional Magnetic Resonance Imaging, Medical Image Processing, Biomedical Signal Analysis

研究計畫 Research Projects

1. 速度選擇動脈氫質子標記法微灌流磁振造影
   Velocity-selective arterial spin labeling perfusion magnetic resonance imaging
2. 四肢肌肉之功能性磁振造影
   Functional magnetic resonance imaging in extremity muscles
3. 使用動態對比劑增強及動脈標定磁振造影技術定量腎臟血流灌注並評估臨床應用之可行性
   Clinical feasibility of dynamic contrast enhanced MRI and arterial spin labeling MRI in quantitative assessment of renal perfusion

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Dean, College of Medicine, National Taiwan University
Research Fellow, Institute of Biomedical Sciences, Academia Sinica
Academician, Academia Sinica

我們主要研究工作有下列四方面（1）找尋國人肺癌之危險基因。（2）建立體外癌轉移模式，全基因體搜尋癌轉移相關基因。（3）發現新的癌轉移基因及機轉做為診斷及治療標的。（4）研究癌細胞與周邊微環境之交互作用，特別是發炎細胞與癌細胞的互動。我們以cDNA基因微陣列研究基因之調控，訊息傳遞及功能。在基因流行病學研究我們已找到數個國人肺癌之危險基因，我們更以自己建立之肺腺癌之細胞株，利用侵襲篩選之細胞培養方式，篩選出高侵襲能力之子細胞株，並在老鼠實驗動物模式證明高侵襲肺癌細胞株也同時具有高轉移能力，利用以一體外模式及cDNA微陣列，我們可以全基因體找尋癌轉移之相關基因，在含9600基因之微陣列中我們找到近600個基因與肺癌轉移有關，我們將利用這些基因製成癌轉移檢測晶片推廣至臨床使用。同時在這些癌轉移相關基因中，我們發現新的抑癌轉移基因及促癌轉移基因如Collapsin Response Mediator Protein-1 (CRMP-1)，LCRMP-1，HLJ1及Slug等。這些基因在癌轉移之分子調控機制為目前主要研究之重點，且此類新的癌轉移相關蛋白也成為治療主要標誌分子，我們也用基因微陣列之研究模式，剖析這些基因之下游基因。最近，我們正著重於研究這些新的癌轉移相關蛋白之訊息傳遞途徑及功能和蛋白交互作用機制。

Our research teams are interested in studying the molecular pathogenesis of lung cancer in Taiwan and mechanisms of cancer metastasis. We focus on four aspects: (1) identification of novel risk genes for lung cancer in Taiwan, (2) molecular signature for prognostic prediction and personalized therapy of lung cancer, (3) identify novel genes and mechanisms involved in cancer metastasis for potential diagnosis and treatment targets, and (4) interaction of cancer cells and microenvironments, especially the cross talks between cancer cells and microenvironment inflammatory cells. Our team has identified several candidate risk genes for lung cancer. Cancer metastasis is a complicated process that may involve numerous genetic changes. To identify invasion/metastasis associated genes, we used DNA microarray and invasion/metastasis lung cancer cell line model and identified a panel of genes associated with lung cancer metastasis. We also developed gene expression signature and microRNA signature that can predict survival and metastasis of lung cancer patients. These molecular signatures may be helpful for personalized therapy of lung cancer patients. We have also identified novel invasion/metastasis suppressor genes such as collapsin response mediator protein-1 (CRMP-1), long form CRMP, HLJ-1 and invasion promoting gene slug. Currently, we are investigating the molecular mechanisms and signaling pathways and protein interaction maps of these novel metastasis related genes.

主要研究領域 Major Research Areas

基因體醫學、細胞生物學、轉譯醫學
Genomic medicine, Cell Biology, Translational Medicine

研究計畫 Research Projects

1. 探討HIPK2與Slug在致癌性及癌轉移的角色
   HIPK2 regulates slug-mediated tumorigenesis and metastasis
2. 研究促癌轉移基因 Slug 在細胞週期扮演的角色
   The invasion promoter Slug is a novel cell cycle regulator
3. 整合性功能基因體學核心實驗室II
   Integrated Core Facility for Functional Genomics (II)
4. 多功能轉錄因子YY1和肺癌生成關係之探討
   Multifunctional Transcription Factor YY1 and Lung Cancer Progression
5. 整合性功能基因體學核心實驗室I
   Integrated Core Facility for Functional Genomics (I)
6. 癌轉移之外基因調控
   Epigenetic Control of Cancer Metastasis

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柒 發表論文 Publications

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2. K. H. Chiang, K. C. Chang-Chien, R. F. Chang, and H. Y. Yen, "Tamper Detection and Restoring System for Medical Images Using Wavelet-based Reversible Data Embedding," J Digit Imaging, vol. 27, no. 3, pp. 320-330, Mar 2008.
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