國立臺灣大學
生醫電子與資訊學研究所

Graduate Institute of
Biomedical Electronics and Bioinformatics,
National Taiwan University

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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，特別合聘醫學院楊泮池院長、王水深教授、成佳憲副教授、黃俊升副教授加入本所陣容，以提昇本所在生物醫學及臨床醫學的研究能量，楊院長與本所相關的專長主要是分子生物學、 超音波學，其研究成果非常傑出，也是中央研究院的院士；王教授是心臟外科權威，在心臟輔助器的研究非常突出；成醫師身兼附設醫院放射腫瘤科主任，專長是放射生物學，在國內居於領先地位；黃醫師是乳房外科權威，對醫學影像的研究非常投入，成果卓越。

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三屆台大生醫電資營，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，顯見經過了連續三屆的活動舉辦，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，並於今年三月準通過認證 (因尚無畢業生)，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，本所也與日本及韓國在台北共同舉辦2009國際醫學影像論壇 (International Forum on Medical Imaging in Asia, IFMIA 2009) 增加本所在醫學影像研究的國際地位及知名度。

本所成立至今已三年，非常感謝大家的努力及團隊合作，其中李百祺所長的卓越領導更是功不可沒，我們希望所有同仁都能積極參與所務，共同合作執行計畫，對外更要加強不同學門間的合作關係，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

2009年8月

In the past year, promoting multidisciplinary research and teaching in the areas of Biomedical Electronics and Bioinformatics continued to be our main mission. Four new faculty members joined our institute in the last semester, including Professor Pan-Chyr Yang, Professor Shoei-Shen Wang, Associate Prof. Chia-Hsien Cheng and Associate Prof. Chiun-Sheng Huang all from the college of medicine. The related research interests of Dean Yang include molecular biology and supersonics who is also an academician of the Academia Sinica. Prof. Wang is a leading expert in surgical cardiology, part of his research interest is in the design of left ventricle assisted device. Dr. Chen is the director of division of radiation oncology, NTU Hospital and his excellent expertise is in radiological biology. Dr. Huang is very famous in the area of breast tumor and he has done very good research in the related medical images. 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 third 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 quasi-pass approval, because there was neither Master nor Ph.D. degrees had ever been granted to our students. We have very good reputation and performance in the review categories of faculty, teaching, research, funding and equipments. We and our partners from Korea and Japan together held an International Forum on Medical Imaging in Asia, IFMIA 2009 at Taipei in last January. Through this effort, it helped to promote the international reputation of our distinguished researches in medical imaging.

As always, we are very thankful for all the supports that we have received, especially the great leadership from the ex-director Prof. Li. It has been three 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

August, 2009.

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31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 NationalTaiwan University was formally founded on August 1, 2006. In a way, it is a very uniqueinstitute among those in College of Electrical Engineering and Computer Science, NationalTaiwan University, in that the fields of expertise are diversified but our efforts remainextremely focused. The main mission of the institute is to promote multidisciplinaryresearch and education in respond to the rapid advancement of biotechnology. In thisregard, the following areas have been identified as our focus areas which we have beenputting 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 theseareas and to bring up research synergy, integrative efforts from different disciplines arenecessary.

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 31 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、楊泮池教授 Pan-Chyr Yang, Professor

Current position and relevant experience

- M.D., College of Medicine, National Taiwan University, 1979
- Ph.D., Graduate Institute of Clinical Medicine, National Taiwan University, 1990
- Professor, Department of Internal Medicine, College of Medicine, National Taiwan University, 1993 – Present
- Research Fellow, Institute of Biomedical Sciences, Academia Sinica, 1993 – Present

Honor & Award

- Distinguished Teacher Award, National Taiwan University, 1999
- Academic Award, Ministry of Education, ROC, 2002
- Academician, Academia Sinica, 2006
- Distinguished Professor, National Taiwan University, 2006
- National Chair Professor, Ministry of Education, Taiwan ROC, 2007
- Academician ,The Academy of Sciences for the Developing World, 2008

二、王水深教授 Shoei-Shen Wang, Professor

心臟血管外科王水深教授主要的研究包括免疫抑制在心臟移植的運用和輔助循環(包括葉克膜體外維生系統、心室輔助器)在嚴重心臟衰竭的治療。他是台大醫院心臟移植及心肺移植召集人。

王水深教授在1977年完成台大醫學院醫學系學士學位，1987年以大鼠心臟移植的免疫學研究完成醫學博士學位。1997年為台大外科教授。2002年到2004年為台灣胸腔及心臟血管外科學會理事長。2005年為台灣血管外科學會創會(第一屆)理事長。王水深教授出版台灣第一本心臟移植教科書和其它有關心臟血管外科方面的書籍。王水深教授經常受邀講演並發表超過300篇心臟血管領域的論文。

Dr. Shoei-Shen Wang is Professor of Cardiovascular Surgery. His main research interests concern immunosuppressive treatment in heart transplantation, and assist circulation including extracorporeal membrane oxygenation support (ECMO) and ventricular assist devices (VAD) for intractable heart failure. He is director of heart transplantation and heart-lung transplantation at the National Taiwan University Hospital.

Dr. Wang received his M.D. degree in 1977 and presented his Ph.D. thesis in rat heart transplantation in 1987. In 1997 he was appointed Professor of Surgery at the National Taiwan University. From 2002 to 2004 he was elected President of Association of Thoracic and Cardiovascular Surgery, Taiwan. He founded Taiwan Society for Vascular Surgery in 2005. He published the first Chinese textbook of heart transplantation and other Chinese textbooks on cardiovascular surgery. He is a frequently invited lecturer and has published more than 300 original articles and reviews in cardiovascular field.

貳 新進教師介紹
New Faculty

三、黃俊升副教授 Chiun-Sheng Huang, Associate Professor

Chiun-Sheng Huang is an attending surgeon and director of breast center at the National Taiwan University Hospital and associate professor at the National Taiwan University College of Medicine, Taipei, Taiwan.

Dr Huang obtained his MD and PhD from the National Taiwan University College of Medicine in Taipei, Taiwan, and obtained a Master of Public Health degree from the Harvard School of Public Health. After completing his residency in general surgery at the National Taiwan University Hospital, he went on to become a Research Fellow in Pediatric Hematology/Oncology at the University of California Medical Center, San Diego, US.

Dr Huang has dedicated his career to the prevention and treatment of breast cancer. Dr Huang’ s expertise in breast surgery and ultrasound has allowed him to actively participate in professional societies, including teaching ultrasound courses. His areas of research include: the use of ultrasound in breast cancer screening; estrogen and genetic polymorphism as susceptibility and prognostic factor for breast cancer; and new regimens and biomarkers of neoadjuvant therapy. He is currently the chief 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.

四、成佳憲副教授 Chia-Hsien Cheng, Associate Professor

成佳憲老師1994年畢業於國立陽明大學醫學系，隨即進入和信治癌中心醫院放射腫瘤科接受住院醫師訓練，1997-1998年於美國華盛頓大學醫學中心Mallinckrodt Institute of Radiology 接受住院醫師訓練進修，1998年回國後於和信醫院擔任主治醫師，2002年獲邀加入台大醫院腫瘤醫學部放射腫瘤科主治醫師陣容，隨後並兼任科主任至今。2005年獲本校電機工程學研究所醫工組博士學位。成老師於2006年起專任於台灣大學醫學院臨床醫學研究所教職，目前是醫學院腫瘤醫學研究所專任副教授，並同時合聘於醫學院臨床醫學研究所及電資學院生醫電子與資訊學研究所。

成老師為一臨床醫師出身的醫師科學家，臨床專科為放射腫瘤科，專長以放射線治療癌症，成老師的研究方向涉及醫學物理和放射生物兩大方向。由於腫瘤放射治療使用多種精密儀器設備，如高能直線加速器、電腦斷層機、X光模擬攝影機，以及身體固定或呼吸調控裝置，因此成老師在醫學物理方面的研究主要在影像物理及設備物理上，進行與病人治療遭遇的問題有關之實驗。如測試最理想的呼吸調控模式及劑量影響，或影像導引治療模式的影像最佳化等，進行這些實驗的地點是在台大醫院放射腫瘤科。另一方向則是基礎研究的放射生物相關實驗，進行腫瘤受放射線照射後致死機轉的細胞實驗及動物實驗，及強化放射線效果的藥物實驗，於台大醫院放射腫瘤科放射生物實驗室從事這些研究，並使用台灣大學校區內唯一可以進行類似人體精準放射治療的鈷60治療機進行放射照射實驗。

成老師的研究團隊位在醫院臨床部門，因此生活步調與醫療人員聲息相聞，不同於單純校園的感覺。研究方向也在訓練學生成為臨床部門醫學物理師所需的技能，與醫學物理或放射生物科學家的入門準備。成老師十分歡迎研究所的碩博士學生投入團隊共同研究，創造有益於臨床基礎醫學研究的未來遠景。

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。

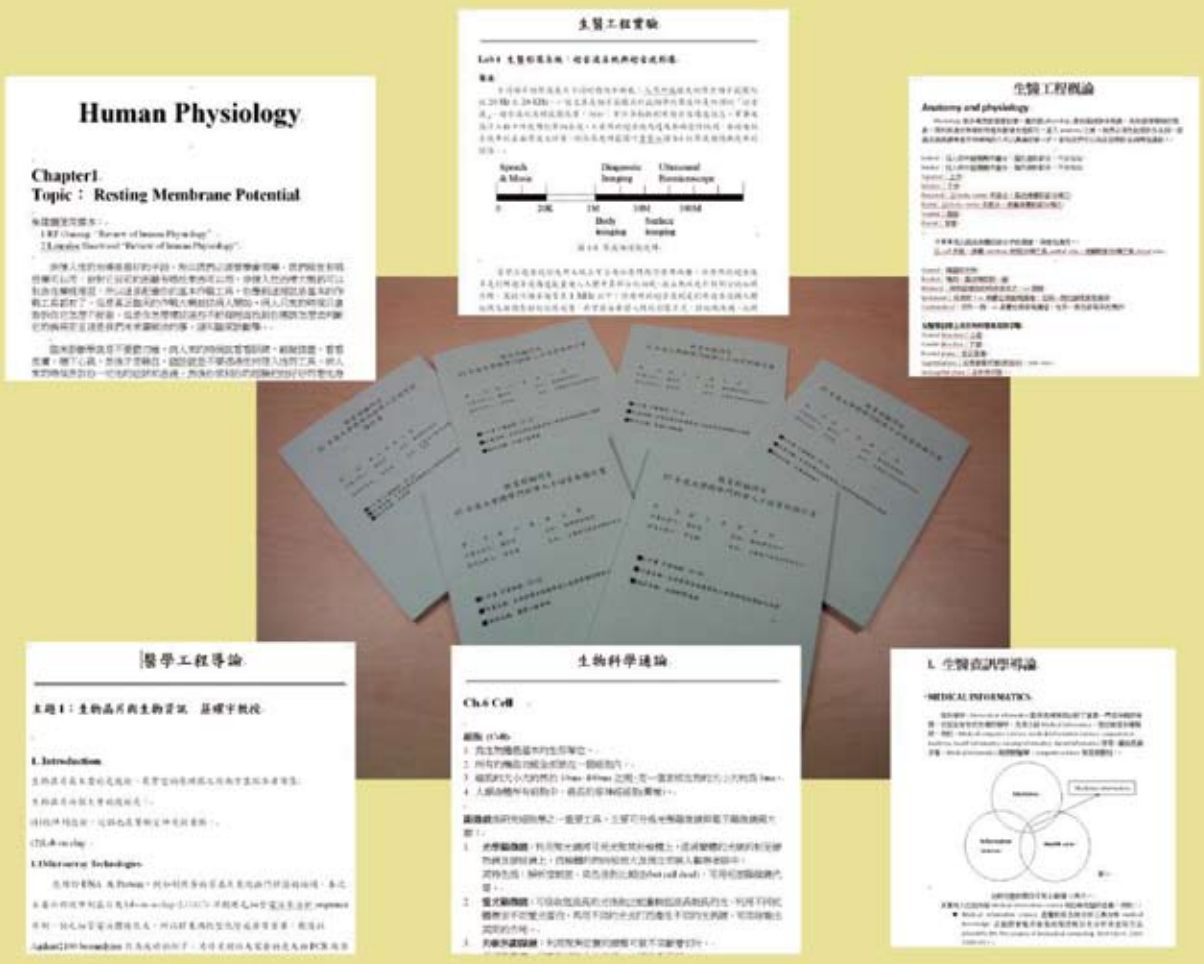
We dedicate our resources on the cutting-edge topics such as "biomedical data analysis and mining", "computational system biology", "computational pharmacology and chemistry". In the area of biomedical data analysis and mining, our major research includes: biochip (Micro-array) data analysis, DNA and 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：生命科學生物醫學及工程學跨領域課程之規劃
The Interdisciplinary Training Program for Talented College Students in Science : cross-disciplinary courses between Life Science, Electrical Engineering and Computer Science

參與單位 Participants:

國立臺灣大學電機資訊學院 College of Electrical Engineering and Computer Science, NTU
國立臺灣大學生命科學院 College of Life Science, NTU



計劃簡介 Project Description:

本子計畫為臺大生命科學院與電資學院之共同合作，透過二院教師之整合參與，結合豐富多元、深入淺出的課程規劃，向電機資訊學院有意朝此領域更深入研究之學生介紹跨領域的銜接知識，進行跨領域人才培訓，以期未來具備結合尖端電子資訊技術，進行前瞻生物醫學研究之能力。

本計劃於97學年度上學期開設課程，並初步發展各課程教材，亦結合學校資源投入，計畫執行成效良好，但礙於學期尚未結束之因素，教材完整度稍有不足，為求課程教材之完整性與連貫性，本計劃將延續上一年度成果，繼續開設六門課程：生物科學通論、生理學、生醫工程概論、醫學工程導論、生醫資訊學導論、生醫工程實驗等，以跨學門整合為首要目標，精簡課程，並依學生回饋調整課程主題、深度、比重，精進第一年之成果，強化教學能量，加強各課程之銜接。

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

The sub-project is collaboration between College of Life Science and College of Electrical Engineering and Computer Science of National Taiwan University. Through integration, consolidation and participation from faculty members of two colleges, 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 the biomedical engineering field.

Last semester, we offered six courses, which were: Introduction to biological science, Physiology, Introduction to biomedical engineering, Introduction to biomedical engineering, Topics in medical engineering, Topics in biomedical informatics and biomedical engineering lab. To achieve our goal, we tried our best to develop partial teaching materials and provide resources (both hardware and software) to faculties and students. This year, we are planning to go to the next step: an integration of interdisciplinary—improving courses and focusing on the needs of students to complete the training program.

Through the sub-project, we will be able to offer students a wide range of courses with fundamental knowledge in various fields. These courses will be a bridge to connect two different fields and can meet the goal of this project.

二、醫療器材人才培訓研習班
Talents Cultivation Program for Advanced Medical Device

參與單位 Participants:

國立臺灣大學生醫電子與資訊學研究所 Graduate Institute of Biomedical Electronics and Bioinformatics, NTU
永齡生醫工程中心 YongLin Biomedical Engineering Center
國立臺灣大學進修推廣部 School of Professional and Continuing Studies, NTU

計劃簡介 Project Description:

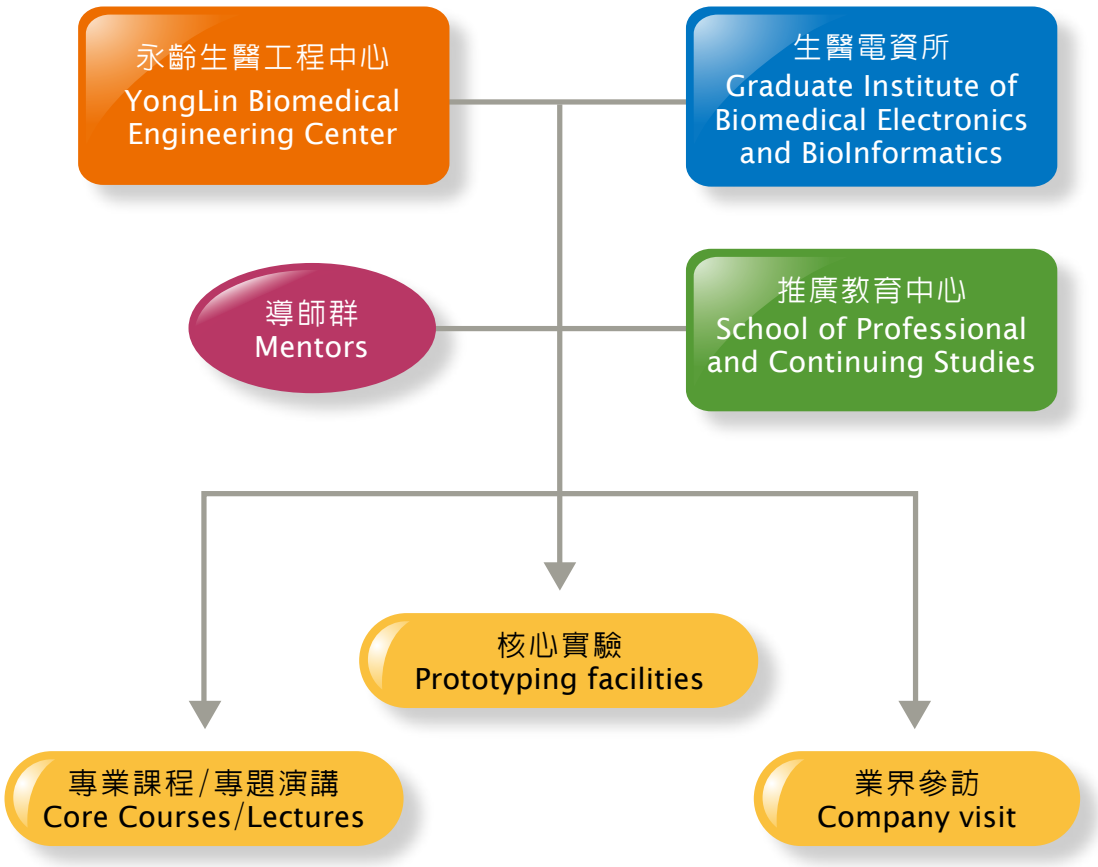
為培育臺灣高階醫療器材的跨領域人才，本所與永齡生醫工程中心及進修推廣部共同開設醫療器材人才培訓課程，其內容強調跨領域合作、臨床需求導向、創新產品研發與新事業開創等核心精神，以期能協助建立台灣醫療器材產業之優勢，並促進產學合作成效。

課程規劃包括：專業課程、核心實驗、專題演講、業界參訪及小組創業提案競賽。在專業課程設計中，涵蓋臨床需求、創新創業、法規認證、專利與智財管理、工程技術與創新研發等內容，邀請相關領域傑出人士授課。除上述課程外，本課程亦將建立一導師制度(mentor program)，結合臨床、法規、創業育成與產業界資源，給予學員在培訓各階段之諮詢與支援。

To train multidisciplinary talents for promoting the medical device industry in Taiwan, YongLin Biomedical Engineering Center, School of Professional and Continuing Studies and our institute have been executing the Advanced Medical Device Training Program. This program emphasizes on cross-disciplinary collaboration, clinical needs finding, innovative product developments, and entrepreneurship, hoping that by discovering and training new talents, it can assist in building the competitive edge of Taiwan’s medical device industry, and promote the synergy of collaboration between academia and industry.

The program consists core courses, hand-on facilities, company visit and group contest. The core courses also include aspects of clinical needs finding, innovation, entrepreneurship, regulatory affairs, patents and intelligent properties, engineering technologies, and creative developments. We invited outstanding experts from these various fields to ensure the success of this program. Moreover, there is also an accompanying mentor program, so that students can seek advice from mentors during the training process.

計畫架構 Project Structure:



三、碩班甄試說明會 BEBI introduction to prospective students

(一) 2008/10/14 第一場：電資學院
Part I, College of Electrical Engineering and Computer Science

(二) 2008/10/16 第二場：生命科學院　Part II, College of Life Science

四、期末聚會活動 Year-end Gathering

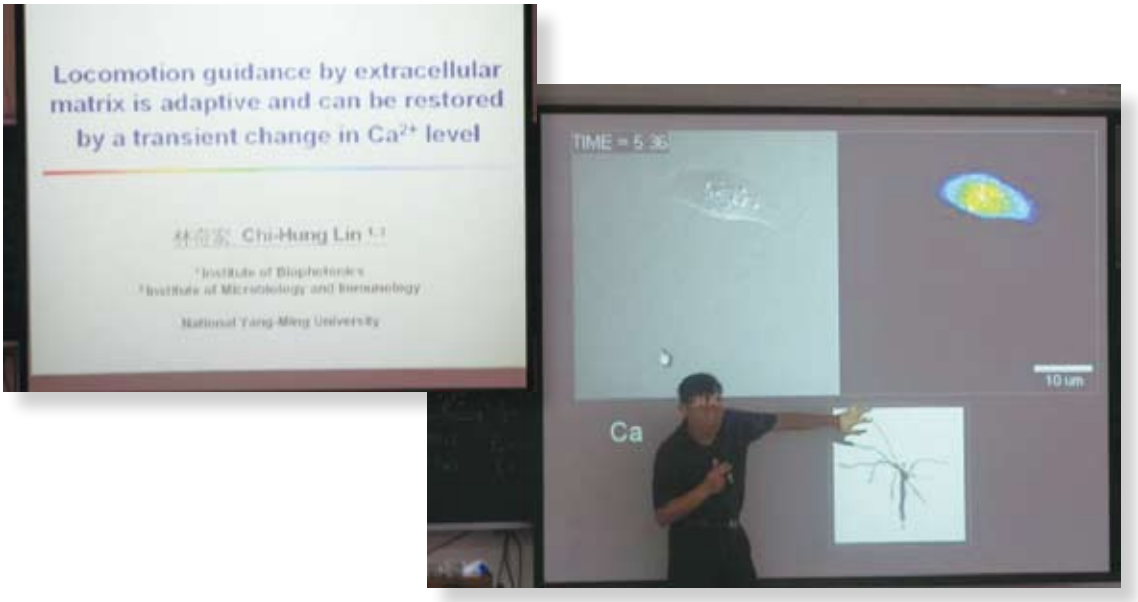
Bowling Game

Kickball Game

Farewell Party

五、IEET實地訪評 IEET Accreditation

六、演講 Lectures



1. 97.09.22，林奇宏 所長，陽明大學微生物及免疫學研究所
   Topic: Locomotion guidance by extracellular matrix is adaptive and can be restored by Ca2+ transient


2. 97.10.13，熊克平 教授，美國南加州大學 Topic: High frequency ultrasound

3. 97.10.20，張大慈 教授，清華大學生命科學系 Topic: Old Enzyme's New Look


4. 97.10.27，陳家進 教授，成功大學醫學工程研究所
Topic:應用神經工程方法於重複經顱磁刺激治療帕金森大鼠的研究/Neural Engineering Approaches for Repetitive Transcranial Magnetic Stimulation (rTMS) Treatment on Parkinson's Disease Rats

5. 97.10.31, Professor Matt O'Donnell, Dean of College of Engineering, University of Washington
   Topic: Cardiac Activation Mapping using Ultrasound Current Source Density Imaging

6. 97.11.03，黃明經 研究員，中央研究院生物醫學科學研究所
   Topic: Bioinformatics and Genome-Based Biomedical Research

7. 97.11.10，李克昭 所長，中央研究院統計科學研究所
   Topic: Statistical analysis of voluminous genomics data and systems Biology

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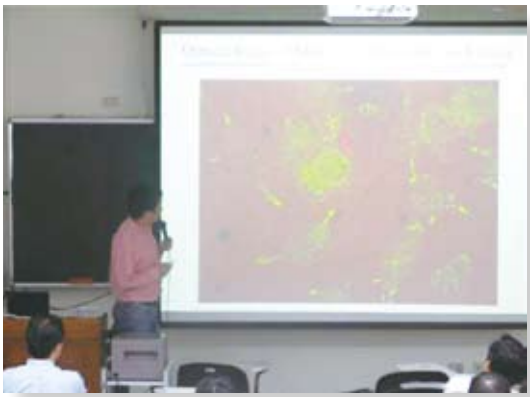

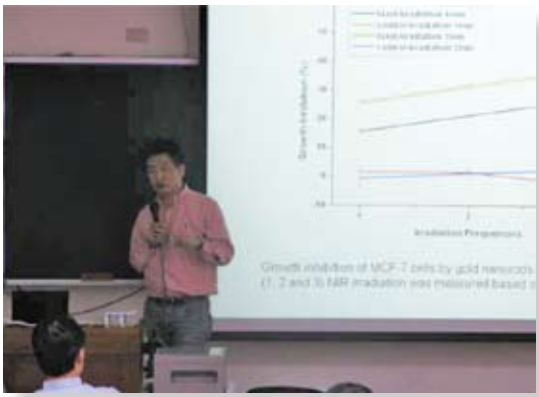

8. 97.11.17，陳家俊 教授，師範大學化學系 Topic:奈米材料在生物醫學上的應用

9. 97.11.24，楊重熙 主任，國衛院奈米醫學研究中心
   Topic: Monitoring of Nanoparticles In Vivo and the Biomedical Applications

10. 97.12.01，張慧嫻 小姐，臺灣大學環境衛生所 Topic:實驗室安全衛生與管理

11. 97.12.08，謝達斌 醫師，成大醫院牙醫部 Topic: 轉譯奈米醫學Translational Nanomedicine

12. 97.12.15，Professor Xiaochuan Pan，University of Chicago Medical Center
Topic: A Brief Overview of Modern CT Technology and Applications

13. 97.12.29，張俊哲 助理教授，臺灣大學昆蟲學系暨研究所
Topic: The Making of the Fittest in the Lab

14. 98.02.16，李超煌 博士，中央研究院應用科學中心
Topic：Studies on membrane activities of living cells using high-resolution optical microscopy

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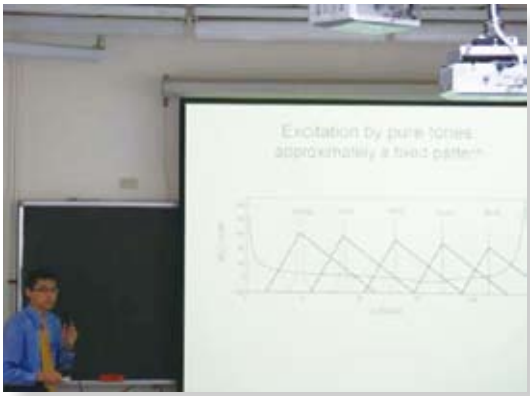
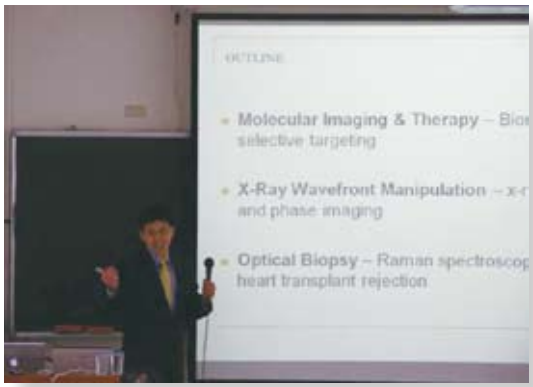


15. 98.02.23，Dr. Yi-Wen Liu，Center for Hearing Research, Boys Town National Research Hospital
Topic：Signal processing mechanisms in the inner ear - mysteries of high sensitivity and fine tuning

16. 98.03.02，何信瑩 副院長，交通大學生物資訊及系統生物研究所
Topic：Intelligent Evolutionary Algorithm and Its Applications in Bioinformatics

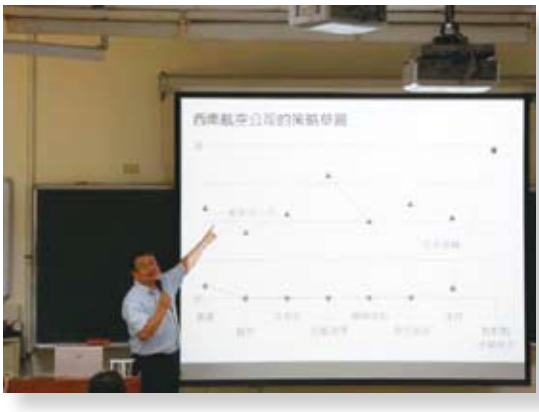


17. 98.03.09，張 昶 博士，Drexel University
Topic：What do EUV Lithography and Metastatic Colorectal Cancer have in common?
- A journey from sophomore electromagnetics to positron emission tomography

18. 98.03.16，曾繁根 教授，清華大學工程與系統科學系
Topic：From High Efficient Protein Micro Chip Toward Ultra High Sensitive Single Protein Molecule Array

19. 98.03.23，呂平江 教授，清華大學生物資訊與結構生物研究所
Topic：Computational Structure-Based Protein Design of Plant Defensin

20. 98.04.13，王水深 教授，臺大醫學院心臟血管外科
Topic：Heart Transplantation Bridged with Mechanical Circulatory Support



21. 98.04.20，王榮春 教授，東吳大學 心理學系　Topic：站在有光的地方- 從藍海策略談職涯發展

22. 98.04.27，吳漢章 執行長，eCareme Technologies, Inc.
Topic：一個築夢者的創業與學習歷程分享

23. 98.05.04，郭宏基 教授，張老師基金會 Topic：職場人際互動

24. 98.05.11，成佳憲 醫師，臺大醫學院腫瘤醫學部
Topic：Diversities in Radiation Oncology Research

25. 98.06.01，楊基寬 董事長，104資訊科技股份有限公司
Topic：英雄-職場必勝之道

26. 98.06.08，高建民 教授，University of Chicago
Topic：Instrumentation and System Design for Positron Emission Tomography

肆 學術活動
Academic Activities

七、九十七學年生醫電資所畢業典禮
2008 Commencement of College of electrical Engineering and Computer Science NTU

八、 2009/06/29~07/01生醫電子資訊營
Biomedical Electronics and Bioinformatics Camp

為響應前兩年生醫電資營參與學員之鼓勵與建議，延續規劃2009臺大生醫電子資訊營，於6/29(一)~7/1(三)假臺大博理館舉行研習，活動透過規畫設計的課程及課後的競賽活動，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。透過主題課程的設計及實驗室參觀，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，並為國家培養生物科技與醫療電子資訊的學術與產業人才。

課程涵括神經電子、生醫工程、生醫影像、基因晶片、微感測器、生醫光電、醫學資訊、生物資訊、系統生物學等，並安排實驗室活動。

此外，本所亦十分榮幸邀請臺大醫學院內科特聘講座教授陳定信院士為本活動演講「科技進展對醫學進步的影響」，並鼓勵學員從事跨領域團隊合作，對學員們有相當程度的提升及啓發。

本次活動共116人報名參加，大學部學員約佔62%。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97%，整體而言頗受好評，給予本計劃辦理跨領域交流活動相當大的鼓勵。

2009 Biomedical Electronics and Bioinformatics Summer Camp, known as BEBI summer camp, was held on 6/29-7/1 at Barry building in NTU. The main theme of this event was introducing the advanced technologies to promote the fundamental life science researches and applied medical treatments. Based on the course designs and lab tours 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.

Our curriculum consisted of the following courses: neuron-potential, biomedical engineering, biomedical image, gene-chip, biomedical micro sensor, biomedical optics, medical informatics, bioinformatics, systematic biology, and laboratory tours.

肆 學術活動
Academic Activities

In addition, we were honored to invite Dr. Ding-Shinn Chen, an academician of Academia Sinica, to give a special talk entitled "the impact of technology development toward medical science". Dr. Chen also encouraged students to devote themselves to interdisciplinary collaboration.

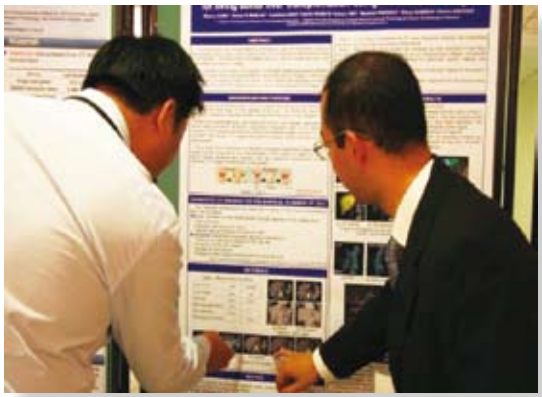
We had a total of 116 participants with diverse backgrounds (engineering and life science), and half were undergraduate. A 97% satisfaction rate was achieved.

National Taiwan University

伍 國際交流
International Exchanges

一、2009國際醫學影像論壇
International Forum on Medical Imaging in Asia(IFMIA) 2009

由本所、日本及韓國共同舉辦之2009國際醫學影像論壇()於98年1月19-21日舉行，除三國學者外，並廣邀其他各國頂尖學者參與。其中，大會特地邀請美國芝加哥大學的頂尖學者來台指導，包括Dr. Maryellen L. Giger及Dr. Chin-Tu Chen。兩位學者除發表Keynote speech外，亦進行Tutorial，向大師學習，對於與會者是一個難得的機會。本次會議共有208位國內外相關與會者，除一般論文發表外，更規劃有壁報論文展示，總計發表156篇論文，經與會學者熱烈討論，成果豐碩。



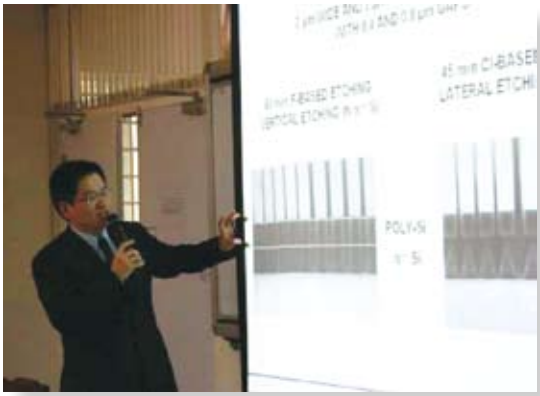
International Forum on Medical Imaging in Asia (IFMIA) was held on January 19-21, 2009 at National Taiwan University. The invited speakers included Dr. Maryellen Lissak Giger and Dr. Chin-Tu Chen from University of Chicago. We had 208 attendees from various countries and 156 presentations (including oral presentations and posters) covering medical imaging, CAD techniques, and medical informatics etc..

二、外賓參訪 International Visits

1. 2009.01.19~21，Professor Maryellen Lissak Giger，University of Chicago

伍 國際交流
International Exchanges

2. 2009.01.19~21，Professor Chin-Tu Chen，University of Chicago



3 2009.03.03，田維誠博士，GE Global Research Center

4. Prof. John Harris

5. 2009.03.17，深圳理邦精密儀器公司
6. 2009.04.20，Prof. Mari Ostendorf，University of Washington

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
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 702
	楊泮池 Pan-Chyr Yang	臺大醫院 NTUH
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
	王水深 Shoei-Shen Wang	臺大醫院 NTUH NTUH
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
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
醫學影像實驗室/磁共振影像頻譜實驗室 Medical Imaging Lab.	陳志宏 Jyh-Horng Chen	明達館706 MingDa Building 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 604
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
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

實驗室名稱 Name	主持教授 Advising professor	地點 Room
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 704
超音波影像實驗室 Ultrasonic Imaging Lab.	李百祺 Pai-Chi Li	明達館731 MingDa Building 731
放射物理生物實驗室 Laboratory for Radiation Physics and Biology Lab.	成佳憲 Chia-Hsien Cheng	臺大醫院 NTUH
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 Barry Lam Hall 405
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 701
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
生物醫學信號實驗室 Biomedical Signal Lab.	郭德盛 Te-Son Kuo	明達館 705 MingDa Building 705
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 703
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
整合神經生理學實驗室 Integrative Neurophysiology Lab.	林則彬 Tzer-Bin Lin	中山醫學大學 基礎醫學大樓
細胞行為實驗室 Cell Behavior Lab.	郭柏齡 Po-Ling Kuo	明達館207 MingDa Building 207

陸 實驗室及教師
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
低功率超大型積體電路實驗室 Low Power VSLI Lab.	賴飛羆 Fei-pei Lai	資訊館346 CSIE Building, Room 346
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 410
生物資訊實驗室 Bioinformatics Lab.	高成炎 Cheng-Yan Kao	資訊館401 CSIE Building, Room 401
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
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 Build Room 432
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
演算法實驗室 Algorithmic Research Lab.	呂學一 Hsueh-I Lu	資訊館406 CSIE Building, Room 406
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
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

張璞曾 副教授 *Chong, Fok-Ching,* Associate Professor

國立台灣大學生醫電子與資訊學研究所 副教授
國立台灣大學電機工程學系 副教授

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

生醫系統與電磁實驗室
Biomedical System and Electromagnetism Lab.

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

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

計畫名稱: 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
補助單位:學術領域全面提升計畫
計畫期間: 2006-2007

肝癌在世界上是最常見的癌症。肝癌是致命的癌症，因此一旦罹患癌症的病患其生命大多不超過一年。世界衛生組織在1990年估計全世界約有四十三萬新增案例，且全球約43萬死於肝癌。其中有3/4的病患集中在東南亞(中國，香港，台灣，朝鮮和日本)。這顯示肝癌發生率在亞洲是比其他地區還要高，這是因為肝癌與慢性 B 型肝炎感染有密切相關。肝功能是目前常用的檢驗病患肝是否正常的指標。肝臟一旦受損，在血液中天冬胺酸轉胺酶(Aspartate Aminotransferase，AST)，丙胺酸轉移酶(Alanine Aminotransferase，ALT)，丙麥胺酸轉轉移酶(Gamma Glutamyl Transpeptidase，GGT)和α-胎兒蛋白(α-Fetoprotein，AFP)這些酵素都會有上升的趨勢。因此肝細胞大量死亡時這些酵素或者相關蛋白全部都會從肝細胞釋放到血液中。冬胺酸轉胺酶(AST)雖然是反映出對肝細胞的損害，但是並非是特異性高的酵素。丙胺酸轉移酶(ALT)僅在肝細胞中產生，因此當肝細胞受到損傷或者死亡時，血液中的丙胺酸轉移酶(ALT)就會因此而上升。除此之外，任何造成肝細胞損傷的疾病都會使得血液中丙胺酸轉移酶(ALT)濃度上升。因此藉著丙胺酸轉移酶(ALT)的靈敏度，丙胺酸轉移酶(ALT)是一個很好的肝功能指標。

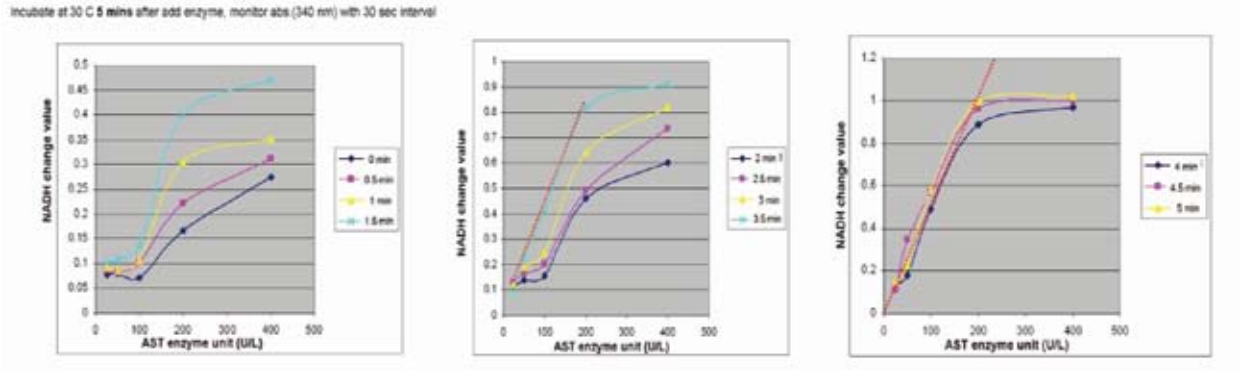
“預防勝於治療”這觀念必須植入在每個人心裡，因此定期性的健康檢查便可以使人遠離肝癌且能使肝的功能能長久進而使人的壽命變長。為了此目的，我們結合生物化學、臨床醫學及電子三大領域來研製肝功能監控系統，此系統命名為“Liver function meter (或簡稱 Lifemeter)”。此系統可以量測兩個重要肝功能酵素指標：天冬胺酸轉胺酶(Aspartate Aminotransferase，AST)及丙胺酸轉移酶(Alanine Aminotransferase，ALT)。此外居家照護是現在及未來醫學檢測上的方式，因此此系統結合了無線技術，將量測的數值記錄下來並藉由無線技術傳至醫療院所，使得醫護人員即時監控病患的健康狀況。

Project name：The development of the homecare health detector –
unction indicator AST (GOT) / ALT(GPT) monitoring system
Subsidiary organization：The project of advancement in academic fields
The duration of the project：2006-2007

The liver cancer is the most common cancer in the world. Since liver cancer is deadly, patients suffering from cancer rarely last for more than one year. The World Health Organization estimated that in 1990 there were approximately 430,000 new cases around the world. About 430,000 died because of the liver cancer; among these patients 3/4 of them are in the Southeast Asia (China, Hong Kong, Taiwan, Korea and Japan). This shows that the chance of having liver cancer in Asia is higher than that in other regions, because liver cancer and infected chronic hepatitis B are closely related. Liver function is the most commonly used indicator to assess the condition of the patient's liver. Once liver is damaged, Aspartate Aminotransferase(AST), Alanine Aminotransferase(ALT), Gamma Glutamyl Transpeptidase(GGT) and α-Fetoprotein(AFP) in blood, will all tend to rise. So these ferments or relevant albumens will all be released from liver cell in blood when a large amount of liver cells die. Though Aspartate Aminotransferase(AST) reflects the harm to the liver cell, it is not a peculiar high ferment. Alanine Aminotransferase(ALT) is produced only in the liver cell, so while the liver cell is damaged or die, Alanine Aminotransferase(ALT) in blood will thereby rise. In addition, any disease that causes liver cell damage will make the concentration of Alanine Aminotransferase(ALT) in blood rises. So the sensitivity of Alanine Aminotransferase(ALT) makes it a very good indicator of liver function.

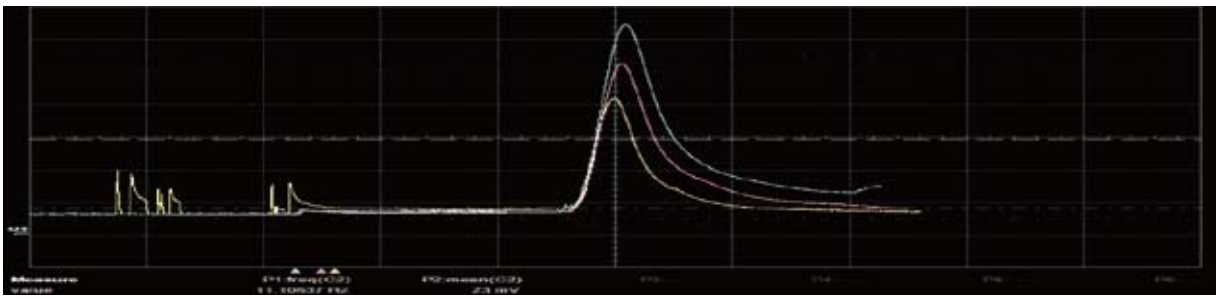
The idea of "prevention is better than treatment" must be kept in mind. Regular health examination can prevent people from liver cancer and can prolong the function of the liver as well as human life-span. For this purpose, we combine three major fields of biochemistry, clinical medicine and electron to develop the monitoring system of liver function, which is named "Liver function meter (or abbreviated as Lifemeter)". This system can examine two important liver function ferment indicators：Aspartate Aminotransferase(AST) and Alanine

Aminotransferase(ALT). In addition, since homecare is the current and future medical measurement, this system combined wireless technology to record the data of measurement and transmit them to the medical institutes by wireless technology. This enables medical staff to monitor the patient's health condition at any time.



此圖為不同單位的酵素在不同時間下所量測到的化學反應，可觀測到一致性的變化

This figure shows the chemical reaction measured at different time and on different ferment of units, which allows for the examination of the consistency of change.



此為在不同膽固醇濃度下 在示波器所呈現的波形，已經具有足夠的解析度計算對應的數值

This is in the wave form that the oscillograph appears under the concentration of different cholesterol. This has enough resolution to calculate corresponding value.

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主要研究領域 Major Research Areas

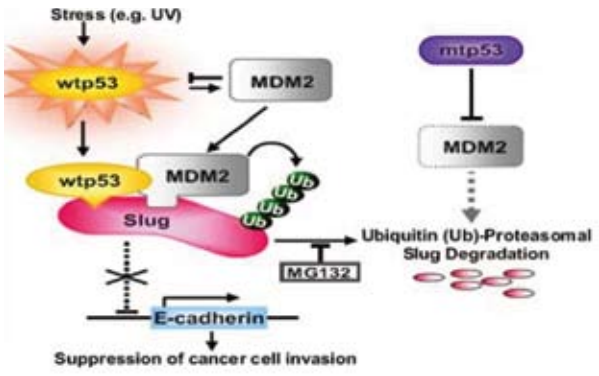
基因體醫學、細胞生物學、轉譯醫學
Genomic medicine, Cell Biology, Translational Medicine

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

研究興趣 Research Interests

Our major research interests are lung cancer genomics, molecular mechanisms of cancer metastasis and translational research related to personalized therapy of lung cancer. We have discovered novel genes and pathways that associated with lung cancer pathogenesis and progression. They also identified specific gene expression signature and microRNA signature that can predict the treatment outcome and may be useful for designation of personalized therapy for lung cancer patients.



We recently identified that p53 can control cancer cell invasion and metastasis through the p53-MDM2-Slug pathway. The wild-type p53 (wtp53) forms a wtp53-MDM2-Slug complex that induces Slug degradation, thereby suppresses cancer cell invasion. In contrast, mutant p53 (mtp53) inactivates Slug degradation and increases cancer cell invasion.

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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，是台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，我們也會研究窄頻紅外線光源照射對植物產生抗氧化性之行為表現。

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.

Our lab has developed the narrow bandwidth, tunable wavelength and room temperature operated infrared thermal emitter utilizing the surface plasmon. It has been applied successfully to the study of gene expression during the growth of plants. In the future, we plan to investigate the growth of Arabidopsis and the signal transmission of neuron when irradiated by this narrow bandwidth light source.

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

研究計畫 Research Projects

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. 家用型雙波段乳癌紅外線診斷系統
   A Novel Household Dual-Spectrum IR Imaging System for Breast Cancer Detection

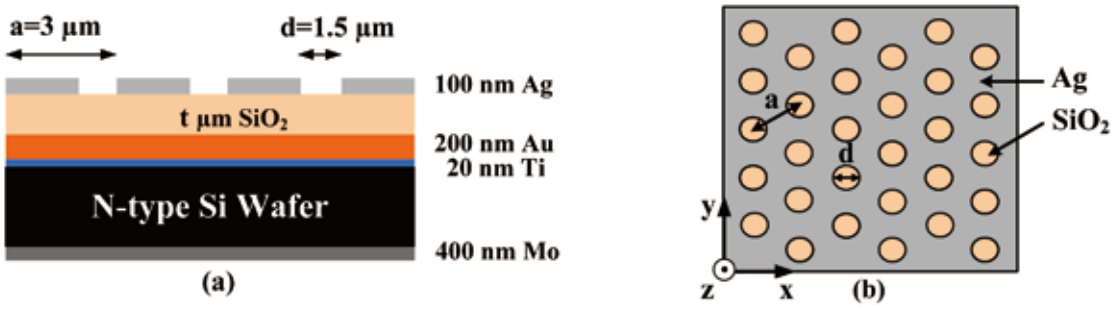
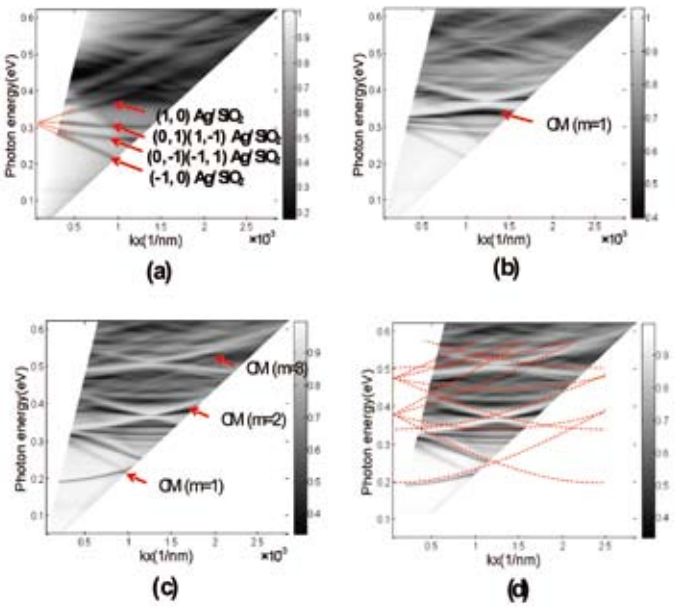


Fig.1 Schematic diagram of the (a) side and (b) top view of the Ag/SiO2/Au plasmonic thermal emitter, the top metal is perforated with hexagonal hole array.

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。

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) 0.7 μm, (b) 1.1 μm, and (c) 2.6 μm. 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2.6 μm，理論的計算結果顯示於圖二(d)，其結果與實驗[圖二(c)]相同。



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：國科會

計畫期間：2008/08/01-2009/07/31

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1.1 μm，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0.7 μm)，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1.1 μm (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2.6 μm (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。

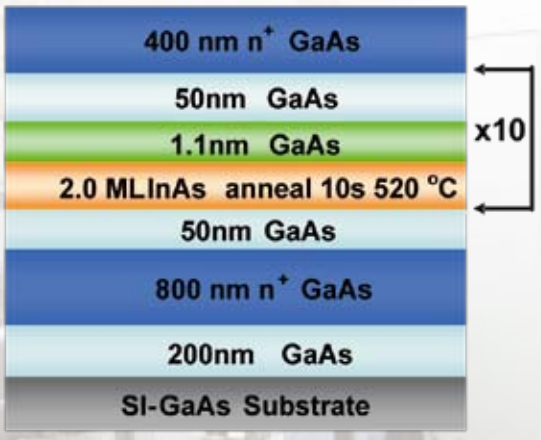


Fig.3 The QRIP device structure with 10 periods of 2.0-ML InAs QDs, 1.1-nm GaAs capping layer and 50 nm GaAs barrier layer.

圖三　為紅外線量子環偵測器之結構示意圖。其中量子環是由2.0-ML的砷化銦及1.1-nm的砷化鎵覆蓋層所組成。

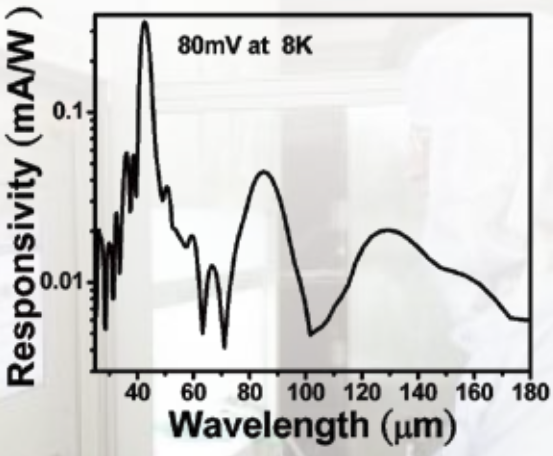


Fig.4 The responsivity of QR terahertz photodetector measured at 8 K under a bias of 80 mV. Three peaks at 42 μm, 85 μm and 130 μm are observed and cutoff wavelength is at 175 um.

圖四　表示我們所製作的紅外線量子環偵測器在80K的環境操作下，其響應頻譜可達175 μm(1.7THz)。

Project title: The narrow bandwidth infrared emitter and detector with applications in plants and neuron cells
Supported by: NSC
Project period: 2008/08/01-2009/07/31

The emission spectra of Ag/SiO2/Au tri-layer cavity thermal emitters (CTE) were investigated. When the SiO2 thickness exceeded 1.1 μm, 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.

A InAs/GaAs quantum ring infrared photodetector (QRIP) has been fabricated using molecular beam epitaxy (MBE) successfully. The real operation temperature can be raised up to 80 K. The photodetector demonstrates a cutoff wavelength at 175 μm (1.7 THz) and the detectivity of 1.3×107 cmHz1/2/W at 80 K.

A flexible Ge-on-polyimide photodetector is demonstrated for telecommunication wavelength. The direct band transition can be enhanced by increasing injection level, biaxial tensile strain, and the elevated temperature.

These data indicates that GASA4, an Arabidopsis homolog of mungbean VrGIR1, indeed plays a vital role to regulate hypocotyl elongation, the expression of CHS and RbcS, and physiological responses including anthocyanin accumulation in response to IR irradiation.

To measure the signal of neuron cells, neuron cells should be patterned on the electrodes precisely. we have achieved a nano-technique for extracellular matrix patterning, i.e. biomolecular patterning in sub-micrometer size. The fundamental idea is integrating two physical characteristics, hydrophobicity and dielectricphoresis.

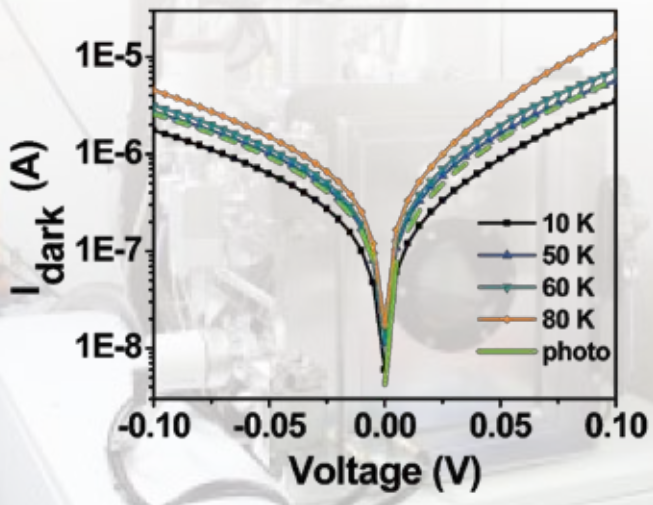


Fig. 5 The dark and photo I-V curves of the QR terahertz photodetector at different temperatures. The BLIP temperature is about 50 K

圖五 表示我們所製作的紅外線量子環偵測器在不同的溫度操作下，照光及非照光下暗電流對電壓之曲線圖，本元件約可在50K下的環境下操作。

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Professor, Graduate Institute of Biomedical Electronics and Bioinformatics/ Division of Cardiovascular Surgery, National Taiwan University
Director, Heart Transplantation and Heart-Lung Transplantation, National Taiwan University Hospital

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、尿毒症血液透析之血管手術等
- 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

- Cardiac Surgery：Coronary Artery Disease Surgery、Valvular Heart Disease Surgery、Aortic Surgery、Arrhythmia Surgery、Surgery for Heart Failure
- Vascular Surgery：EndoVascular Stent-grafting for Thoracic Aortic Aneurysm or Abdominal Aortic Aneurysm、Revascularization for Peripheral Arterial Occlusive Disease、Varicose Vein Surgery、Arteriovenous Fistula Creation
- Mechanical Circulatory Assist：Extracorporeal Membrane Oxygenation、Ventricular Assist Device
- Transplantation：Heart Transplantation、Heart-Lung Transplantation

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數位信號處理實驗室
Digital Signal Processing Lab.

Medical Ultrasound Imaging
Bio-signal Analysis
Underwater Acoustic Communication

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

研究計畫 Research Projects

- 超音波對比劑於組織參數估測之應用(1)
- 超音波對比劑於組織參數估測之應用(2)

計畫名稱：超音波對比劑於組織參數估測之應用
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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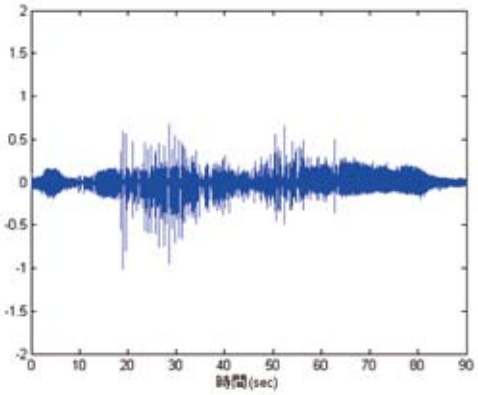
統計信號處理實驗室
Statistical Signal Processing Lab.

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。

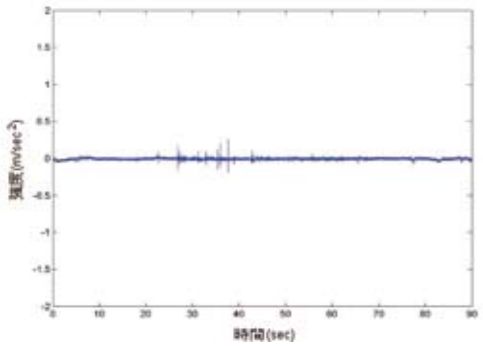
I. BASIC DIGITAL SIGNAL PROCESSING：
   (1) Techniques for the Design and Implementation of 1-D and 2-D FIR and IIR Digital Filters.
   (2) Techniques for Design and Implementation of 1-D and 2-D FIR and IIR Digital Filter Banks (Multi-rate Digital Signal Processing)

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

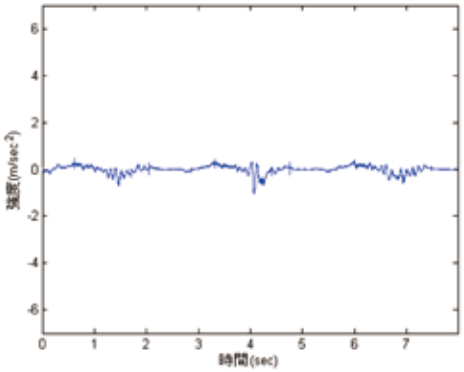
III. PROCESSING AND ANALYSIS OF BIOMEDICAL SIGNALS ：
   Analysis and Processing of Joint Vibration Signals for the Diagnosis of Cartilage Pathology
   (1) Signal Processing Techniques for Vibration Signals of Human Knee Joints
   (2) Signal Processing Techniques for Vibration Signals of Equine Knee Joints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



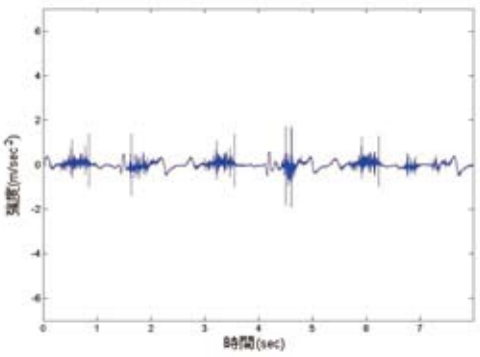
(A) 正常著膝關節在慢速擺動下所產生的振動訊號 (Physiological Patellofemoral Crepitus;PPC)



(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

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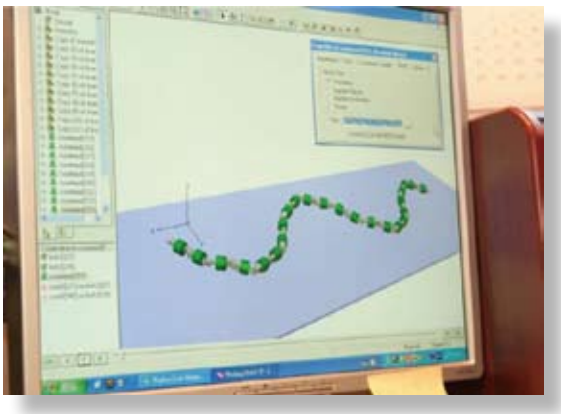
智慧型及精密運動控制實驗室
IPMC Lab.

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。

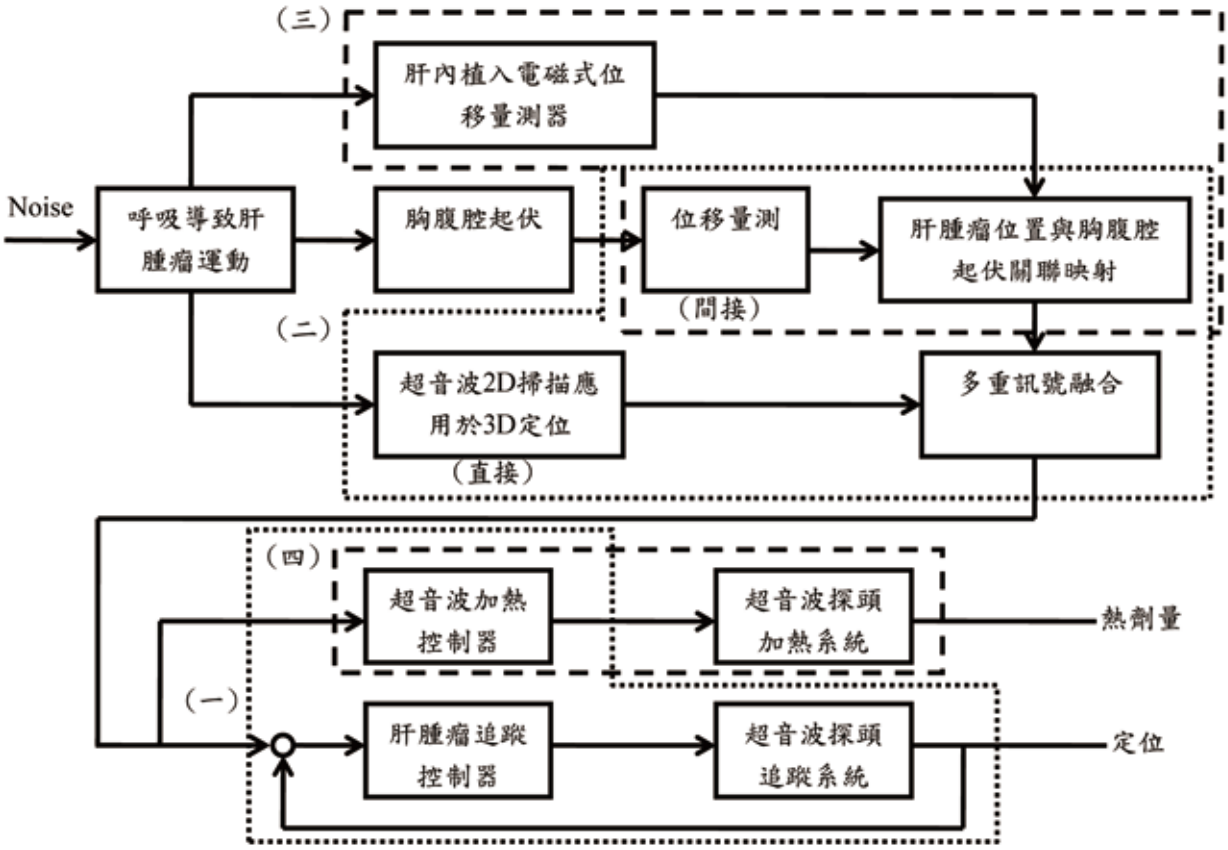
反向光學微影技術的研究是針對在IC製程上小尺度的光罩所產生的繞射現象，在光罩設計時將繞射現象考慮進去，設計出最佳的光罩形狀。電子束微影系統的研究是在IC製程中的電子束蝕刻時，對電子束做位置的訊號回授控制以修正電子移動時所產生的漂移現象。姿態辨識的研究是利用人工智慧的方式來處理影像中的資訊，本實驗室建立影像的監視系統應用在老人看護上。另外在聲音處理的方面是利用訊號處理的方式將聲音中的雜訊濾除，進而研究聲音本質與語者分析。仿生機械人的研究是模仿生物的運動模式，將生物的優點轉換成電機領域的應用，近期的研究是將蛇的運動設計成新型的載具。超音波熱療的研究是發展新的預測方式，來追蹤人體中因呼吸而上下運動的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



圖一 子計畫關聯性之控制方塊圖

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 applications for thermal therapy
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

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(總計劃)

補助單位：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，本計畫結合國立台灣大學電機/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, Taiwan
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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Professor, Graduate Institute of Biomedical Electronics and Bioinformatics/ Department of Electrical Engineering, National Taiwan University

醫學影像實驗室
Medical Imaging Lab.

醫學影像實驗室目前位於台灣大學明達館七樓 (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。

磁共振影像頻譜實驗室
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

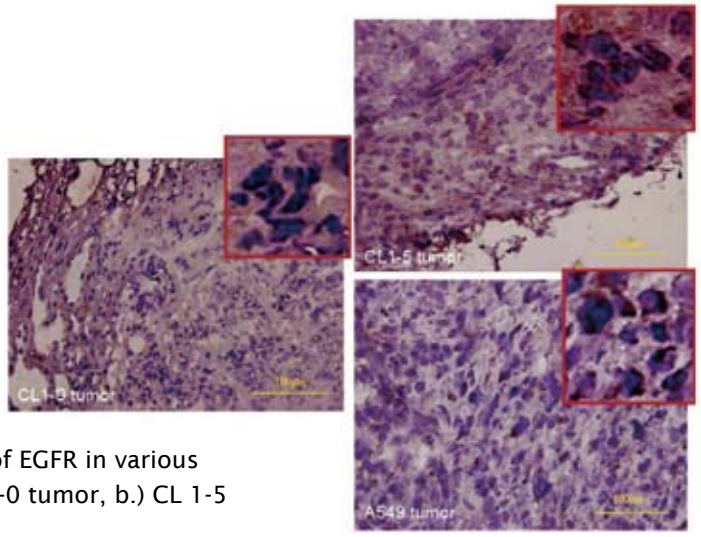
研究計畫 Research Projects

1. 大腦功能影像技術平台建立
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. 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)
5. 新世代磁共振成像術之研發II-超高速磁振成像系統之研究：
   以寬頻無線通訊理論建構之新世代MRI (子計畫一)
   Program for Promoting Academic Excellence of Universities(Phase II): Development of An Ultrafast MR Imager: A New Generation MRI Based on Broadband Wireless Communication Theory
6. 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?
7. 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：針對肺癌診斷與治療評估之核磁共振分子影像技術平台：具標定功能氧化鐵奈米粒子之發展
補助單位：行政院國家科學委員會
計畫期間：2007/08/01-2008/07/31

本計畫的研究目為發展生醫分子及活體細胞追蹤之磁振造影技術，並研究其在早期偵測並評估肺癌細胞小鼠模式之腫瘤血管新生型態功能及其轉移。主要內容為發展動態顯影磁振造影之血管新生評估技術、開發對細胞分子表現特異性鑑別之奈米磁振顯影劑、並且利用高溫超導射頻線圈及平行影像重建法來達到高訊雜比及高效率之磁振造影技術，用來研究肺癌細胞與肺臟轉移小鼠模式。結合上述技術之開發則可更進一步提供病灶分子病理資訊並設計多功能甚或智慧型藥劑，使醫師得以即時知道用藥之效能與投遞分布情形以最佳化治療策略。

此計畫針對肺癌之疾病模式作為主要之疾病研究標的，其主因為肺癌之臨床特徵為不易早期診斷，並常早期發生轉移，尤其是肺腺癌更常在疾病發現初期，即有遠處轉移之現象，並且常有手術後復發之情況。就目前的治療成效，非小細胞肺癌對放射線治療及化學治療之反應也較差。因此研究發展早期診斷肺癌、早期偵測肺癌轉移、評估腫瘤血管新生能力以及監測肺癌治療反應之新方法，即成為刻不容緩之課題。於此，本團隊已建立VEGF(vascular permeability factors)與EGFR超表現或低表現之鼠肺癌活體模型之標準化誘導程序，可快速以正位手術移植法重現，將作為本研究標的。



The immunohistochemical staining of EGFR in various tumor cell line in SCID mice. a.) CL 1-0 tumor, b.) CL 1-5 tumor;,and c.) A549 tumor.

In the Figure the imaging of immunohistochemical staining showed that the expression of EGFR had different level in various tumor cell line. Herein, we found that the CL 1-5 and A549 have more EGFR expression on cell membranes of tumor section. Furthermore, we could apply the Fe3O4-anti EGFR antiboby nanocontrast agents for tumor region targeting in MR in vivo assay.

Project title: The development and preparation of targeted Fe3O4 nanoparticles as MR contrast agent; its application for MR molecular imaging in lung cancer diagnosis and treatment
Supported by: National Science Council
Project period: 2007/08/01-2008/07/31

In this research, we aim to develop a platform of nanocontrast agents and molecular MR imaging system that specifically recognizes cancer cells and exerts its therapeutic efficacy while enables real-time tracking of the drug distribution. This kind of system will provide not only valuable molecular pathological information but also real-time therapeutic efficacy evaluation for personalized healthcare treatment strategy.

Among various disease models, lung cancer is one of the most common causes of cancer-related death in Taiwan (top 2nd) as well as other industrialized nations. The prognosis of lung cancer is poor as compared with other malignancies. Therefore, the research for early diagnosis, early detection of metastasis, and tumor-associated angiogenesis process, and assessment of therapeutic response become more and more important for lung cancer diagnosis and treatment. In this study, pulmonary tumor implantation animal models in mice with high and low VEGF (vascular permeability factors) and EGFR expression lung cancer cell carcinoma model were established by our team and will be used through the whole three years.

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國立台灣大學電機工程學系 教授

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

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

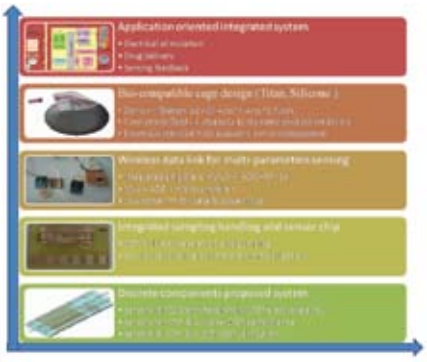
生物微感測器與系統、生醫晶片、生醫光電、類神經網路、醫材法規
Bioelectronics、Biomedical Micro sensors and System、Biochip、Biomedical Optics、Artificial Neural Networks, Regulatory Affairs

研究計畫 Research Projects

1. 光生化型晶片系統於藥物篩選與疾病檢測之研發
   Drug Screening and Diseases Diagnosis with Multifunctional Opto-electronic Biochip Systems
2. 光生化型晶片系統於藥物篩選與疾病檢測之研發-(子計畫二)整合式蛋白質生醫晶片系統
   Integrated Protein Chip System
3. 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
4. 整合式奈米氣體陣列感測器於有毒氣體分析之研發
   Integrated gas nanosensor array for the analysis of volatile mixtures

5. 先進無線生醫保健監測系統之開發三年計畫第2期計畫
   Wireless Health Advanced Monitoring Bio-Diagnosis, WHAM-BioS (Phase II)
6. 即時性可拋式軟性有機電激表面電漿子生物感測元件(總計畫)
   A Disposable Soft Material-based OLED SPR Biosensor for Real Time Applications (Co-PI)
7. 非線性光學顯微術於奈微米尺度下生物分子動態檢測之研發
   Nonlinear microscopy developments for investigations of biomolecules in micro- and nanodomains (Co-PI)
8. 以海鱸、海藻及濾食性貝類整體育種、飼養、銷售、智慧財產保護平台之海產食物供應鏈研究－子計劃六：智慧財產權佈局與品質安全規範研析
   Sea food supply chain - Analysis of Intellecture Propertis & Regulatory affairs(Co-PI)
9. 永續智慧人本住家(子計畫二)—居家醫護屋
   Development of a smart sustainable human-centric home- Smart Medical Home(Co-PI)

計畫名稱：Efficacy studies of RF Stimulation on Lumbar DRG
補助單位：台懋生技股份有限公司
計畫期間：2009/02/02-2009/07/30



本計畫在台懋公司的經費援助下，以先期參與之合作模式，共同投入針對上述之微小化脊椎電刺激系統於頑固性下背痛患者使用之驗證研究，本期研究將以下列重點為主

1. 相關智慧產權評估與專利地圖分析
   (Sluijter, Kim, DRG, RFID, reference articles> 1996-2004)
2. 於下背痛之脊椎動物模型進行有關體內植入電刺激參數在DRG部位的刺激之功效確認，進行單極與雙極電刺激參數之效能驗證.
3. DRG電氣參數之量測.
4. 植入式電極與無電源植入刺激系統之最佳設計技術報告

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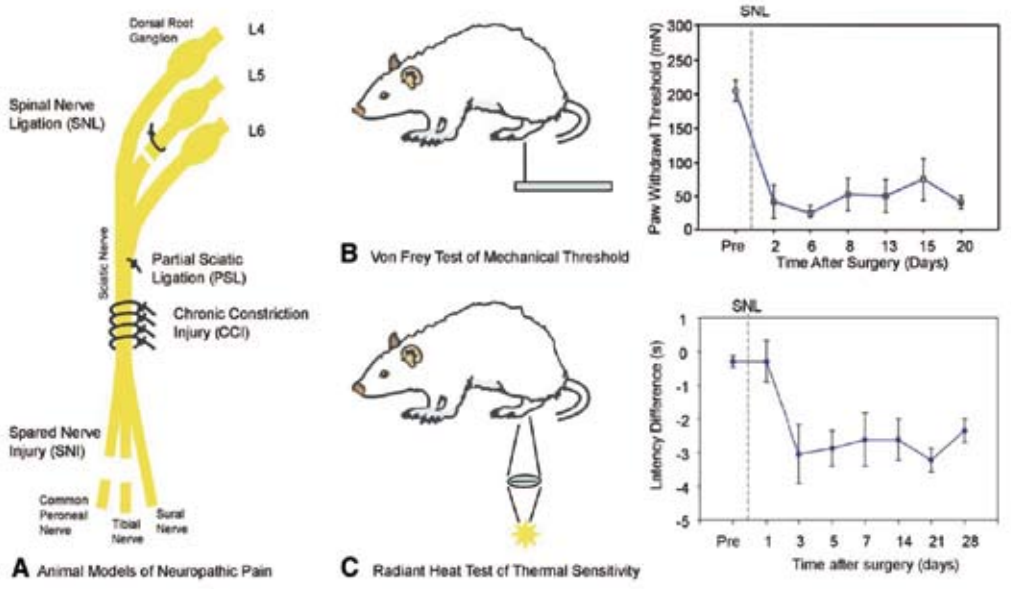
Project title：Efficacy studies of RF Stimulation on Lumbar DRG
Supported by：Taimed Corp.
Project period：2009/02/02-2009/07/30

Objective: To assess the efficacy and specific electrical characteristics of RadioFrequency on treatment of Low Back Pain.

Study Design: An in vivo animal study use 30 mice for RF-DRG on neuropathic pain with design output of stimulating electrode and validation of subthreshold (< 1 V) RF pulse patterns for efficacy along with the specific electrical properties of DRG under such a condition for possible clinical applications.

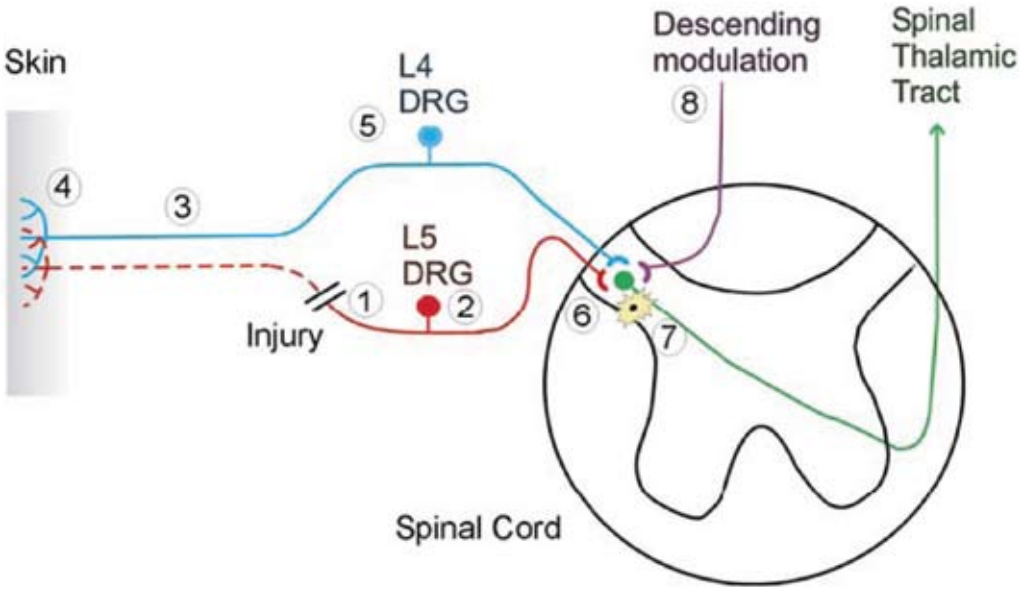
Expected outputs:
1. IP lanscape assessment & patent map (Sluijter, Kim, DRG, RFID, reference articles> 1996-2004)
2. Animal model for experimental validation of mono and bi-polar sub-threshold stimulation effects.
3. A set of electrical parameters on DRG characterizations.
4. A set of optimal design for implantable electrode & battery-less implantable stimulus sysetm.

本研究團隊在溫永銳醫師的多年努力下已成功建構如圖一之改良式Chung model，可在下背神經的相關部位進行不同程度的損傷以模擬不同形式的脊椎損傷，並配合不同行為試驗方法，測試評估損傷程度與後續治療方法所引起的改善程度，以與臨床行為建立相比對之量化數據。



圖一

Animal Models of Neuropathic Pain. (A) Four different nerve injury models are shown, spinal nerve ligation (SNL) model (Kim and Chung, 1992), the partial sciatic ligation (PSL) model (Seltzer et al., 1990), the chronic constriction injury (CCI) model, and the spared nerve injury (SNI) model (Decosterd and Woolf, 2000). Each of these nerve injury models leads to hyperalgesia, which is manifest by enhanced responses to mechanical, heat, and/or cooling stimuli. (B) To test for mechanical hyperalgesia, Von Frey monofilaments with different bending forces are applied to the plantar surface of the foot. The threshold force for paw withdrawal decreases dramatically after the nerve injury (adapted with permission [Li et al., 2000]). (C) To test for heat hyperalgesia, a radiant heat source is focused onto the plantar surface of the foot, and the reaction time for paw withdrawal is measured. The difference in reaction time between the ipsilateral and contralateral foot is calculated.



圖二

更進一步的在此計畫中我們將利用免疫螢光染色法進行組織切片的量測分析，以建立如圖二所式之疼痛機制模型中相關分子的表現，特別用以比對在低位準電刺激DRG後所引起的變化。

A Spinal Nerve Injury Leads to Alterations at Many Sites along the Neural Axis for Pain. Eight different sites of pathophysiological changes are shown.

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紅外線暨生醫奈米元件實驗室
Infrared and Bio-Chemical Nano-Device Lab.

- 電子束直寫顯影實驗室、電子束掃瞄及顯影實驗室
  (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.)

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

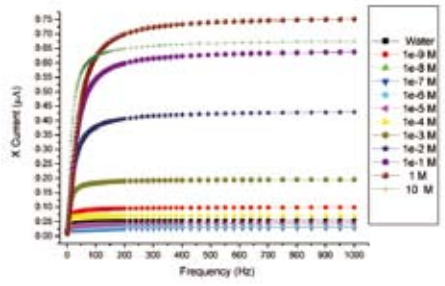
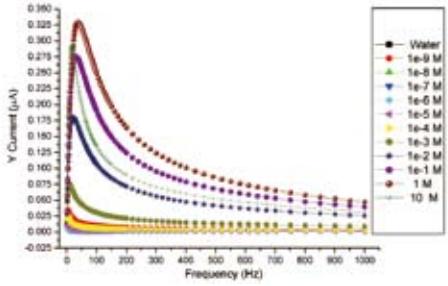
計畫名稱：離子的高敏感度交流電性量測並以紅外線頻譜作輔助分析
補助單位：行政院國家科學委員會
計畫期間：2007/08/01-2010/07/31

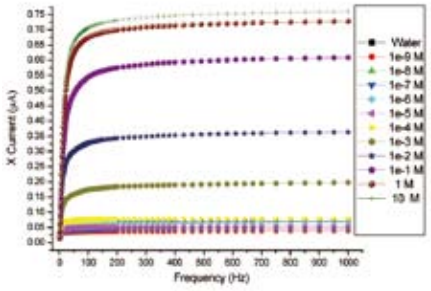
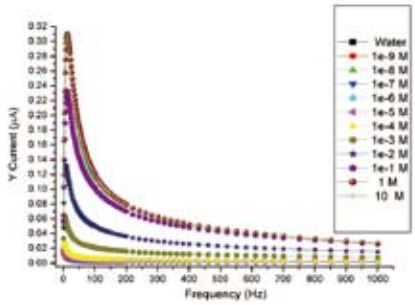
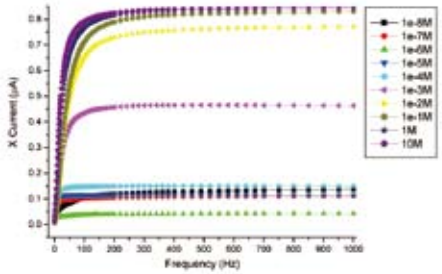
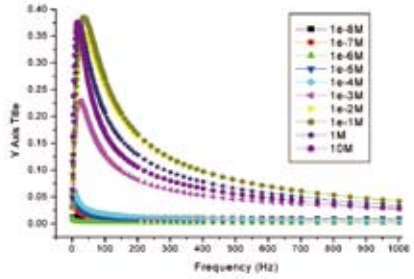
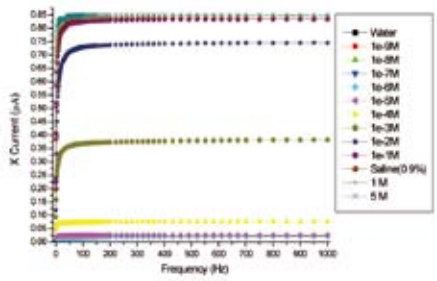
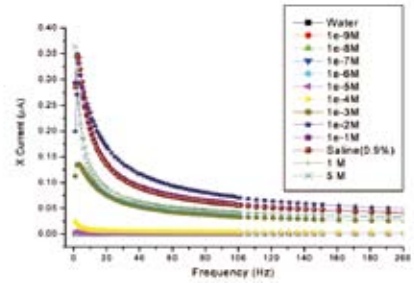
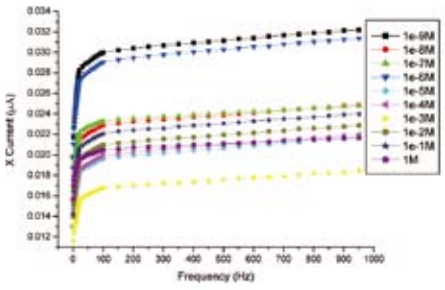
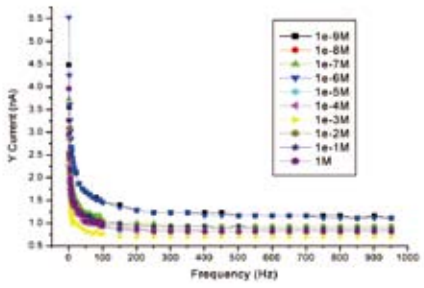
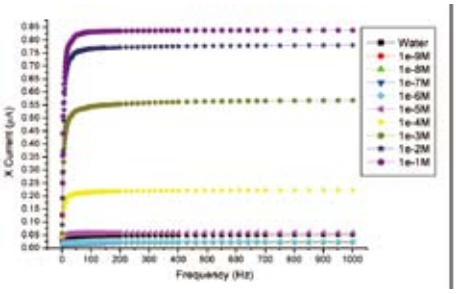
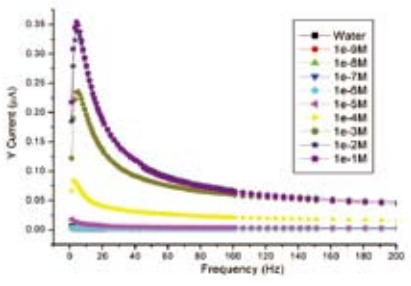
傳統微電泳通道外加電場普遍為直流電源，在電壓持續提供下，會造成單方向電荷持續累積，此意味著量測環境將隨電荷累積持續變化，降低量測結果重複性。我們採用交流訊號量測方式使量測環境形成規律之充放電反覆循環，避免電荷持續累積，並確保量測環境不隨時間改變，以將雜訊成分降到最低，同時可大幅提高訊號／雜訊比。藉由待測分子在交流響應中表現出來之相位延遲，精準擷取出複數形式的響應參數，再將此同一機制下產生之虛部除以實部，得到各種不同待測分子之特徵響應。此種以鎖相放大器量測系統進行之量測，可實現高敏感度，依此構想期望研發一種新型生物分子ID建立方式。

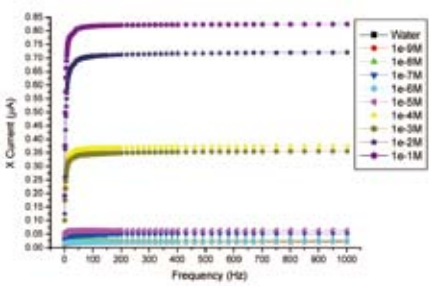
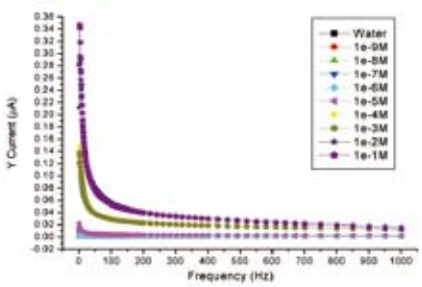
在本計畫中，我們以二氧化碳雷射雕刻壓克力基板，設計封閉式微電泳通道元件，以改善先前之玻璃基板半導體製程所遭遇的水溶液蒸發問題；發現經過改良後，實部與虛部電流之趨勢均較先前穩定。而接續前一年度的研究進程，考慮寡核苷酸樣本內的背景鹽類可能帶來之干擾，我們另外採用一些高純度的簡單分子水溶液樣本來做分析，包括醋酸、氨水、磷酸、葡萄糖、氯化鈉，以及健大黴素、萬古黴素兩種抗生素，分別配製十一種數量級的濃度作分析。上述各種樣本分子各具不同解離特性以及大小離子質量比（M/m），是我們選擇這些樣本分子之理由。

我們初步成功架設一套鎖相放大器量測系統來精準量測微電泳晶片的訊號，並且創新地提出以交流電訊號來分析生物分子微電泳響應的新方法，從目前的實驗結果已足夠證明當初所預期的一些重要現象如高重複性、低誤差率的量測結果等。並且初步驗證了交流電分析的可行性及其所獨具的各項優點，如充放電反覆循環的優點使量測環境不隨時間改變，所以這種晶片可做為長時間的分析應用，較一般微電泳晶片更節省樣本消耗。而從交流電分析取得之複數形式響應數據，本研究準確量測出生物分子在微電泳中的相位延遲資訊，並從這些資訊我們也定義了不會隨量測環境改變的生物分子之特徵響應值（tan θ）。同時我們也建立了離子運動的理論模型來研究生物分子的交流電泳響應，在經過此理論的電腦模擬與實際實驗結果的比對，我們也發現出生物分子的交流響應擁有模型化的可行性。

圖為不同濃度之七種樣本分子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)。
The Figure shows AC current responses of seven different chemical solution.(a)Real part currents(J_x)and (b)Imaginary part currents(J_y)

	（a）實部電流（J_x）	（b）虛部電流（J_y）
醋酸 CH_3COOH		

	（a）實部電流（J_x）	（b）虛部電流（J_y）
氨水 NH_4OH		
磷酸 H_3PO_4		
氯化鈉 NaCl		
葡萄糖 $C_6H_{12}O_6$		
建大黴素 Gentamicin		

	(a) 實部電流 (J_x)	(b) 虛部電流 (J_y)
萬古黴素 Vancomycin		

Project title: High-sensitivity AC electrical signal measurement and infrared spectrum assistant analysis
Supported by: National Science Council
Project period: 2007/8/1-2010/7/31

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 exists 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 CO2 laser to fabricate the PMMA substrate with a cover slide as a close-ended chip to avoid evaporation. The present data shows highly stable and repeatable after improvement. Continuing the last year progress, in order to exclude interferences of background salt in the oligonucleotides, we utilized some simple, pure chemicals like acetic acid, ammonia, phosphoric acid, glucose, sodium chloride, and two antibiotics, gentamicin and vancomycin. All chemicals possesses various ionization characteristics and M/m ratios, which were prepared in eleven orders of concentrations to be analyzed.

We have successfully established a lock-in amplifier systems focus on AC measurement, and also demonstrated a new model to analyze the biomolecular AC signal response. Although the present data amount are not very much enough , it is sufficient to prove some important phenomena like highly repeatable and low error range of the present experimental results. And we ensure the advantages of charge recycling effect remains measuring environment doesn’ t change with time, so the biochip can be applied in long time analysis, decrease wasting of samples. We precisely obtained the information of phase delay in microelectrophoresis and defined the environment-independent characteristics response ( ) .We also established the theoretical model of ion movement to study biomolecular AC response. After comparing the computer simulation and data, we found out the capability in modeling the biosystems.

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

醫用磁振造影實驗室
Magnetic Resonance in Medicine Lab.

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15名，碩士班研究生2名。博士班畢業生16名，碩士班畢業生11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. 平衡穩定態自由旋進磁振造影
   平衡穩定態自由旋進為新興之高效能高信雜比快速磁振造影技術，多使用於心臟造影中。本計畫將拓展此技術，以多頻率葉片式內插混成技術，針對事前選擇之特定區域從事對比之最佳化，並應用於高解析度神經系統功能性造影。

Founded in July 2000. Supervisor: Prof. Hsiao-Wen Chung. This lab currently (2009) has 15 Ph.D. students and 2 M.S. students, plus 16 Ph.D. graduates and 11 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. Balanced steady-state free precession MR imaging Balanced SSFP is a rapid SNR-efficient MR imaging technique mostly used in cardiac imaging. This project aims at high-resolution functional imaging in the central nervous system by means of multi-frequency interleaving to optimize functional contrast in specific regions of interest.

主要研究領域 Major Research Areas

醫用磁振造影
Biomedical magnetic resonance imaging

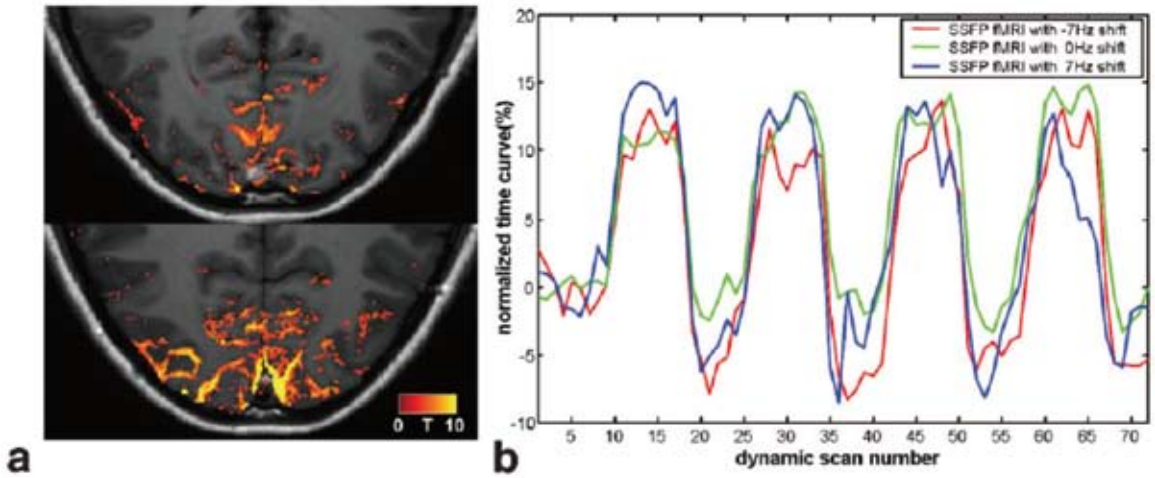
研究計畫 Research Projects

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：國科會工程處
計畫期間：2007/08/01-2010/07/30

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, Engineering Division
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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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. 使用奈米金粒子之多目標光熱治療與光聲影像技術
   Gold nanoparticles for multiple selective photothermal therapy and photoacoustic imaging
2. 乳癌治療抗療性之整合研究
   Integrated approach to dissecting resistance of anti-cancer treatment
3. 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
4. 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

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：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。

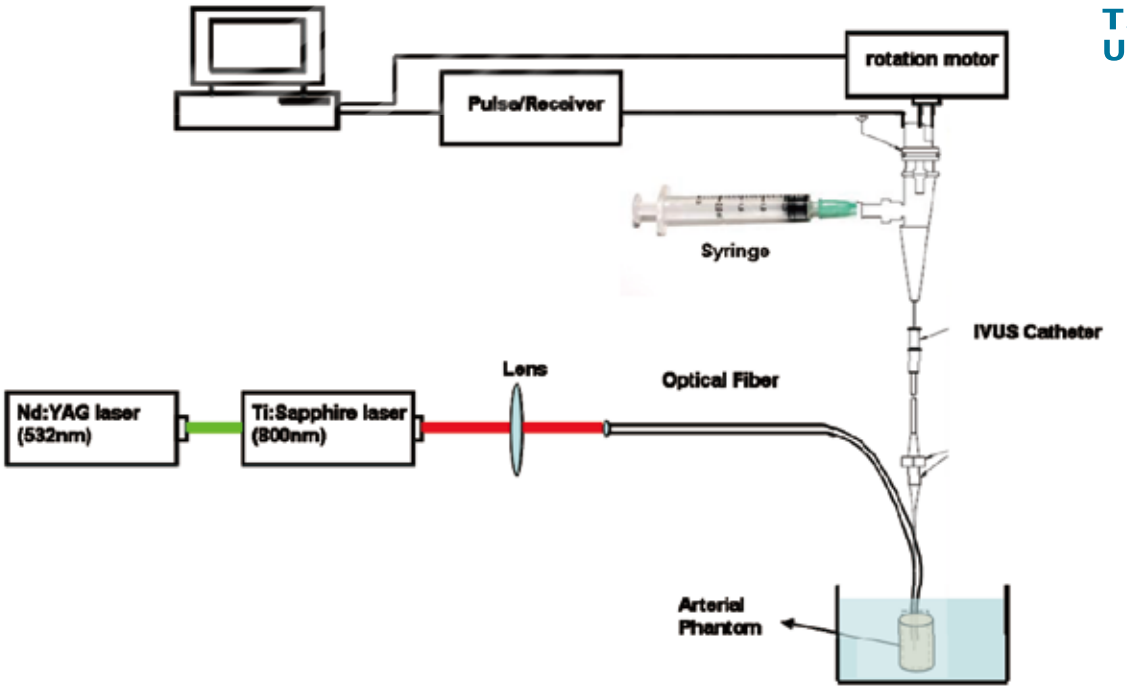

Fig.1 Laboratory prototype IVUS/IVPA imaging system setup

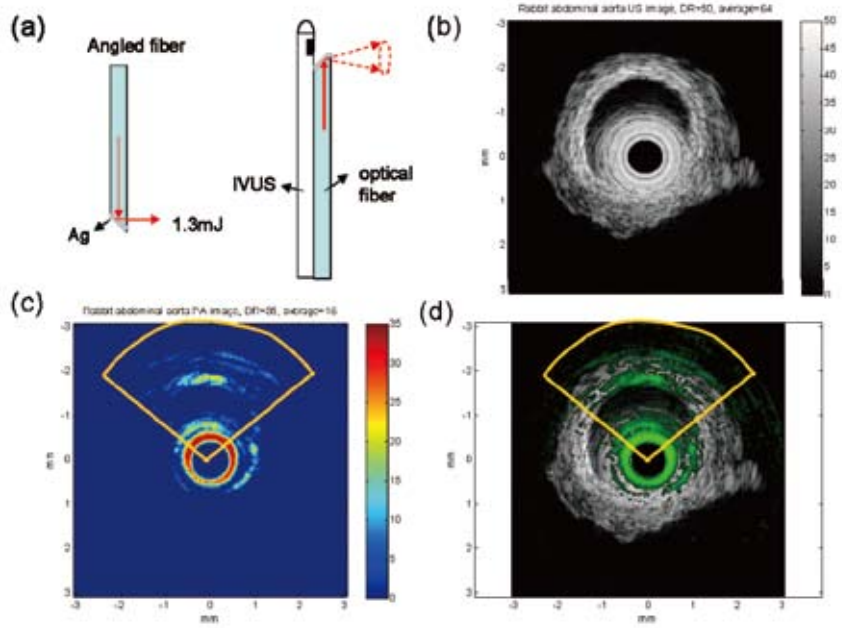

Fig.2 (a) Configuration of integrated IVUS/IVPA transducer, rabbit abdominal aorta (b) IVUS image (c) IVPA image, and (d) IVUS/IVPA fusion image

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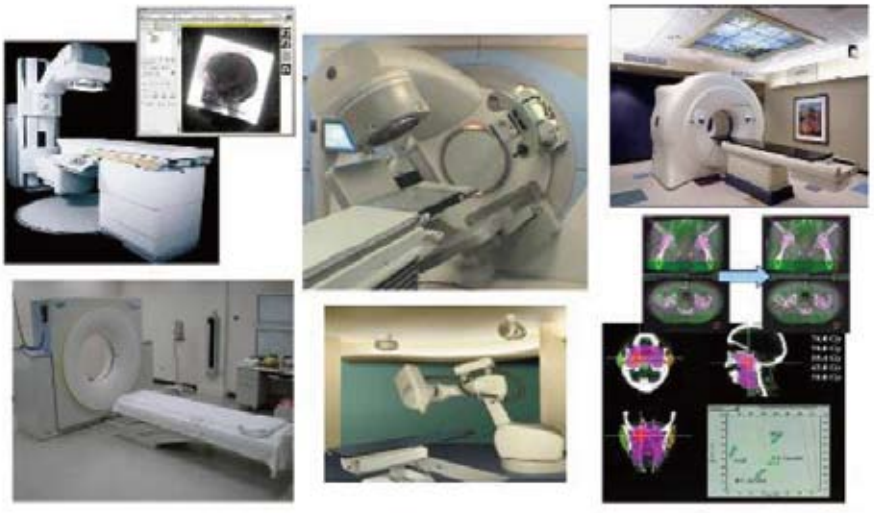
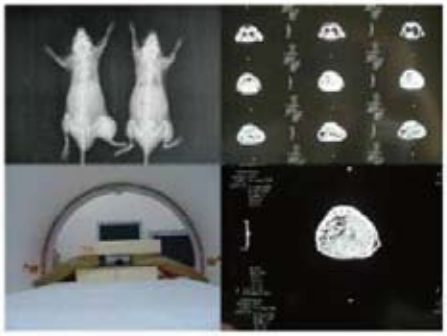
本實驗室由成佳憲副教授於2002年起隨同整建台大醫院腫瘤醫學部放射腫瘤科時設立，主要從事放射治療物理學與放射生物學相關研究，目前以設備技術物理與腫瘤放射治療轉譯醫學等領域為研究重點。本實驗室在影像導引放射治療領域與肝癌放射治療領域已產出許多具體貢獻。本實驗室之成員來自台大醫院腫瘤醫學部放射腫瘤科醫學物理師、放射師、及放射生物醫學領域研究人員，多年來亦積極與國內外單位進行合作。

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. 放射線引發人類血管內皮細胞產生介白質六之機轉與功能研究
   Mechanism and functional study of radiation induced IL-6 in human endothelial cells
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. 放射線引發乙型病毒肝炎發作的旁觀者效應研究
   Bystander Effect Study of Radiation-Induced Viral Hepatitis B Reactivation
4. 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

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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五大領域

- 生醫MRI,PET影像處理
- 生醫行動資訊系統
- 數位電路之最佳化
- 可製造性設計
- 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 5 major projects:

- Biomedical MRI,PET Imaging processing
- Digital Circuit Optimization
- Design for Manufacturabiliy
- Statistical Static Timing Analysis
- High Performance Circuit Design

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1012)。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: 2007/08/01-2010/0/07/31

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.

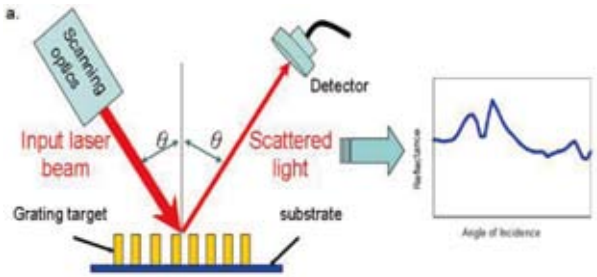
However, due to the everlasting shrinking process feature sizes, the values for the physical parameters of a grating may deviate significantly from the original design in our SEM chart as shown in fig. 1a (fig. 1b demonstrate the Optical Scatterometry Experimental Setup). Therefore, enormous amounts (more than 1012) 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:

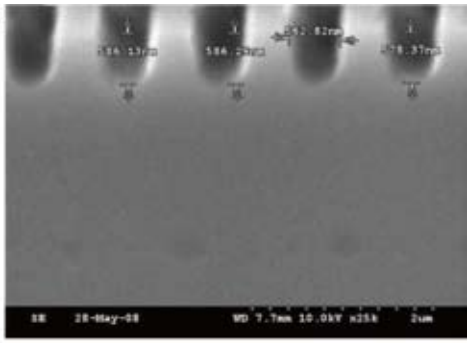
First, a segmented statistical moment matching method has been developed to do a first filtering for possible matching patterns. In the beginning, all of the spectrum in the database will be classified and hierarchically sorted according to the values of the first few segmented moments such as mean, 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.

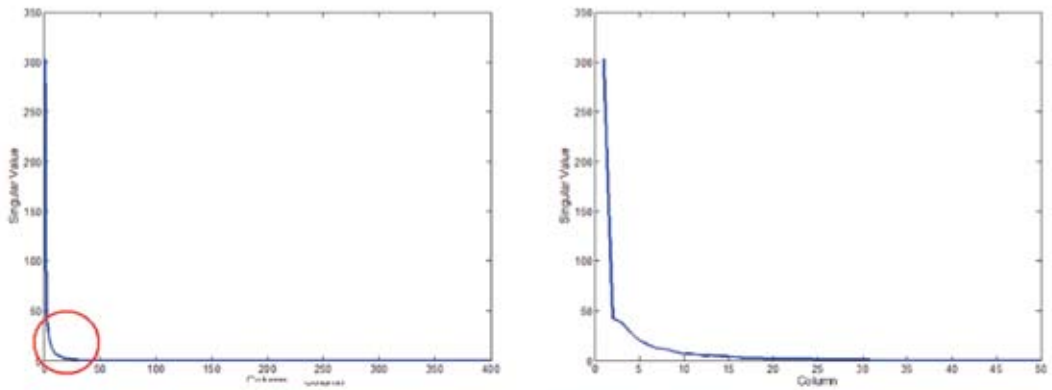
Second, to ensure the best fit (minimum error) of the result, the Singular Value Decomposition (SVD) technique has been employed. After applied SVD to the original database, a, the database can be decomposed into a product of 3 matrices, USVT, where U and V are orthonormalized basis and S contains singular 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.

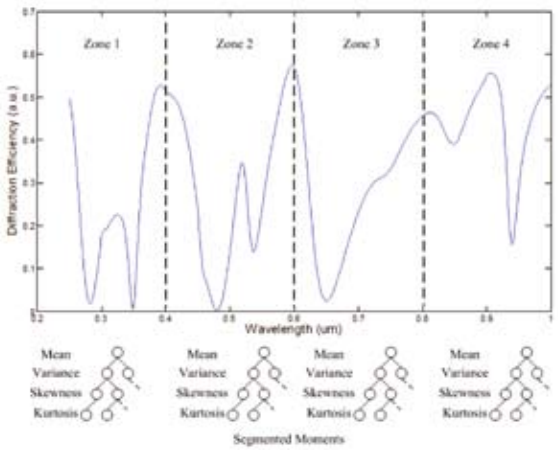
B. Acknowledgements
The authors would like to thank ITRI for providing partial support to the work through the grant number 7301XS7400.







Singular Value Distribution



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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, R.O.C(TAIWAN)
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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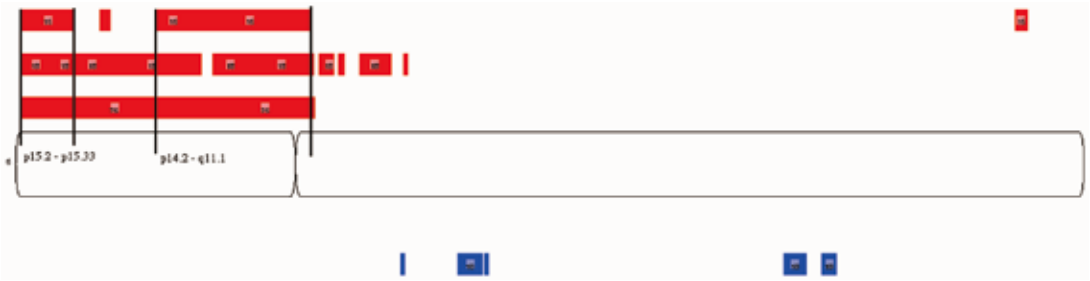

目前已利用whole-genome sampling analysis (WGSA)，完成6個檢體初步之GeneChip Mapping 500K分析，在染色體5p附近有三組樣本在相同區域有DNA高度複製的狀況，進一步研究這些區域發現SKP2, GDNF, NF-kappaB 基因與前人研究肺癌形成有關。並依GeneChip Human Genome U133 Plus 2.0基因表現之初步結果，發現140個於肺癌檢體與正常組織表現有顯著不同表現的基因。經IPA綜合分析GeneChip Mapping 500K與基因表現的結果，顯示染色體變異區域上的基因確實與癌症的形成有相關性。

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.

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

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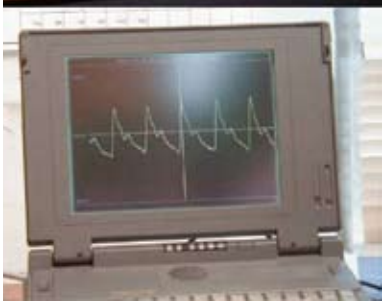
非侵入式生理量測實驗室
Non-Invasive Physiological Measurements Lab.



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

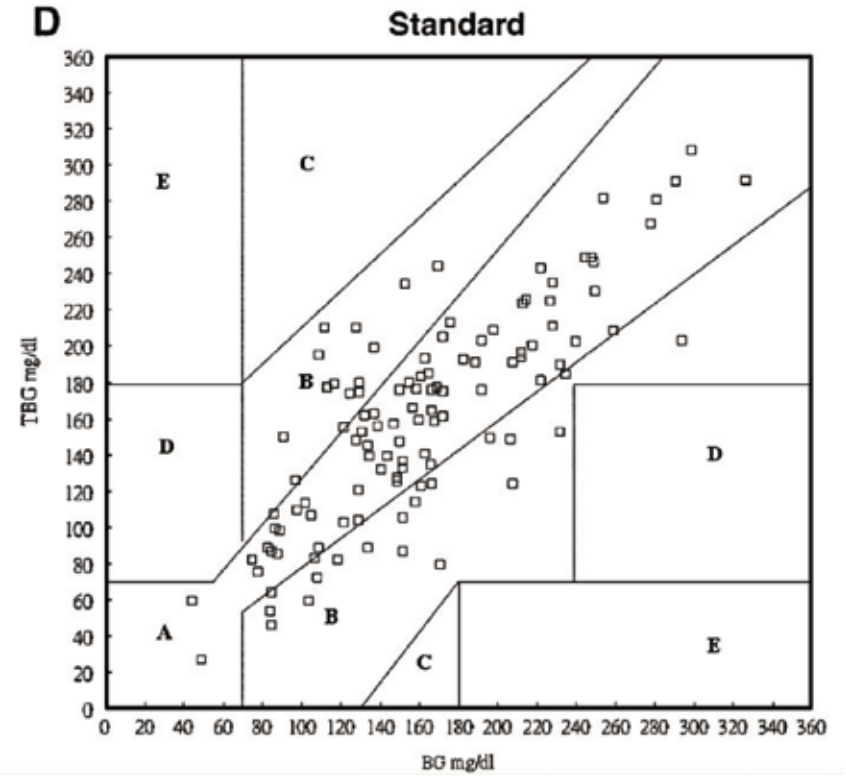
Major Research Areas: Non-invasive physiological measurement

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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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
補助單位：行政院國科會
計畫期間： 2008/08/01-2009/07/31

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。

Project title: Healing Partner System for the Elderly Healthcare at Home
Supported by: NSC
Project period:2008/08/01-2009/07/31

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

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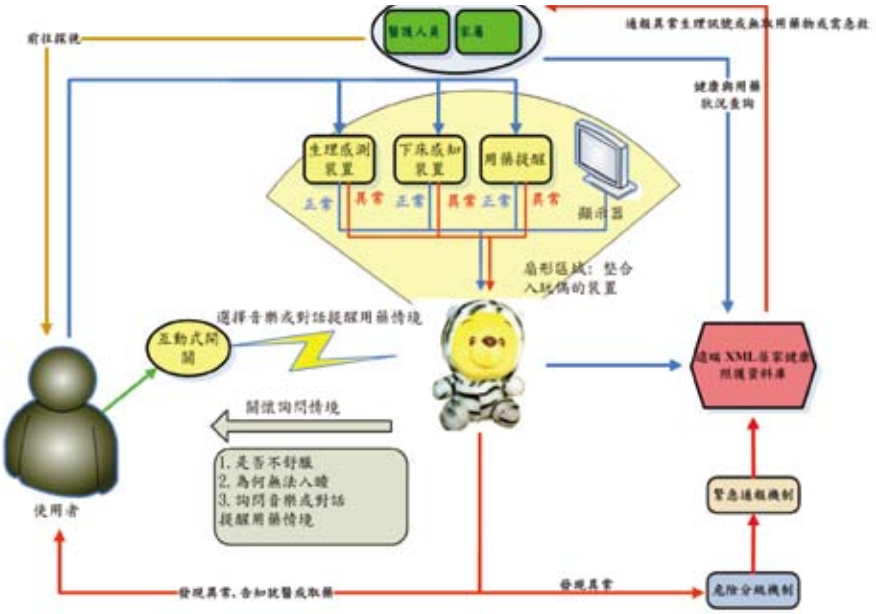
alleviating insomnia, the monitoring for vital signs such as blood pressure, body temperature, and blood oxygen saturation at the appropriate time , the connection & activation of the emergency alert system for immediate attention or rescue. That means a user-friendly healing partner system can help 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.



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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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

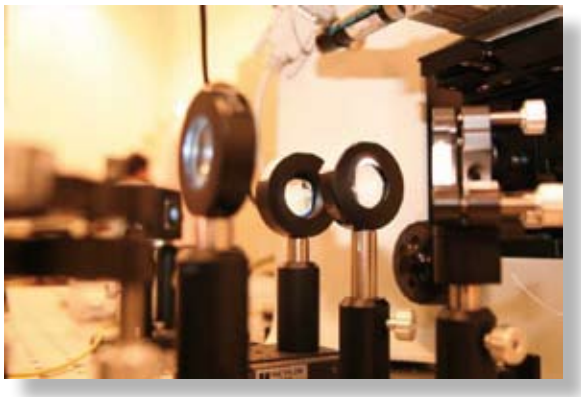
生醫工程、生醫光電
Biomedical engineering, Biophotonics

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. 整合蛋白質樣本濃縮與無標記感測之系統
   An integrated system for sample preconcentration and label-free detection of protein biomarkers
3. 紅外共焦顯微量測模組技術開發
   Development of a micro-measurement module using near infrared confocal microscopy
4. 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

計畫名稱：整合蛋白質樣本濃縮與無標記感測之系統
補助單位：國科會
計畫期間：2008/08/01-2009/07/31

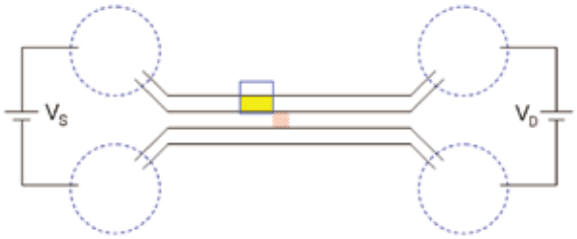
本計畫之目標為設計、建構與測試一個新的結合樣品前濃縮以及無標記生物分子感測的微奈米流體系統，以達成蛋白質生物標記分子的高靈敏度檢測。若能在整合的晶片型微實驗室上進行高靈敏度之免疫分析，將非常有助於在傳染性疾病檢測與癌症篩檢上，提供更普及的醫療服務。我們製作微流體晶片，使用奈米尺度的流道篩選帶電離子與分子並配合加速的電滲流，將蛋白質樣本高度濃縮，並以螢光及自製之表面電漿共振(SPR)生物感測器，在樣本濃縮區域進行高靈敏度的抗體抗原接合偵測。進行SPR免疫分析時必須將捕捉抗體固定在金膜表面，我們將利用樣本濃縮效應加速抗體的吸附。更重要的是，樣本濃縮效應可用於增加受測抗原與抗體接合速度，以克服在微米尺度下的免疫分析受到受測分子擴散速率的限制，進而提升免疫分析的靈敏度，而不需要以增長反應時間來達到加強信號的目的。未來我們將把此方法擴充到在複雜的蛋白質混合樣本中同時檢測多種生物標記分子。由於我們將免疫分析的步驟最簡化，加上SPR生物感測器非常適合



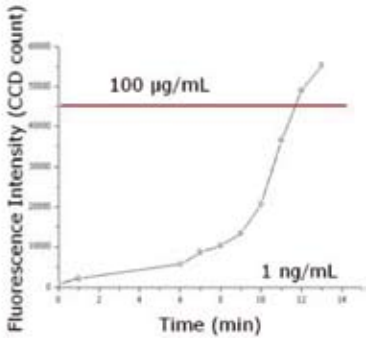
進一步地微小化，因此若能成功達成本計畫的工作目標，相信可以對微量低濃度蛋白質生物標記的免疫分析提供新而有效的方法，也朝發展小型平價檢驗工具的長遠目標邁進一步。

Project title: An integrated system for sample preconcentration and label-free detection of protein biomarkers
Supported by: National Science Council
Project period: 2008/08/01-2009/07/31

The objective of this project is to design, construct and test a novel micro/nanofluidics-based system that combines sample preconcentration and label-free biosensing to achieve highly sensitive detection of protein biomarkers. The capability to perform sensitive immunoassays on integrated lab-on-a-chip devices could lead to significant advances in the diagnosis of infectious diseases and the screening of cancers at the point of care. In this project, we build a microfluidic device that achieves highly concentrated protein sample using an ion-selective nanofluidic channel and high-speed electroosmotic flow. Sensitive detection of antibody-antigen binding event is performed at the site of sample preconcentration using fluorescence detection and a home-made surface plasmon resonance (SPR) biosensor. We immobilize capture antibody onto SPR-active Au film under the influence of the protein preconcentration effect to minimize the time for antibody immobilization. In order to overcome the limitation of sensitivity of the immunoassay due to diffusion, we use sample preconcentration effect at the site of antigen-antibody binding to boost the rate of signal development. Therefore, sensitivity can be significantly improved without impractically long period of incubation. For future work, we will demonstrate sensitive immunoassay of multiple biomarkers in complex protein mixtures. Thanks to the extremely simple assay format and the relative ease to miniaturize SPR biosensors, we believe that successful completion of this project would provide a novel and promising approach to performing immunoassays of low abundance proteins with microfluidics-based devices, which would make a step closer to our long-term goal of developing miniaturized and cost-effective diagnostic tools for point-of-care healthcare.



(a) 微奈米流道晶片的示意圖
Schematic diagram of the micro/nano-fluidic chip.



(b) 螢光標記之蛋白質樣本濃縮效應
Preconcentration effect of fluorescence-labeled protein

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無線生醫晶片系統實驗室
Wireless Bio-Electronics-System 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：2009/08/01-2012/07/31

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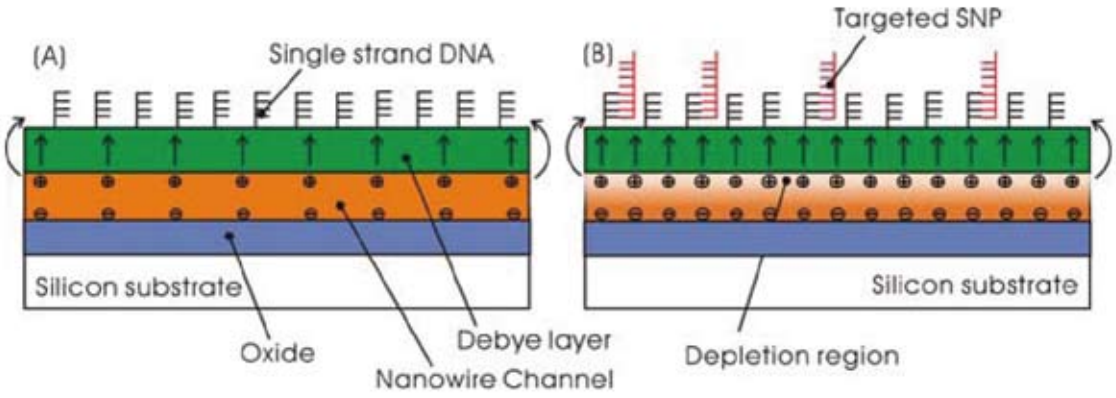
Project title: The Design and Implementation of DNA System-On-Chip for Heart-Failure Patient Response in Beta-Blocker
Supported by: National Science Fundation
Project period: 2009/08/01- 2011/07/31

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.



場效基因感測元件運作示意圖。(A)單股DNA黏附上元件表面時，即對高參雜的傳導通道產生感應電荷，(B)當目標SNP因生物分子特定結合的特性與單股DNA結合時，進一步於高參雜的傳導通道中形成一近似低參雜之區域(depletion region)使此一傳導通道電子特性改變。

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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：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。

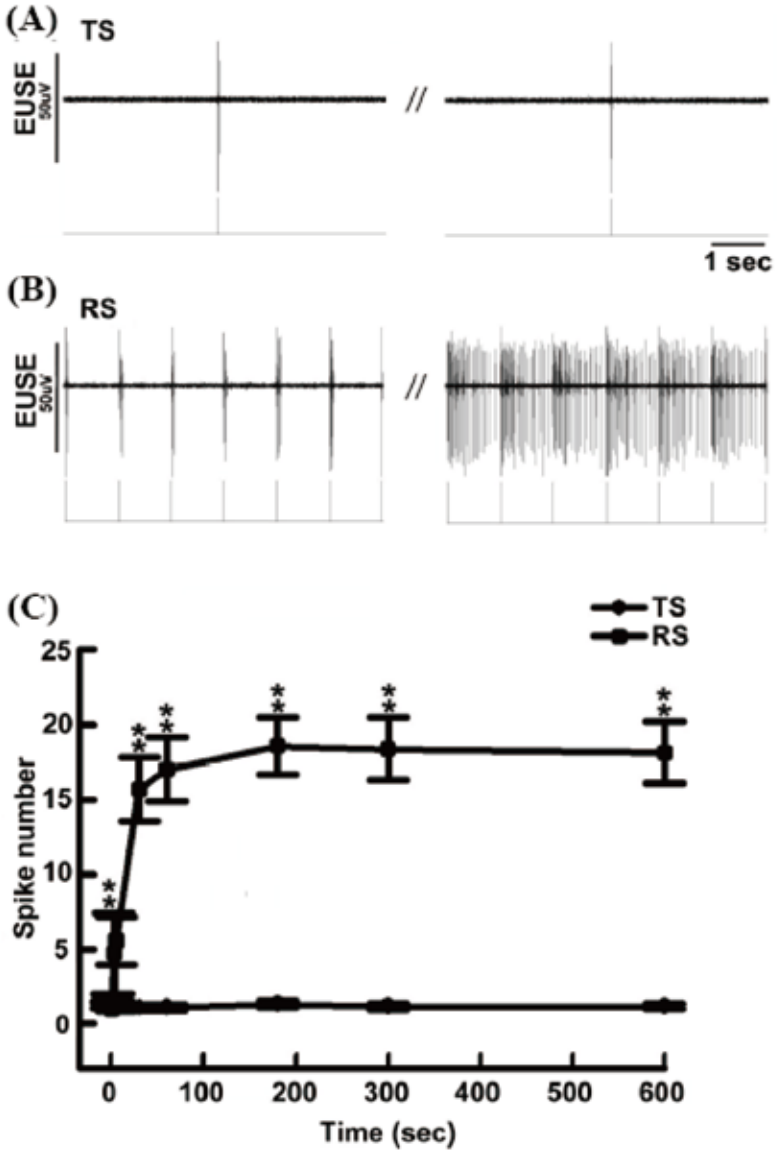
第一年：以1Hz 頻率重複通電刺激大白鼠子宮穴深處腹肌，誘導URP 形成後，經由椎管內分別注射麩胺酸接受器的拮抗劑(NBQX 及APV)；或在基本反射活性(1/30Hz 頻率不會引發URP) 時，由椎管內分別注射麩

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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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

研究計畫 Research Projects

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

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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國立台灣大學電機工程學系 教授
國立台灣大學資訊工程學系 教授

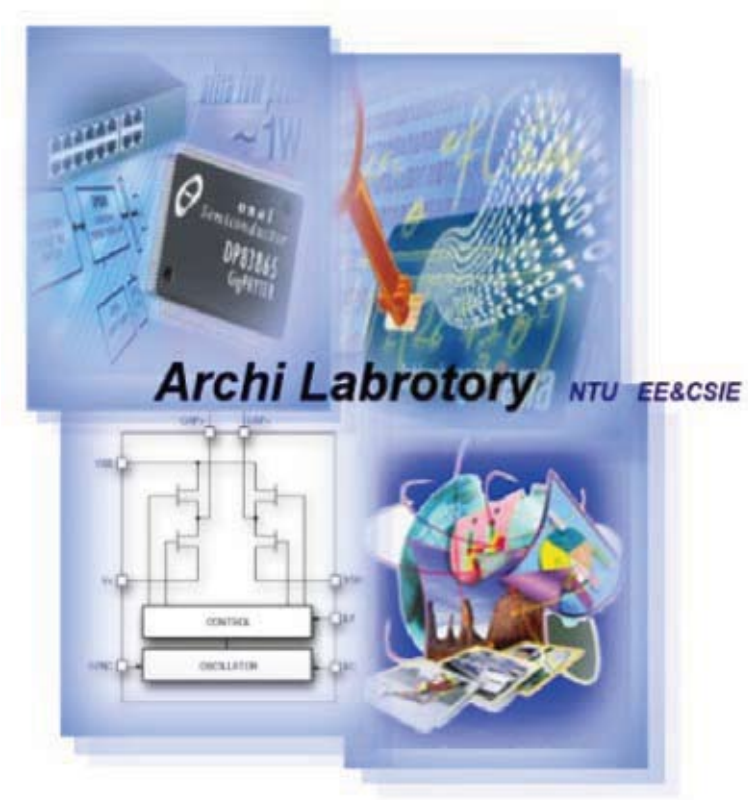
Professor, Graduate Institute of Biomedical Electronics and Bioinformatics/ Department of Electrical Engineering/ Department of Computer Science & Information Engineering, National Taiwan University

低功率超大型積體電路實驗室
Low Power VSLI 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約三十餘名。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為主，近年來改以低功率系統晶片設計為主要目標，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, leads 14 Ph.D. students and 24 master students in this lab. The major research area in the lab includes Low Power SOC Design, Security, and Medical Information System. Our members participate in the research and development of the medical information system in Nation Taiwan University Hospital. Besides, our lab cooperates with numerous IT companies and other overseas universities including Dortmund University in Germany and Calgary University in Canada.



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

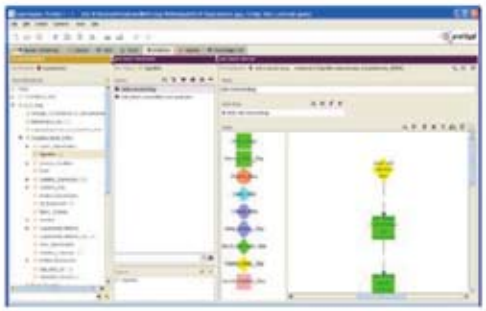
1. 自動化低功率及低漏電流 內容可定址記憶體 產生並模擬及驗證工具集(2009/08/01-2012/07/31)
2. 開放式知識探勘平臺 (2009/08/01-2012/07/31)
1. An automatic tool set for generating, simulating and verifying low power and low leakage content addressable memory
2. Sharable Knowledge Mining Platform

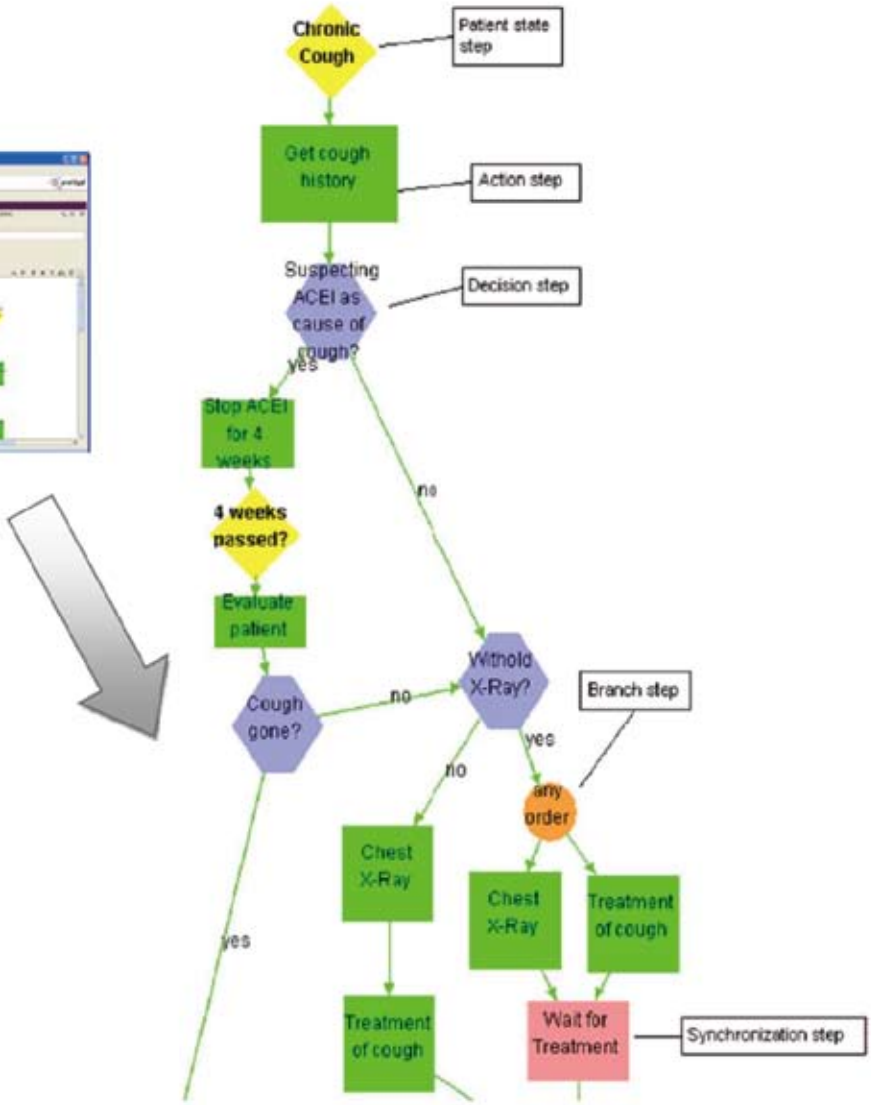
計畫名稱： 開放式知識探勘平臺
補助單位： 行政院國家科學委員會
計畫期間： 2009/08/01-2012/07/31

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。

Project title: Sharable Knowledge Mining Platform
Supported by: National Science Council
Project period: 2009/08/-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.





使用Protégé 編輯由GLIF3 所表示之慢性咳嗽之臨床指引

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分子生醫資訊實驗室
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

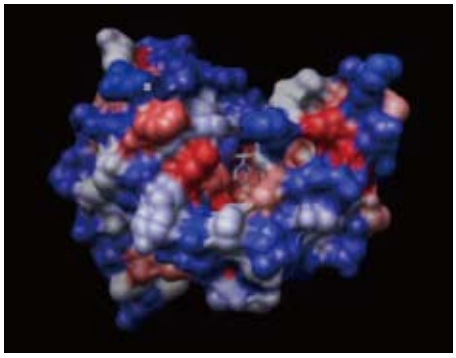
The Molecular Biomedical Informatics (MBI) laboratory focuses on design of advanced machine learning algorithms for systems biology research. During the past few years, the MBI team has proposed three innovative machine learning algorithms and has exploited these algorithms to develop various bioinformatics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

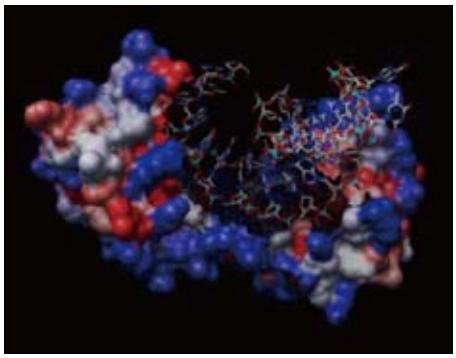
1. HomoClust — construction of protein family hierarchy based on sequence alignment;iPDA — prediction of disorder regions in protein sequences;
2. Proteminer and Protemot — prediction of protein functional sites based on local structural alignment;
3. MEDOCK — emulation of protein-ligand docking;
4. 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.

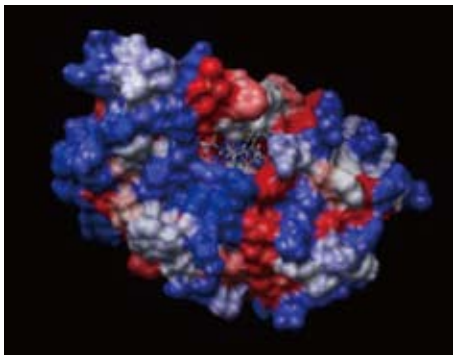
主要研究領域 Major Research Areas

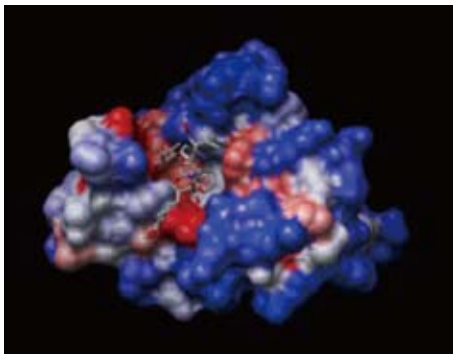
生物資訊學、資料檢索/機器學習
Bioinformatics, Machine Learning

研究計畫 Research Projects









1. 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
2. 計算生物學先導型研究計畫
   Pilot Research Program of Computational Biology

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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Professor, Graduate Institute of Biomedical Electronics and Bioinformatics/ Department of Computer Science and Information Engineering, National Taiwan University

生物資訊實驗室
Bioinformatics Lab.

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

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

計畫名稱：網路生物學整合分析平台之建構與應用
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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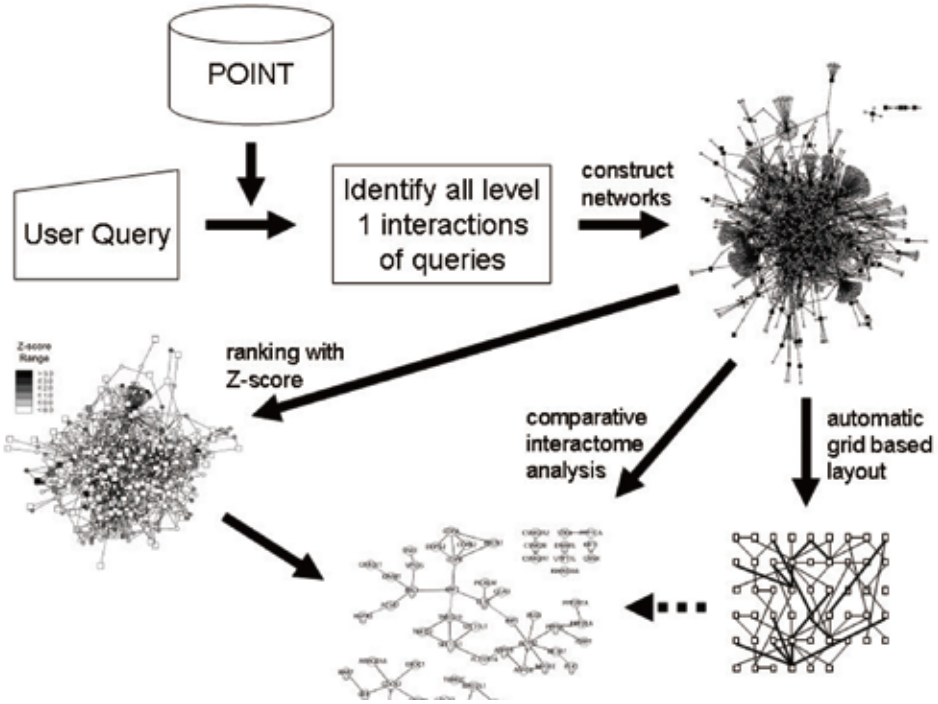
Project title: Construction and Application of Intergrated Network Biology Analysis Platform
Supported by: National Science Council
Project period: 2009/08/0-2011/07/31

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

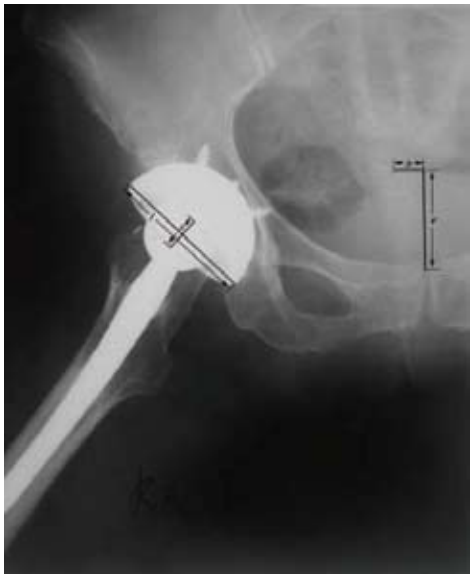
本實驗室由傅楸善教授成立於2003年，主要從事數位相機與電腦視覺相關研究。歷年來已執行多項研究計畫，目前以生醫數位相機、影像處理與自動光學檢測等領域為研究重點。本實驗室在上述領域已產出許多具體貢獻並在全世界有很高之能見度。此外，本實驗室之成員來自電子、資訊及醫學等各領域，多年來亦積極與國內外單位進行合作，合作夥伴包括產、研、學各界，例如：光寶科技、致伸科技、太欣半導體、創惟科技、由田新技、德律科技等。提升數位相機與自動光學檢測技術及其生醫應用，是本實驗室之成立宗旨與具體目標。

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：國科會
計畫期間：2009/08/19-2012/07/31

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: 2009/08/19-2012/07/31

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.

Original Noiseware: 0 votes Our Method :21 votes

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. 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。
2. 乳房彩色彈性超音波之電腦輔助診斷。
3. 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。
4. 乳房磁振造影電腦輔助偵測與功能性評估系統之研發。
5. 家用型雙波段乳癌紅外線診斷系統。
6. 微流體平台進行藥物篩選與化療療效監測。
7. 經前婦女可切除乳癌之CYP19(TTTA)重複多型性研究。
8. 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.
9. 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.
10. 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 HerceptinÒ, 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.

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11. 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
12. 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
13. 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：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：
(1) 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。

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國立台灣大學資訊網路與多媒體研究所 合聘教授

Professor, Graduate Institute of Biomedical Electronics and Bioinformatics/ Department of Computer Science and Information Engineering, National Taiwan University
Adjunct Professor, Graduate Institute of Networking and Multimedia, National Taiwan University

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. 數列分析演算法及其在基因組序列分析上的應用
   Constrained Heaviest Segments in a Number Sequence and Their Applications in Genomic Sequence Analysis

計畫名稱：單一核苷酸多型資訊運用的演算法設計
補助單位：國科會
計畫期間：2005/08/01-2008/07/31

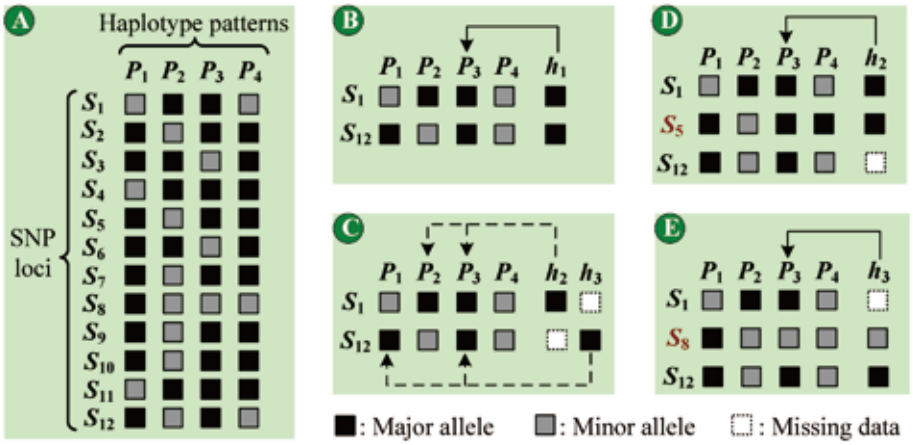
本計畫我們將致力於設計並實作一系列演算法，使得SNP和單套型的資訊運用在關連性研究與連索性分析上，能發揮出最大效益。第一年我們專注於研發從基因型資料推斷單套型資料之相關演算法。第二年我們致力於設計與標籤SNP選擇相關之演算法，以解決目前各種定序實驗上會遭遇的問題。第三年我們研究如何使用基因型和單套型資料，設計出切割單套型區段與標籤SNP選擇之演算法。

本計畫產出一系列與SNP和單套型相關之演算法和軟體。我們以各種數學模型分析所設計的演算法，而且每個提出的演算法都實作出軟體。我們將收集各種模擬資料與實際生物資料，針對每個軟體規劃實驗並加以佐證。我們相信本計畫所提出的方法與開發的軟體，不僅可以提升SNP和單套型資訊在關連性研究與連鎖性分析上之效益，更可以提出一些創新的思維與想法，以解決相關難題。

Project title: Efficient Algorithms for Utilizing SNP information
Supported by: NSC, Taiwan
Project period: 2005/08/01-2008/07/31

In this project, we aim to design and implement algorithms which can improve the power of using SNPs in association studies and linkage analysis. In the first year, we focus on the design and implementation of algorithms for inferring haplotypes data from genotype data. In the second year, we emphasize on solving the problems of tag SNPs selection with poor genotyping quality or genotyping errors. In the third year, we stress on the design and implementation of algorithms for haplotype block partition and tag SNPs selection directly using genotype or haplotype data.

We use different mathematical models to analyze each proposed algorithm. In addition, the proposed algorithms have been implemented and tested on a variety of simulated and biological data. The developed software along with the corresponding experimental results are available to the public. We believe that the results of our studies will not only improve the power of using SNPs in association studies and linkage analysis, but also provide more insights for solving related problems.



失誤資料對單套體辨認的影響。
The influence of missing data when identifying haplotype samples.

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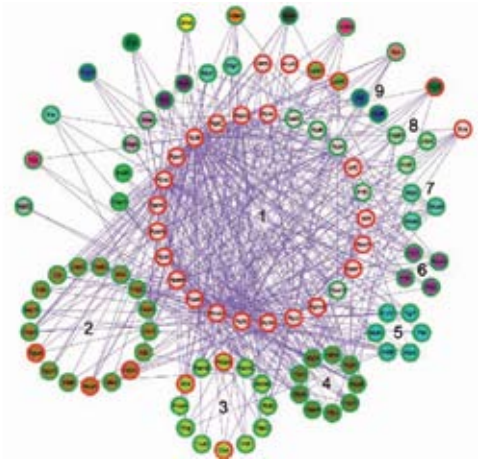
系統生物學研究室
Systems Biology Lab.



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. 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.
2. 以生質能源應用為導向之光合菌Rhodopseudomonas palustris系統與計算生物學研究
   ystems and Computational Biology of Rhodopseudomonas palustris Aimed for Bioenergy Application.
3. 光合菌Rhodopseudomonas palustris 功能性基因體研究
   Functional genomics of Rhodopseudomonas palustris.
4. 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：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
補助單位：基因體醫學國家型計畫 (衛生署)
計畫期間：2009/05/01-2011/04/30

肺癌是世界上造成癌症死亡的頭號殺手，每年約造成130萬人死亡。其五年的總存活率只有15%，而且近幾十年來並沒有改善的跡象。即便是手術治療、放射線療法及化療，病人預後仍相當差，所以找到新的抗肺癌藥物是迫切需要的。系統生物學是生物學中一個新興的研究領域，著重於以系統的觀點來了解生物體的運作。近年來高通量藥物合成、蛋白質體、微陣列及生物資訊技術的發展，促使系統生物學能加快闡明生化路徑、藥物開發與應用於疾病治療的速度。

癌組織標靶治療是加速抗癌治療最有效的方法之一，尋找有效的標靶一例如在不正常的特定區域中大量表現的蛋白質一在癌症治療上是重要的研究主題。先前我們利用系統生物學方法找到新一類的抗癌化合物一ATP合成酶抑制劑，可做為治療乳癌的標靶藥物。除了乳癌之外，我們最近的初步研究發現，ATP合成酶也會在肺癌病人的癌化組織中高度表現；以ATP合成酶抑制劑處理肺癌細胞進行實驗，觀察到肺癌細胞會遭受毒殺，但對正常細胞給予相同劑量時卻無影響。

本計畫主要的目標是利用系統生物學研究法找到抗肺癌藥物並研究以ATP合成酶抑制劑為主的標靶治療及其作用的分子機制。

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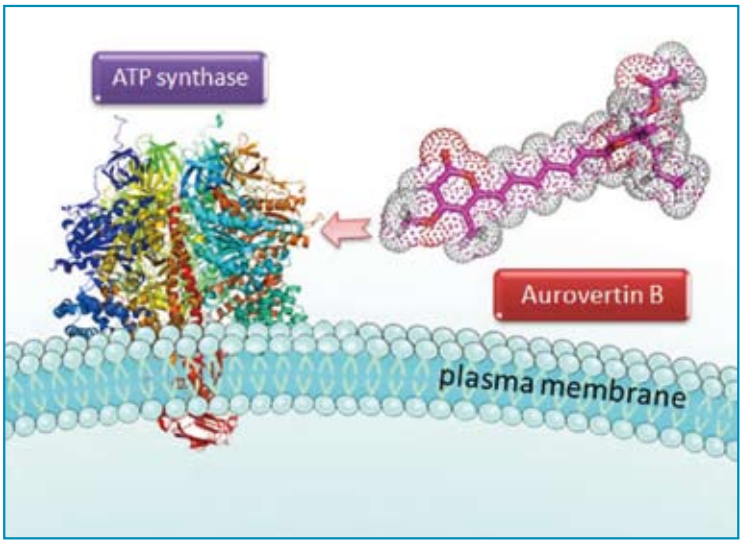
Project title: Applying systems biology for anti-lung cancer drug discovery: targeting therapy by ATP synthase inhibitors and molecular mechanism study
Supported by: National Research Program for Genomics Medicine (National Institute of Health)
Project period: 2009/05/01~2011/04/30

Lung cancer is the most common cause of cancer death in the world and causes 1.3 million deaths per year worldwide. The five-year, overall survival rate is 15% and has not been improved over many decades. Even with improving efficacy of surgical treatment, radiation therapy, and chemotherapy, prognosis for lung cancer patients is still poor. Identification and discovery of novel drugs for lung cancer therapy is therefore imperative. Systems biology is a new field in biology that focuses on understanding functional activities from a system-wide perspective. With the advent of high-throughput drug synthesis, proteomics, transcriptomics and bioinformatics technologies, systems biology has become a viable approach to improve our knowledge of health and disease. This holistic approach will enable more rapid advances in elucidating biomolecular pathways and identifying targets for drug discovery and disease therapies.

Targeting tumor tissues is one of the most powerful approaches to accelerate the efficiency of anticancer treatments. The investigation of effective targets, including proteins specifically and abundantly expressed in abnormal regions, has been one of the most important research topics in cancer therapy. Recently, we have applied systems biology approach on drug discovery for breast cancer and the results suggest that ATP synthase inhibitors may represent a new approach for fighting breast cancer and other cancers. Besides breast cancer, we also observed that ATP synthase was up-regulated in lung tumor tissues. In our preliminary studies, we treated the lung cancer cells with an ATP synthase inhibitor, Aurovertin B, and observed strong inhibition on the proliferation of several lung cancer cell lines but little influence on the normal cell line IMR-90.

The broad and long-term objectives of this proposal are to apply systems biology for anti-lung cancer drug discovery and to study the targeting therapy by ATP synthase inhibitors and their related molecular mechanism.



本圖顯示ATP合成酶抑制劑可與ATP合成酶結合而可做為治療癌症的標靶藥物。

ATP synthase inhibitors can bind to ATP synthase and may represent a new approach for fighting cancer.

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演算法實驗室
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

平面圖之「簡潔編碼」與「簡潔呈現」演算法
動態簡潔資料結構

algorithms for succinct encodings and compact drawings of planar graphs Succinct dynamic data structures

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計畫名稱： 動態簡潔資料結構
補助單位： 國科會
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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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、台大醫院、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：國科會
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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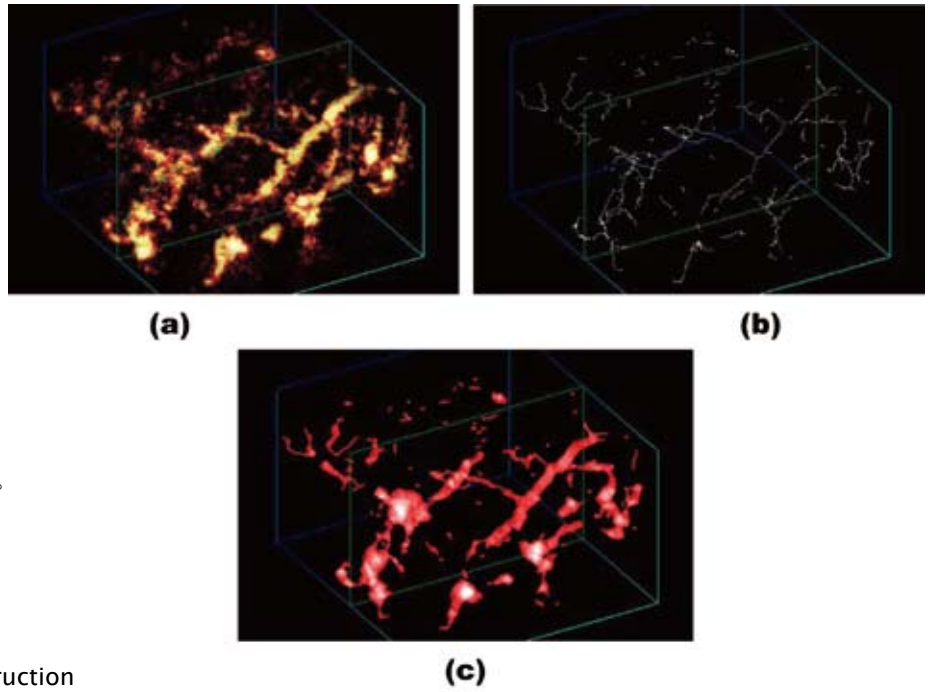
Project title: Computer-aided Diagnosis for 3-D Doppler Breast Ultrasound
Supported by: National Science Council
Project period: 2007/08/01-2010/07/31

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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生物資訊與化學資訊實驗室
Bioinformatics and Cheminformatics 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： 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。

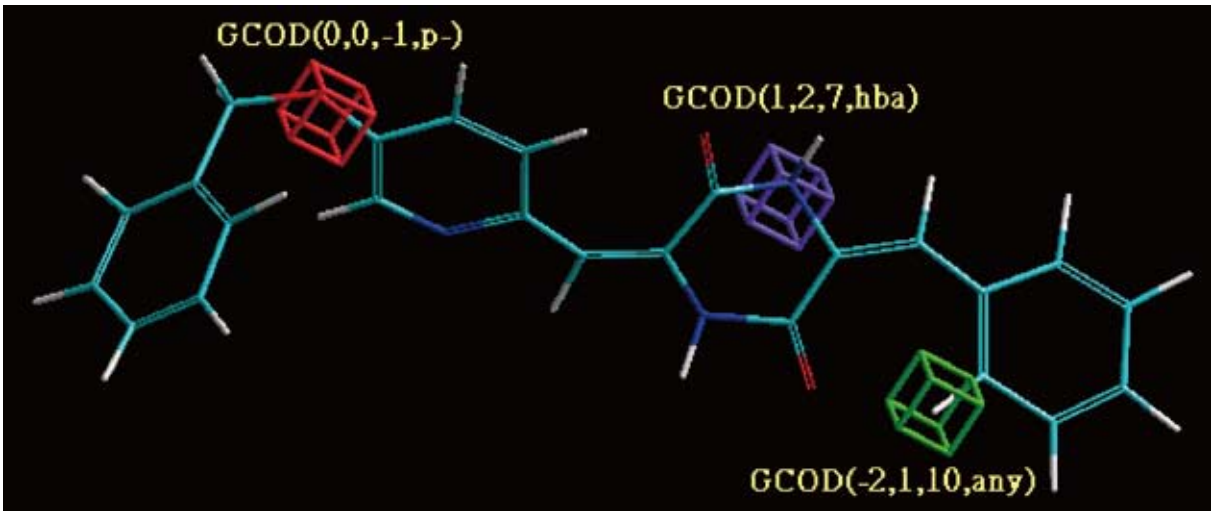
先前在激酶與ATP主要結合區域的基團研究中，結合模式高度地與散佈在蛋白質基酶ATP結合區域的疏水和芳香族基團有關，從4D-QSAR的基團模型與文獻推論，我們判斷ATP結合區域是TW01類似物最有可能的標的。

Project title: In silico platform for anti-angiogenesis screening
Supported by: NSC
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.

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