中央研究院 應用科學研究中心

Research Center for Applied Sciences Academia Sinica

目　　錄

中研院應用科學研究中心介紹

中央研究院 應用科學研究中心

任　　務

運用最尖端、新穎的科技成果，進行跨領域的基礎科學與應用研究，以期達到在地影響力及國際卓越。

應用科學研究中心包含四大專題中心：智慧生物工程、綠色科技、量子光電及量子電腦。

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101/12/03	國立東華大學物理學系
101/07/31	以色列耶路撒冷希伯來大學 (The Hebrew University of Jerusalem)
102/01/24	國立台灣大學分子生醫影像中心
102/08/14	國立中山大學光電系 / 材光系 / 物理系 / 機電系
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103/02/18	國立陽明大學生物醫學暨工程學院
103/12/22	日本北海道大學電子科學研究所
103/07/17	國立台灣大學應用物理研究所暨物理學系
104/05/01	國立成功大學光電科學與工程學系
105/08/26	國立清華大學材料科學工程學系
109/03/25	國立台東大學應用科學系
109/07/27	東京大學工學院
109/08/01	Abbe Center of Photonics, Friedrich Schiller University Jena
110/01/01	Leibniz – Institut für Photonische Technologien e. V.

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- 國立陽明交通大學 光電學院
- 國立陽明交通大學 材料科學與工程學系
- 國立陽明交通大學 生物科技學院
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Prof. Jackie Y. Ying

A*STAR Senior Fellow, NanoBio Lab, Institute of Materials Research and Engineering, Agency for Science, Technology and Research, Singapore

新加坡科技研究局材料學與工程研究所

*Sorted by alphabetical order

智慧生物工程專題中心

智慧生物工程專題中心的任務是運用本中心在基礎領域已開發之新穎感測、影像分析及製造技術來解決生物醫學的重要議題，尤其聚焦在具有高影響力之臨床應用且具有產業價值的主題。智慧生物工程專題中心由十一位研究員組成，成員包含執行長陳培菱博士、魏培坤博士、鄭郅言博士、楊富量博士、李超煌博士、林榮信博士、薛景中博士、董奕錘博士、郭志禹博士、陳壁彰博士和林鈺容博士，以及兩位研究技師，謝東翰博士和謝書宜博士。本專題中心與中央研究院生命科學組及台灣各大學醫學院皆有密切的合作關係。

智慧生物工程專題中心的主要研究領域包括 1）開發超高解析度顯微鏡和光譜工具，用以研究細胞和細胞及細胞與其微環境之交互作用。並結合化學、物理、力學和遺傳學等方法進行分析；2）製造用於藥物傳遞或標記的奈米生物感測器和奈米粒子；以及 3）利用機械學習及人工智慧來計算生物分子交互作用和模擬生物醫學上重要之作用機制。

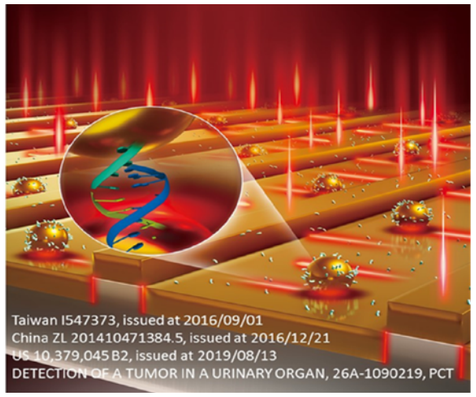
智慧生物工程專題中心在過去幾年中取得了顯著的成果。在影像和感測領域，成功建立了層光膨脹顯微鏡，使其達到電子顯微鏡的解析度相。我們也使用簇離子束和二次離子質譜來研究有機 - 無機複合物質。此外，本專題中心建立了利用細胞牽引力的高速藥物篩選平台。我們亦開發了一種利用表面電漿共振（SPR）的數位奈米等離子體測量（DiNM）方法，在無需標記的情況下，能靈敏地檢測生物分子。我們還利用三維細胞共培養系統測試抗纖維化藥物與抗癌藥物對肺癌細胞與癌關聯纖維母細胞的交互作用，並找到纖維母細胞內四個可能被抗纖維化藥物 nintedanib 抑制的基因。

我們在人工智慧整合方面也取得了重大的進展。我們的「AI 演繹法非侵入式血糖機」獲頒國家新創獎。此外，我們發展了一套全原子圖像生物分子系統的標準自由能計算方法，此計算方法是利用統計力學進行推導，而且已應用在多個蛋白質與蛋白質、蛋白質與胜肽、蛋白質與小分子的交互作用系統中。我們還成功地結合機器學習與拉曼光譜影像分析以應用於毒品檢測。為了幫助開發用於農藥分子的生物醫學感測器，我們合成了各種寡胜肽片段和複合金屬奈米結構。

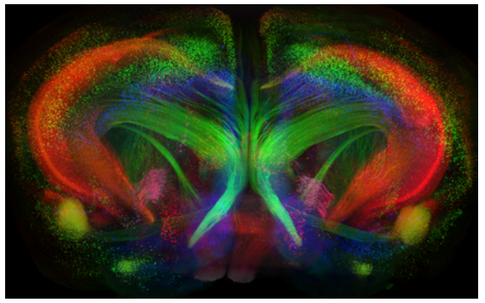
最後，在藥物傳遞領域的部分，我們近期開發了冷模擬物質與熱模擬物質的遞送系統。以薄荷醇做為冷模擬物質，能夠於可溶性水膠中緩慢釋放並誘導脂肪細胞棕化，具有治療肥胖和相關代謝性疾病的潛力。本專題中心還建立了以微流體技術為基礎的體外細胞培養模型，以在更接近體內微環境的條件下研究血管形成過程，如血管生成和血管新生。

為了鼓勵研究員之間的合作，智慧生物工程專題中心在過去幾年提供種子基金資助由幾個實驗室組成之研究團隊從事整合實驗，並利用初步實驗結果申請中央研究院和國科會的大型計畫。在此種子基金的資助下，專題中心已成功申請到多項整合計畫包括奈米細胞力感測器的藥物篩選平台，診斷用的微型核糖核酸檢測系統，以及細胞記憶裝置。此外，我們也進行幾個空間生物學的新研究議題，如使用大樣品膨脹顯微鏡的開發、單細胞分析系統以及使用聚焦離子束掃描電子顯微鏡（FIB/SEM）的 3D 細胞影像。目前，智慧生物工程專題中心正在執行兩個重要整合計畫。在第一個計畫中，我們專注於創建高效藥物開發平台。這個平台包括智慧運算、高效化學合成、數位生物感測以及用於藥物測試的病人衍生類器官模型。在個性化醫療迅速獲得關注的時代，這個計畫既及時又重要。雲端運算和人工智慧的整合可以加速藥物開發，也許能使患者更快地獲得新療法。專題中心的第二個重點議題為建構新型顯微術，提升光學顯微鏡的空間解析度，使其媲美電子顯微鏡，同時保有其化學資訊與 3D 成像能力。這項努力可能會徹底改變我們對生物結構如突觸的理解，例如神經學及相關領域的重點議題 - 突觸，透過提高光學顯微鏡的解析度和能力，我們可以對突觸連結進行更全面的研究，進而更加了解大腦中的訊息傳遞。

Detection of Urinary MiRNA Biomarkers



We have developed a low-cost, high-sensitivity, high-specificity, and multiplex microfluidic nanoplasmonic optical sensing technology for a universal molecular diagnostic testing platform.



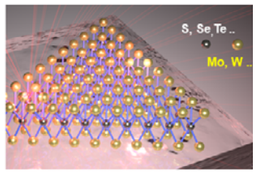
Cleared Thy1-eYFP mouse brain imaged by lightsheet microscopy

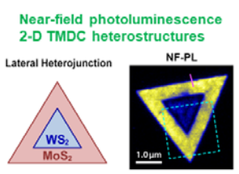
本專題中心的研究目標，旨在探索創新的製造技術與新穎材料，用以加速次世代能源科技的開發與應用，促進更好生活環境和產業技術。主要研究方向包括：（1）節能與產能元件，（2）固態鋰離子電池，（3）先進材料模擬計算。目前專題中心擁有 6 位主要研究者（PIs）：張允崇、程育人、朱治偉、包淳偉、呂宥蓉和方牧懷。

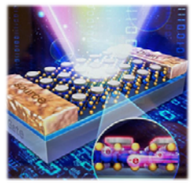
焦點研究計畫

本專題中心內，現共有兩個焦點研究計畫正在執行與開發中：

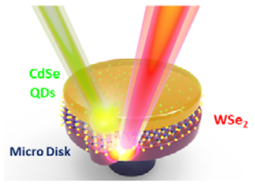
第一個焦點研究方向是利用高品質的二維材料來研發超薄、高效光電元件及系統。過去幾年我們已在應科中心建立及發展用先進磊晶技術來成長高質、晶圓尺度之二維材料，例如石墨烯、二維過渡金屬硫化物（TMDC）及其相關異質結構。除了對新穎二維半導體材料特性的基礎研究外，中心的研究人員同時利用二維半導體材料來發展的下世代奈米光電元件，如 發光二極管（LED）、雷射和光電晶體等重要元件。





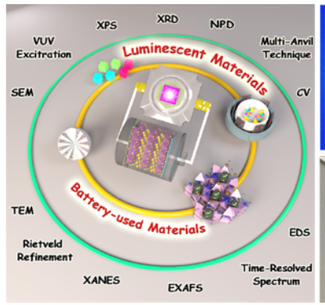


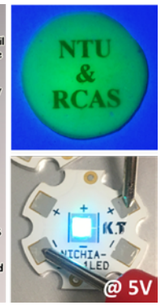
2-D MoS_2 phototransistor with ultrahigh photoresponsivity



Multi-color microcavity laser with 2-D WSe_2 and QDs

第二個焦點研究項目是開發電池用材料與發光材料。應用科學研究中心的研究員們，專注於新穎鈣鈦礦材料的開發，並應用於固態電池、可撓性太陽能電池，以及發光二極體。

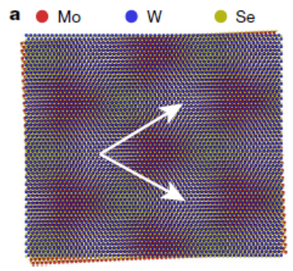


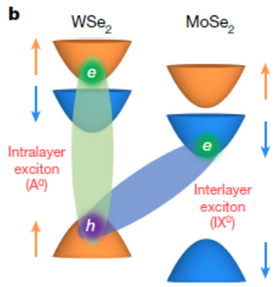


研究成果

WSe2/MoSe2 異質雙分子層中莫瑞三元子的特徵 (*Nature* 594, 46–50 (2021))

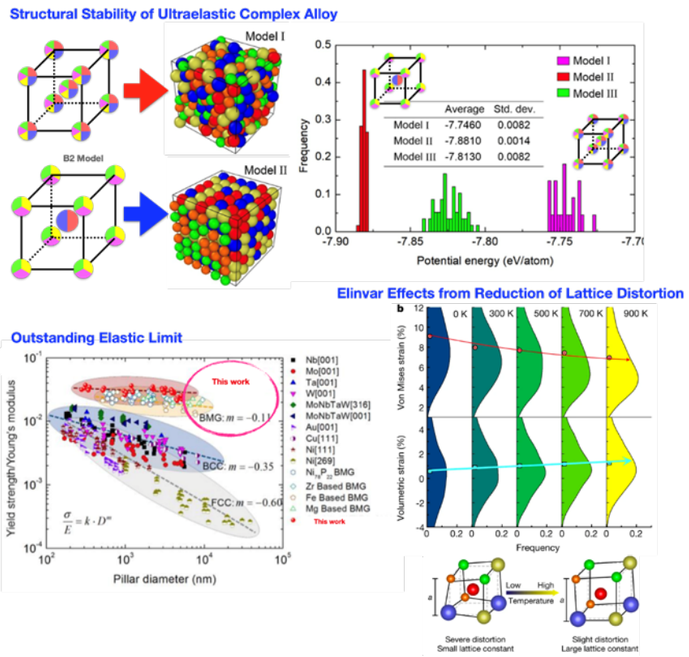
在此工作中，我們研究二維過渡金屬硫化物（TMDC）原子層中莫瑞（Moire）超晶格的三重激子（Trion）和莫瑞電子位能之間的強耦合效應。這些發現將在未來探索光電物理多體現象和下世代量子元件發展中有重要的貢獻。





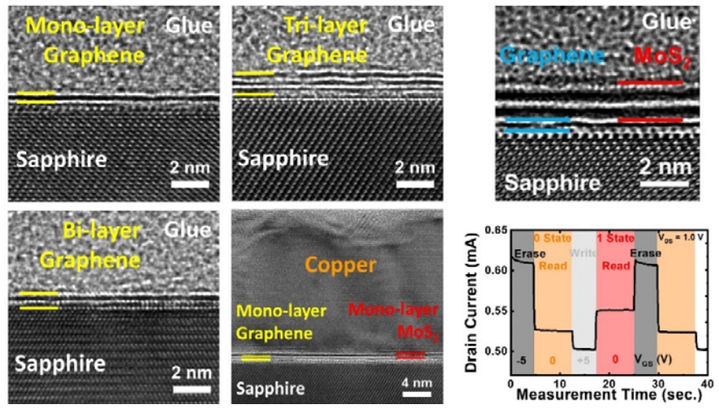
高熵下微觀序列的新可能：超彈性高熵 Elinvar 合金（Nature 602，251-257 (2022)）

通過進行一系列的大規模密度泛函理論計算，我們成功揭示了 Co25Ni25(HfTiZr)50 化學複雜合金的原子結構。藉由巧妙的原子位點安排使得晶體結構能在高達 11% 的原子尺寸差異下保持穩定。我們的原子模擬顯示，巨大的原子尺寸差異引起的強烈晶格變形（9%）是這種複雜合金出色的彈性極限以及 Elinvar 效應的原因。



二維材料在次世代記憶體元件的應用

透過重複的化學氣相沉積成長技術，我們可以在藍寶石基板上達成大面積且均勻的逐層石墨烯成長，使用單層二硫化鉬 / 單層石墨烯作為新穎的襯墊層 / 阻障層的組合，奈米等級的銅薄膜可達到文獻中最低的電阻值。使用二硫化鉬作為電荷儲存層以及石墨烯作為電荷傳輸層，我們以頂閘極電晶體的元件架構製作出第一個全二維材料記憶體元件，該元件展現出超長的電荷儲存時間以及高操作週期可應用於次世代的小線寬記憶體。



本專題中心的研究目標，旨在建造一台超導量子電腦，藉此不僅是可以研究開發量子電腦的硬體架構，也可以提供研究者共同開發優化量子閘之控制機制及提供使用者測試演算法。我們著力於超導量子位元晶片之設計與製作，並持續精進控制與讀取位元的機制，也與合作者開發系統架構朝向雲端服務的目標邁進。專題中心一直都在招募國內外研究者加入團隊，共同為建構超導量子電腦努力。

焦點研究計畫

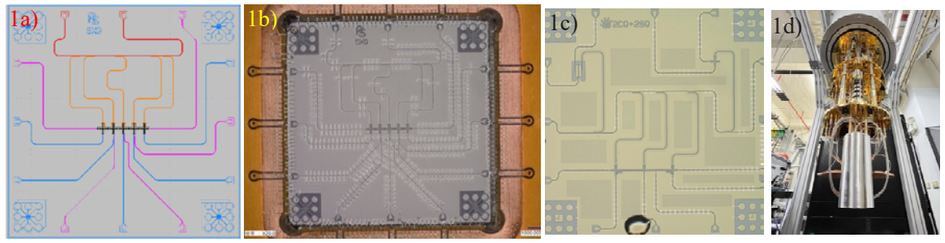
為了建構超導量子電腦，我們有幾項工作焦點：

1. 晶片設計：提供最佳的量子位元控制與讀取線路與連結特性，並降低受電磁輻射的影響
2. 晶片製作：開發精準控制參數、高良率的製程，製作高品質的晶片
3. 系統架構：提供低溫、無電磁波干擾的環境。建構控制系統與程式與高階使用者介面

研究成果

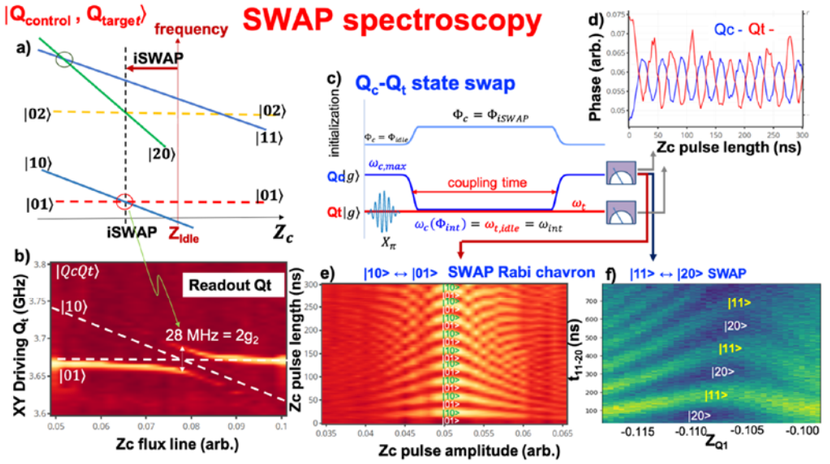
A. **晶片設計**：在持續的微調下，我們會根據量子位元操作之理論與實際系統提出一整套晶片元件的參數，並根據先前的晶片測試結果搭配數值模擬畫出實際晶片的設計圖。我們設計普賽爾過濾器，具有頻率可調耦合位元的雙位元線路（圖 1c），對稱及不對稱、懸浮及一端接地的各種量子位元（圖 1c），也設計各種排列的 5 個頻率可調量子位元的線路（圖 1a）。

B. **晶片製程**：我們採用了全電子束的製程技術，避開了需要處理量子位元下電極與上電極接觸所帶來的複雜影響，目前以這種技術製作出來的量子位元的 T1 時間可以高於 26us（圖 1b），這一品質容許我們快速測試各種新的設計線路。我們同時也與工研院共同開發以鉭作為電容板底電極的量子位元以及空橋的技術（圖 1c）。

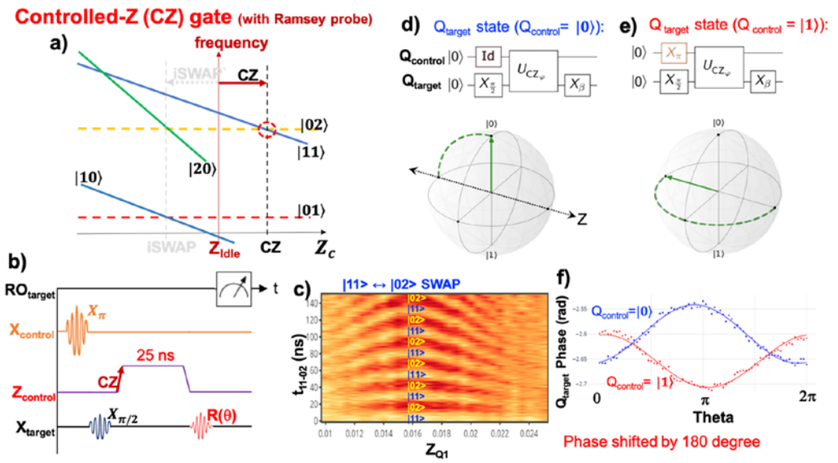


圖一：圖 1a, 一維排列的 5Q 線路設計圖，橘色線為讀取共振腔，藍色線為 Z-gate, 紫紅色線為 XY-gate, 紅色線為讀取線。圖 1b, 製作完成並打線於晶片座 PCB 板的晶片。晶片是以鋁結構製作在矽基板上，並以全電子束曝光製程完成。鋁的打線接合是用以消弭槽線模態，也降低位元間的 XY 及 Z 的串擾。圖 1c, 具有頻率可調的耦合位元的雙位元線路（位於晶片下半部），左上及右上分別為懸浮及一端接地的量子位元。這晶片也有橋底為氧化矽的鋁製空橋。圖 1d. 一個 mu-metal 桶柱樣品座掛在稀釋冷凍機的 10mK 盤上。

C. **系統架構**：晶片盒的光屏蔽、磁場隔離以及位元低溫環境都是得到高邏輯閘保真度的重要因素，為此，我們持續改善晶片盒也同時測試廠商提供的解決方案。另外，我們也開發實驗室的量測程式與數據處理系統，並與控制儀器廠商合作開發進階的量測與使用者介面。



圖二：圖 2a, 直接耦合的控制位元 (control qubit) 與目標位元 (target qubit) 對控制位元 Z-gate (Zc) 的反應。在去除串擾後，目標位元對 Zc 是沒有反應的，因此可以讓控制位元的頻率在一些 Zc 值下與目標位元對齊，並引發兩個位元的耦合。圖 2b, 在 |10⟩ 與 |01⟩ 的交點可以觀測到 coupling 強度是 14MHz. 在這一交點我們可以執行 |10⟩ 與 |01⟩ 的狀態交換 (見圖 2e)。圖 2c 顯示執行的執行方法，在耦合的時間內使用 z-gate 將兩個位元的頻率調到一致，在這段期間兩個位元的狀態交換的速率由耦合強度決定 (見圖 2d)。圖 2f 是在 |11⟩ 與 |20⟩ 的交點觀測到的兩個位元態的交換行為。

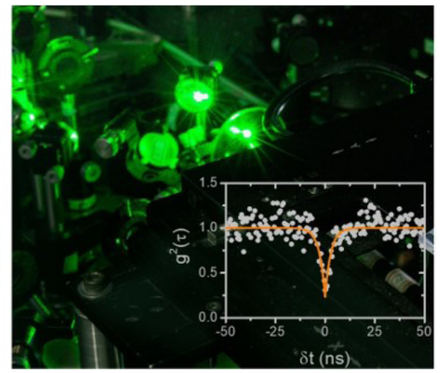


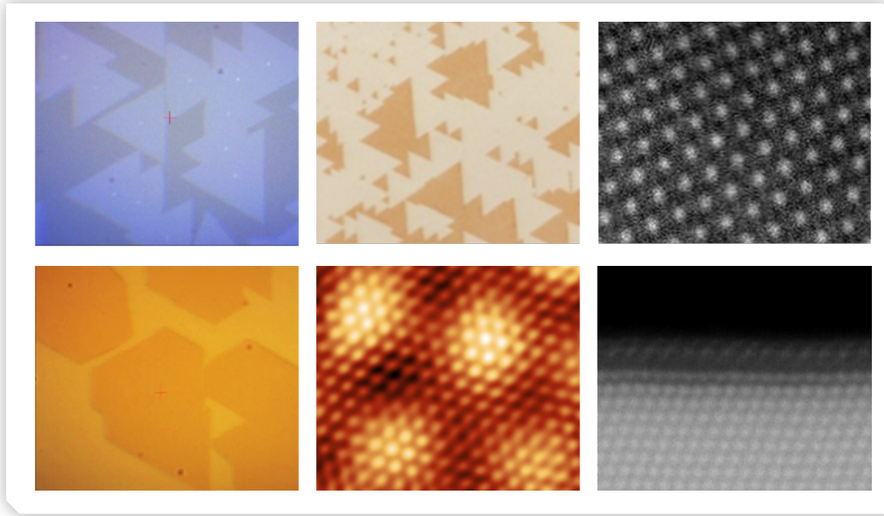
圖三：圖 3a, 同圖 2a 的操作，但將操作點移到 |11⟩ 與 |02⟩ 的交點，可以進行 CZ 閘的運作。圖 3b，CZ 的操作程序就是將控制位元的頻率拉靠近目標位元，可以隨者控制位元的狀態決定目標位元的改變，這兩個位元的角色也可以互換。圖 3c, 在操作點可以觀察到 |11⟩ 與 |02⟩ 的狀態交換。控制位元可以至於基態（圖 3d）或激發態（圖 3e），在 CZ 操作時就會引發目標位元不同的相位角轉換，因而達到控制雙位元相對相位的目的。圖 3f，在適當的操作時間（例如 25ns）可以讓兩者的相位差達到 180 度。

量子光電專題中心

量子光電專題中心主要目標在於發展應用於光量子技術的關鍵材料與元件。本專題中心整合應科中心原有的研究強項，包含材料生長、光譜量測、元件製程以及理論分析，同時亦與國內外先進研究團隊建立合作，藉此槓桿先進技術以期突破應用於光量子技術之材料與元件的技術瓶頸。

本專題中心之中長期目標是發展新材料與元件技術，開發量子光源、單光子偵測器以及光量子晶片。我們期許未來可以在光量子運算與量子通訊應用達成重要的技術突破。





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| 研究人員 |

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研究重點

The Applications of Real-time Intravital Imaging

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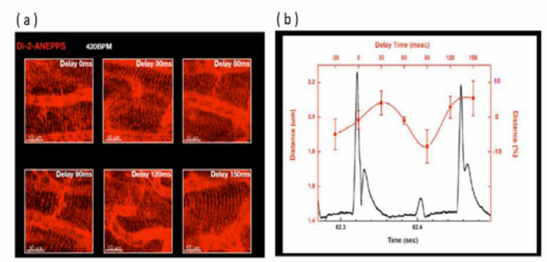
Academic Sinica, Research Center for Applied Sciences

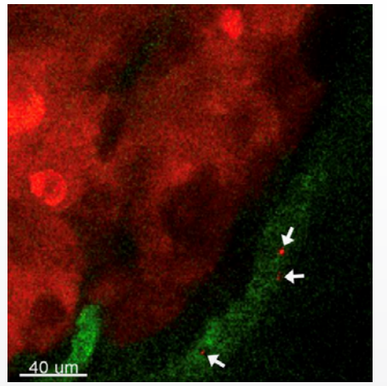
- Frontiers in Bioengineering and Biotechnology, 2022, **10**, 935415
- Circulation, 2022, **146**, 1950
- Science Advances, 2021, **7**, eabf2400
- Circulation, 2019, **139**, 647
- Science Translational Medicine 2016, 8, 365ra160
- J. Nanobiotech 2019, **17**, 26
- J. Clin. Invest. 2021, 131, e130704
- PNAS, 2023, **12**, e2207091120

In our group, we have developed real-time intravital imaging for various disease models. Since the heart diseases and cancers are the top two leading causes of death in United State and Taiwan. We focus on the applications of real-time intravital imaging for these two disease models. In the heart disease model, the beating rate of mouse is about 6-8 Hz, which is about 6 times faster than human heartbeat. If we utilize two-photon microscope with a resonance scanner running at 30 Hz to image the beating heart in a living mouse, we will still get very blurry images. To minimize the influence of heart beating, we synchronized the scanner of confocal microscope to the beating heart. When the imaging system was synchronized with heartbeat, it allowed us to conduct detail analysis of individual cellular behavior in the blood vessels on the beating heart.



(a) a section of the image from different time delay corresponding to a specific portion of the ECG cycle (b) the plot diagram of time delay and Sarcomere lenght displacement in one complete cardiac cycle

In the case of tumor imaging, we are interested in the real-time imaging of the circulating tumor cells (CTCs). The detection of circulating tumor cells (CTCs) is very important for cancer diagnosis. CTCs can travel from primary tumors through the circulation to form secondary tumor colonies via bloodstream extravasation. The number of CTCs has been used as an indicator of cancer progress. However, the population of CTCs is very heterogeneous. It is very challenging to identify CTC subpopulations such as cancer stem cells (CSCs) with high metastatic potential, which are very important for cancer diagnostic management.



CTCs (red cells indicated by arrows) in the blood vessel near solid tumor expressing red fluorescent protein (RFP). The blood vessels (green) were stained with fluorescein isothiocyanate (FITC)-dextran. Tumor cells: BXPC3-RFP.

We developed real-time CTC and CSC imaging in the bloodstreams of living animals using multi-photon microscopy and antibody conjugated quantum dots. When the cancer cells broke away from the solid tumor, CTCs with fluorescent proteins in the bloodstream at different stages of development could be monitored noninvasively in real time. The number of CTCs observed in the blood vessels could be correlated to the tumor size in the first month and reached a maximum value of approximately 100 CTCs/min after five weeks of tumor inoculation. To observe CTC subpopulations, conjugated quantum dots were used. It was found that cluster of differentiation (CD)24+ CTCs can move along the blood vessel walls and migrate to peripheral tissues.

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5. Sheng-Hann Wang; Chia-Wen Kuo; Shu-Cheng Lo; Wing Kiu Yeung; Ting-Wei Chang; Pei-Kuen Wei*, "Spectral Image Contrast-Based Flow Digital Nanoplasmon-metry for Ultrasensitive Antibody Detection", Journal of Nanobiotechnology. 2 20, 6 (2022)
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研究重點

Spectral Image Contrast-Based Flow Digital Nanoplasmon-metry for Ultrasensitive Antibody Detection

Sheng-Hann Wang; Chia-Wen Kuo; Shu-Cheng Lo; Wing Kiu Yeung; Ting-Wei Chang; Pei-Kuen Wei

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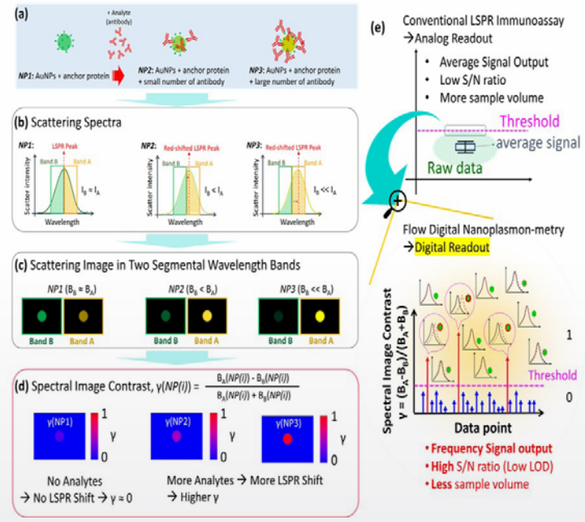
Journal of Nanobiotechnology 2022, DOI:10.1186/s12951-021-01188-6

Gold nanoparticles (AuNPs) have been widely used in local surface plasmon resonance (LSPR) immunoassays for biomolecule sensing, which is primarily based on two conventional methods: absorption spectra analysis and colorimetry. In this work, we developed a new spectral image contrast-based flow digital nanoplasmon-metry (Flow DiNM) to push the detection limit. Comparing the scattering image brightness of AuNPs in two neighboring wavelength bands near the LSPR peak, the peak shift signal is strongly amplified and quickly detected. Introducing digital analysis, the Flow DiNM provides an ultrahigh signal-to-noise ratio and has a lower sample volume requirement. Compared to the conventional analog LSPR immunoassay, Flow DiNM for anti-BSA detection in pure samples has an LOD as low as 1 pg mL-1 within only a 15-min detection time and 500 μL sample volume.



Sensitive Oligonucleotide Detection Using Resonant Coupling between Fano Resonance and Image Dipoles of Gold Nanoparticles

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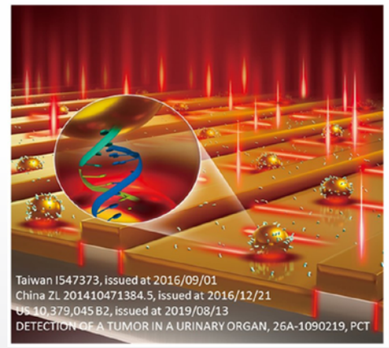
ACS Applied Materials & Interfaces 2022, DOI: 10.1021/acsami.1c21936

The surface plasmon resonance (SPR)-based sensor has been widely used for biodetection. One of the attractive roles is the gold nanostructure with Fano resonance. Its sharp resonant profile takes advantage of the high figure of merit (FoM) in high-sensitivity detection. However, it is still difficult to detect small molecules at low concentrations due to the extremely low refractive index changes on the metallic surface. We propose using the coupling of image dipoles of gold nanoparticles (AuNPs) and Fano resonance of periodic capped gold nanoslits (CGNs) for sensitive small-molecule detections. The 50 nm AuNPs can be detected with a surface density of less than one particle/μm2. With the resonant coupling between Fano resonance and image dipole extinction, the oligonucleotide with a molecular weight of 5.5 kDa can be detected at a concentration of 100 fM. The resonant coupling dramatically pushes the sensitivity boundary, and we report the limit of detection (LOD) to be 3 orders of magnitude lower than that of the prism-based SPR.



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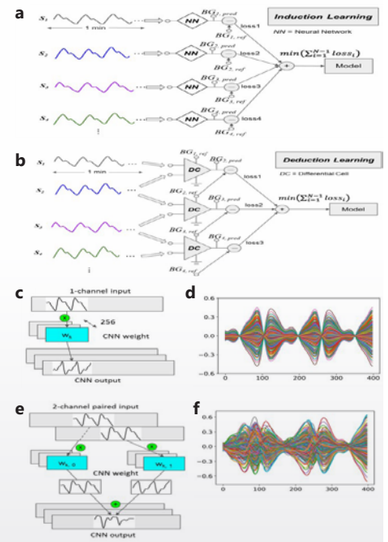
代表著作

1. Wei-Ru Lu, Wen-Tse Yang, Justin Chu, Tung-Han Hsieh & Fu-Liang Yang *. **"Deduction learning for precise noninvasive measurements of blood glucose with a dozen rounds of data for model training"** Scientific Reports volume 12, Article number: 6506 (2022), https://doi.org/10.1038/s41598-022-10360-3
2. Chu, J.; Yang, W.-T.; Lu, W.-R.; Chang, Y.-T.; Hsieh, T.-H.; Yang, F.-L*. **"90% Accuracy for Photoplethysmography-Based Non-Invasive Blood Glucose Prediction by Deep Learning with Cohort Arrangement and Quarterly Measured HbA1c."** Sensors 2021, 21, 7815. https://doi.org/10.3390/s21237815
3. Justin Chu, Wen-Tse Yang, Yao-Ting Chang* and Fu-Liang Yang* **"Visual Reassessment with Flux Interval Plot Configuration after Automatic Classification for Accurate Atrial Fibrillation Detection by Photoplethysmography"** Diagnostics 2022, 12, 1304. https:// doi.org/10.3390/diagnostics12061304
4. Justin Chu, Wen-Tse Yang, Tung-Han Hsieh, Fu-Liang Yang*, Feb. 2021 **"One-Minute Finger Pulsation Measurement for Diabetes Rapid Screening with 1.3% to 13% False-Negative Prediction Rate"** Biomedical Statistics and Informatics 2021; 6(1): 6-13, DOI: 10.11648/j.bsi.20210601.12
5. Bitewulign Kassa Mekonnen, Webb Yang, Tung-Han Hsieh, Shien-Kuei Liaw, and Fu-Liang Yang*, May. 2020 **"Accurate Prediction of Glucose Concentration and Identification of Major Contributing Features from Hardly Distinguishable Near-Infrared Spectroscopy"** Biomedical Signal Processing and Control, Volume 59. DOI: 10.1016/j.bspc.2020.101923
6. Bitewulign Kassa Mekonnen, Tung-Han Hsieh, Dian-Fu Tsai, Shien-Kuei Liaw, Fu-Liang Yang and Sheng-Lung Huang, **"Generation of Augmented Capillary Network Optical Coherence Tomography Image Data of Human Skin for Deep Learning and Capillary Segmentation"** Diagnostics 2021. 11(4), 685; https://doi.org/10.3390/diagnostics11040685
7. Yann-Wen Lan1*, Po-Chun Chen, Yun-Yan Lin, Ming-Yang Li, Lain-Jong Li, Yu-Ling Tu, **Fu-Liang Yang**, Min-Cheng Chen, Kai-Shin Li, Jan. 2019 **"Scalable fabrication of a complementary logic inverter based on MoS2 fin-shaped field effect transistors"** Nanoscale Horizons, DOI: 10.1039/C8NH00419F
8. I-Fang Cheng, Hsien-Chang Chang, Tzu-Ying Chen, Chenming Hu, **Fu-Liang Yang**, Aug. 2013, **"Rapid (<5min) Identification of Pathogen in Human Blood by Electrokinetic Concentration and Surface-Enhanced Raman Spectroscopy"**, Scientific Reports, 2365(3),1-8. DOI: 10.1038/srep02365(SCI) (IF: 2.927; SCI ranking: 15.1%)

研究重點

Deduction learning for precise noninvasive measurements of blood glucose with a dozen rounds of data for model training

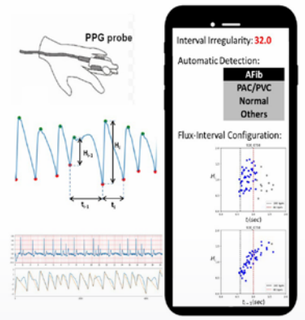
Wei-Ru Lu, Wen-TseYang, Justin Chu, Tung-Han Hsieh, and Fu-LiangYang*



Personalized modeling has long been anticipated to approach precise noninvasive blood glucose (NIBG) measurements, but challenged by limited data for training personal model and its unavoidable outlier predictions. We recently significantly enhanced the training efficiency with the limited personal data by an innovative Deduction Learning (DL), instead of the conventional Induction Learning (IL). DL method involves the use of paired adjacent rounds of finger pulsation Photoplethysmography (PPG) signal recordings as the input to a convolutional-neural-network (CNN) based deep learning model. Our study reveals that CNN filters of DL model generated extra and non-uniform feature patterns than that of IL models. The DL model achieved 80% of test prediction in zone A of Clarke Error Grid (CEG) for model training with 12 rounds of data, which was 20% improvement over IL method. With only a dozen rounds of training data, DL with automatic screening achieved a correlation coefficient (R_P) of 0.81, an accuracy score (R_A) of 93.5, a root mean squared error (RMSE) of 13.93 mg/dl, a mean absolute error (MAE) of 12.07 mg/dl, and 100% predictions in zone A of CEG. The nonparametric Wilcoxon paired test on R_A for DL versus IL revealed near significant difference with p-value 0.06. These significant improvements indicate that a very simple and precise noninvasive measurement of blood glucose concentration is achievable.

Visual Reassessment with Flux-Interval Plot Configuration after Automatic Classification for Accurate Atrial Fibrillation Detection by Photoplethysmography

Justin Chu, Wen-Tse Yang, Yao-Ting Chang*, and Fu-Liang Yang*



Atrial fibrillation (AFib) is a common type of arrhythmia that is often clinically asymptomatic, which increases the risk of stroke significantly but can be prevented with anticoagulation. The photoplethysmogram (PPG) has recently attracted a lot of attention as a surrogate for electrocardiography (ECG) on atrial fibrillation (AFib) detection, with its out-of-hospital usability for rapid screening or long-term monitoring. Previous studies on AFib detection via PPG signals have achieved good results, but were short of intuitive criteria like ECG p-wave absence or not, especially while using interval randomness to detect AFib suffering from conjunction with premature contractions (PAC/PVC). In this study, we newly developed a PPG flux (pulse amplitude) and interval plots-based methodology, simply comprising an irregularity index threshold of 20 and regression error threshold of 0.06 for the precise automatic detection of AFib. The proposed method with automated detection on AFib shows a combined sensitivity, specificity, accuracy, and precision of 1, 0.995, 0.995, and 0.952 across the 460 samples. Furthermore, the flux-interval plot configuration also acts as a very intuitive tool for visual reassessment to confirm the automatic detection of AFib by its distinctive plot pattern compared to other cardiac rhythms. The study demonstrated that exclusive 2 false-positive cases could be corrected after the reassessment. With the methodology's background theory well established, the detection process automated and visualized, and the PPG sensors already extensively used, this technology is very user-friendly and convincing for promoted to in-house AFib diagnostics.

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學歷 | 國立臺灣大學化學系博士（1998）

經　歷

2023- 中央研究院應用科學研究中心副主任
2021-2022 中央研究院應用科學研究生醫應用專題中心執行長
2015-2020 中央研究院應用科學研究中心力學專題中心執行長
2013- 中央研究院應用科學研究中心 研究員
2007- 國立陽明大學兼任
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2006- 國立海洋大學兼任
2001 中央研究院應用科學工程所籌備處助研究員
1998 中央研究院生物醫學研究所 博士後研究員

專長及研究重點

- Cell-based micro analysis: cell responses in weak DC EF, cell-cell interaction co-culture chip, cellular chemotaxis, electrotaxis and metastasis, affinity binding and separation.
- Microfluidic biochip and their applications in biosensing.
- Microarray technologies: flexible in- situ array synthesis, rapid hybridization, mRNA labeling chip, and portable DNA amplification chip.

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1. Huang, W.-C., Wei, C.-D., Belkin, S., Hsieh, T.-H. and Cheng, J.-Y. (2022) Machine-learning assisted antibiotic detection and categorization using a bacterial sensor array. Sensors and Actuators B: Chemical, 355, 131257.
2. Chien, T.Y., Marin-Benavides, R., Belkin, S. and Cheng, J.Y. (2022) Rapid printing of a Bacterial array for a Solid-Phase Assay (BacSPA) of heavy metal ions. Sensor Actuat B-Chem, 359.
3. Chou, S.E., Lee, K.L., Wei, P.K. and Cheng, J.Y. (2021) Screening anti-metastasis drugs by cell adhesion-induced color change in a biochip. Lab Chip, 21, 2955-2970.
4. Chang, H.F., Chou, S.E. and Cheng, J.Y. (2021) Electric-Field-Induced Neural Precursor Cell Differentiation in Microfluidic Devices. Jove-J Vis Exp.
5. Yeung, W.K., Li, H.-F., Chung, C.-L., Lee, K.-L., Wei, P.-K., Lin, H., Chen, H.-H. and Cheng, J.-Y. (2020) Promising urinary miRNA biomarkers t-SPR profiling for urothelial cell carcinoma. Sensors and Actuators B: Chemical, 322, 128605.
6. Chang, H.-F., Yeung, W.K., Kao, W.-C., Ehrhardt, M., Zimmer, K. and Cheng, J.-Y. (2020) Surface micromachining on a polymethylmethacrylate substrate using visible laser-induced backside wet etching with a KMnO4 solution as an absorber. Journal of Laser Applications, 32, 022014.
7. Lu, M.Y., Kao, W.C., Belkin, S. and Cheng, J.Y. (2019) A Smartphone-Based Whole-Cell Array Sensor for Detection of Antibiotics in Milk. Sensors-Basel, 19.
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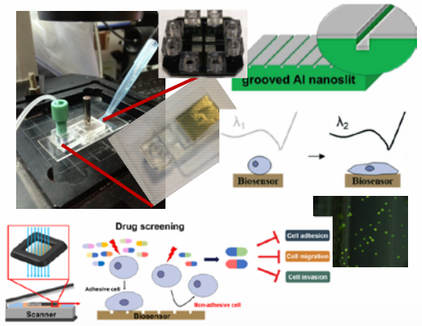
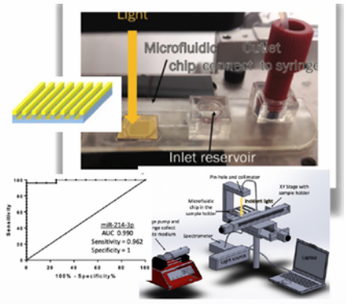
研究重點

Research Highlight -1/2

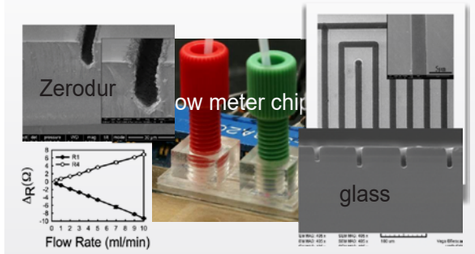
Cell adhesion quantification by nanostructure SPR
Biosensor 2015, 2019; *Sci.Rpt.* 2019; *Lab-on-chip. 2021.*



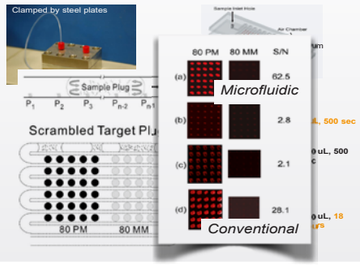
Urinary cancer biomarker detection using nanostructure SPR
Analyst 2013, 2015, 2018, 2021; SnB 2020



Laser microfabrication/Microfluidic flow sensor
JMM 2007, 2011; JLMN 2013, 2106; J. Laser App. 2020

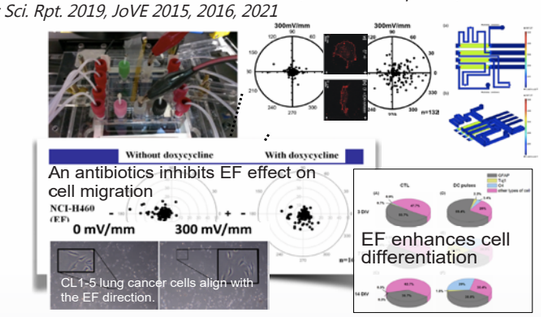


10 min DNA hybridization in microfluidic chip
Nucl. Acid. Res. 2005; Biotech. Bioeng. 2009

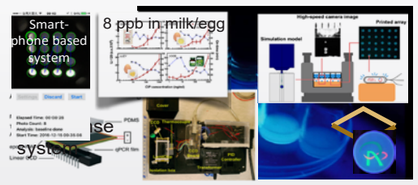


Research Highlight -2/2

Migration and differentiation of adherent cells in EF
Biomicrofluidics, 2008, 2009, 2012, 2014, 2015; Lab-on-a-chip 2009; PlosOne 2011, 2013; Sci. Rpt. 2019, JoVE 2015, 2016, 2021

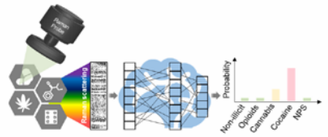


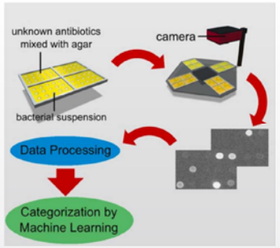
Antibiotics detection and characterization using whole-cell biosensor,
Lab-on-a-chip 2015; Anal. Bioanl. Chem. 2018; SnB, 2022.



AI-assisted categorization of illicit drugs and antibiotics,
SnB, 2021; 2022

Portable Raman spectral imaging system and machine-learning model assists in predicting different illicit drugs with high accuracy.





AI assisted antibiotics categorization using bacterial array.

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2016- 迄今 中央研究院學術諮詢總會副執行秘書
2014-2016 中央研究院應用科學研究中心副主任
2011-2014 國立陽明交通大學生醫光電研究所所長
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2000-2004 中央研究院應用科學研究中心助研究員

榮　譽

2012 中央研究院年輕學者研究著作獎
2010 行政院國家科學委員會吳大猷先生紀念獎

專長及研究重點

- Optical microscopy and related techniques
- Cell–cell and cell–microenvironment interactions
- Biomedical applications of microfluidic devices

代表著作

1. H.-J. Pan, C.-W. Lee, L.-Y. Wu, H.-H. Hsu, Y.-C. Tung, W.-Y. Liao, and C.-H. Lee, "A 3D culture system for evaluating the combined effects of cisplatin and anti-fibrotic drugs on the growth and invasion of lung cancer cells co-cultured with fibroblasts," APL Bioengineering **7**, 016117 (2023).
2. Y.-C. Kao, G.-Y. Lin, J.-Y. Cheng, and C.-H. Lee, "Neurite growth induced by red light-caused intracellular production of reactive oxygen species through cytochrome c oxidase activation," Journal of Photochemistry & Photobiology, B: Biology **241**, 112681 (2023).
3. C.-W. Lee, C.-C. Kuo, C.-J. Liang, H.-J. Pan, C.-N. Shen, and C.-H. Lee, "Effects of the media conditioned by various macrophage subtypes derived from THP-1 cells on tunneling nanotube formation in pancreatic cancer cells," BMC Molecular and Cell Biology **23**, 26 (2022).
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5. H.-H. Hou, H.-J. Pan, W.-Y. Liao, C.-H. Lee, and C.-J. Yu, "Autophagy in fibroblasts induced by cigarette smoke extract promotes invasion in lung cancer cells," International Journal of Cancer **147**, 2587-2596 (2020).
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7. C.-W. Lee, Y.-L. Chiang, J.-T. Liu, Y.-X. Chen, C.-H. Lee, Y.-L. Chen, and I.-S. Hwang, "Emerging roles of air gases in lipid bilayers," Small **14**, 1802133 (2018).
8. Y.-C. Kao, J.-R. Jheng, H.-J. Pan, W.-Y. Liao, C.-H. Lee, and P.-L. Kuo, "Elevated hydrostatic pressure enhances the motility and enlarges the size of the lung cancer cells through aquaporin upregulation mediated by caveolin-1 and ERK1/2 signaling," Oncogene **36**, 863-874 (2017).
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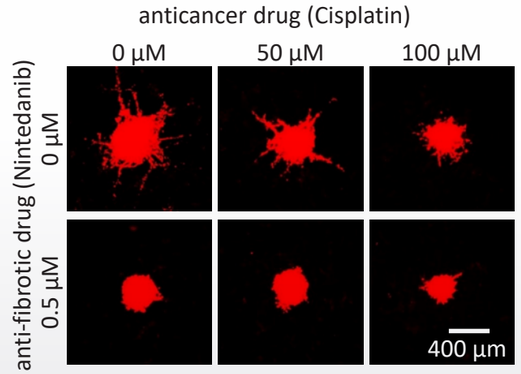
研究重點

A 3D culture system for evaluating the combined effects of cisplatin and anti-fibrotic drugs on the growth and invasion of lung cancer cells co-cultured with fibroblasts

H.-J. Pan, C.-W. Lee, L.-Y. Wu, H.-H. Hsu, Y.-C. Tung, W.-Y. Liao, and C.-H. Lee

Research Center for Applied Sciences, Academia Sinica
APL Bioengineering, 2023, DOI: 10.1063/5.0115464

We developed a 3D co-culture system composed of the mixture of fibrin and Matrigel to mimic the tumor microenvironment for studying the impact of drug combinations on a tumor of lung cancer cells co-cultured with fibroblasts. The results demonstrated that an anti-fibrotic drug, nintedanib, could improve the effect of an anticancer drug, cisplatin, to reduce tumor growth and invasion. We also identified four genes in fibroblasts relevant to cell adhesion, invasion, or ECM degradation that were reduced by nintedanib in this co-culture system. This work was also reported by Genetic Engineering & Biotechnology News, March 29, 2023.

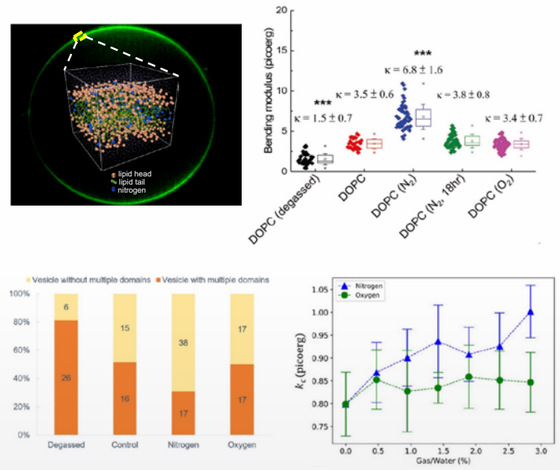


Emerging roles of air gases in lipid bilayers

C.-W. Lee, Y.-L. Chiang, J.-T. Liu, Y.-X. Chen, C.-H. Lee, Y.-L. Chen, and I.-S. Hwang

Institute of Physics and Research Center for Applied Sciences, Academia Sinica
Small, 2018, DOI: 10.1002/smll.201802133

We collaborated with Dr. Ing-Shouh Hwang and Dr. Yeng-Long Chen of Institute of Physics, Academia Sinica, to study the influences of dissolved air gases on lipid bilayers in aqueous solutions. Experimental measurements were based on differential confocal microscopy (DCM) and fluorescence microscopy on giant unilamellar lipid vesicles, as well as atomic force microscopy (AFM) on supported lipid bilayers. In comparison to lipid bilayers in ambient solutions (without gas control), the bilayers in degassed solutions are softer and less stable. High concentrations of N_2 increase the bending moduli and stability of the lipid bilayers, and impede phase separation in ternary lipid bilayers. Molecular dynamic simulations found that N_2 accumulates in the lipid bilayer, and higher N2 affinity to the lipid tails accounts for increased bending rigidity. The results imply that dissolved air gases may affect the properties of similar bilayer structures, such as cell membranes, in aqueous solutions.



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2017-2021 中央研究院院務會議數理科學組研究人員代表
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2015-2020 中央研究院應用科學研究中心生醫應用專題中心 執行長
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2006- 國立臺灣大學醫學院藥學系合聘
2004- 中央研究院生物醫學科學研究所合聘
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2000-2000 德國于利希研究院馮諾曼計算研究所博士後研究員

榮　譽

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專長及研究重點

- Pharmacoinformatics
- Structural biophysics
- Large-scale all-atom molecular dynamics simulations
- Computational drug discovery

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代表著作

1. Dhananjay C. Joshi, Charlie Gosse, Shu-Yu Huang and Jung-Hsin Lin*, "A curvilinear-path umbrella sampling approach to characterizing the interactions between rapamycin and three FKBP12 variants", *Front. Mol. Biosci.* 9: 879000 (2022) DOI: 10.3389/fmolb.2022.879000.
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4. Jung-Hsin Lin*, "Structure- and dynamics-based computational design of anticancer drugs", *Biopolymers* 105: 2-9 (2016)
5. Nanlan Huang and Jung-Hsin Lin*, "Recovery of the poisoned topoisomerase II for DNA religation: coordinated motion of the cleavage core revealed with the microsecond atomistic simulation", *Nucleic Acids Res.* 43: 6772-6786 (2015)
6. Nan-Lan Huang and Jung-Hsin Lin*, "Drug-Induced conformational population shifts in topoisomerase-DNA ternary complexes". *Molecules* 15: 7415-7428 (2014)
7. Jhih-Bin Chen , Ting-Rong Chern , Tzu-Tang Wei , Ching-Chow Chen , Jung-Hsin Lin*, and Jim-Min Fang*. "Design and synthesis of dual-action inhibitors targeting histone deacetylases and HMG-CoA reductase for cancer treatment." *J. Med. Chem.* 56: 3645-3655 (2013)
8. Jui-Chih Wang and Jung-Hsin Lin*, "Scoring functions for prediction of protein-ligand interactions", *Curr. Pharm. Des.* 19: 2174-2182 (2013)
9. Jung-Hsin Lin*. "Target prediction of small molecules with information of key molecular interactions.", Curr. Top. Med. Chem. 12: 1903-1910 (2012)
10. Jui-Chih Wang, Pei-Ying Chu, Chung-Ming Chen and Jung-Hsin Lin*. "idTarget: a web server for identifying proteins targets of small chemical molecules with robust scoring functions and a divide-and-conquer docking approach." *Nucleic Acids Res.* 40: W393-W399 (2012)

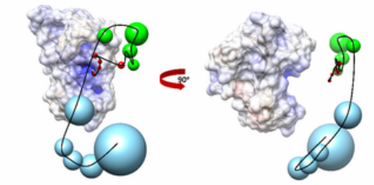
研究重點

Delineating Protein–Protein Curvilinear Dissociation Pathways and Energetics with Naïve Multiple-Walker Umbrella Sampling Simulations

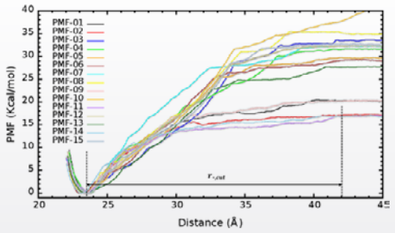
Dhananjay C. Joshi, Jung-Hsin Lin*

Academic Sinica, Research Center for Applied Sciences
J. Comput. Chem., 2019, DOI: DOI:10.1002/jcc.25821

The protein–protein interactiōn energetics can be obtained by calculating the potential of mean force (PMF) from umbrella sampling (US) simulations, in which samplings are often enhanced along a predefined vector as the reaction coordinate. However, any slight change in the vector may significantly vary the calculated PMF, and therefore the energetics using a random choice of vector may mislead. A non-predefined curve path-based sampling enhancement approach is a natural alternative, but was relatively less explored. In this work, dissociation of the barnase–barstar complex is simulated by implementing non-predefined curvilinear pathways in US simulations. A simple variational principle is applied to determine the lower bound PMF, which could be used to derive the standard free energy of binding. Two major dissociation pathways, which include interactions with the RNA-binding loop and the Val 36 to Gly 40 loop, are observed. Further, the proposed approach was used to discriminate the decoys from protein–protein docking studies.



Traces of curvilinear physical transitions for barnase–barstar from sequential US MD simulations.



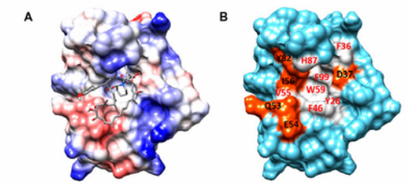
A variational principle-based approach was adopted to selected the PMF.

A Curvilinear-Path Umbrella Sampling Approach to Characterizing the Interactions Between Rapamycin and Three FKBP12 Variants

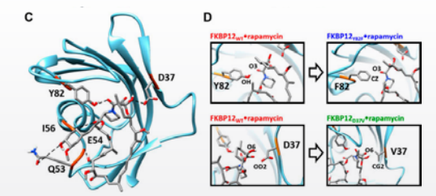
Dhananjay C. Joshi, Charlie Gosse, Shu-Yu Huang and Jung-Hsin Lin*

Academic Sinica, Research Center for Applied Sciences
Front. *Mol. Biosci.* 9: 879000 (2022) DOI: 10.3389/fmol.2022.879000

Rapamycin is an immunosuppressant macrolide that exhibits anti-proliferative properties through inhibiting the mTOR kinase. Despite the availability of structural and thermodynamic information on the interaction of FKBP12 with rapamycin, the energetic and mechanistic understanding of this process is still incomplete. In the present paper, we extend our investigations to a protein-small molecule duo, the FKBP12•rapamycin complex. We estimate the binding free energies of rapamycin with wild-type FKBP12 and two mutants in which a hydrogen bond has been removed, D37V and Y82F. On one hand, removing the carboxylate group of D37 strongly destabilizes the association; on the other hand, the hydroxyl group of Y82 is nearly unnecessary for the stability of the complex because some nonconventional, cryptic, indirect interaction mechanisms seem to be at work.



Structure of the FKBP12•rapamycin complex as determined in PDB 1FKB. (A) Coulombic surface representation (B) Surface representation of the protein alone with the hydrogen-bond forming residues in orange and the hydrophobic residues in gray.



(C) The five hydrogen bonds formed between FKBP12 and rapamycin are shown as dashed lines. (D) Close-up view on the Y82 and D37 residues and resulting starting conformation obtained after either the Y82F or the D37V substitution.

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- Ta-You Wu Memorial Award（吳大猷先生紀念獎）, National Science Council, 2013.
- Career Development Award（前瞻計劃）, Academia Sinica, 2012-2016.

專長及研究重點

- Functional materials (for electronic, chemical and biomedical applications).
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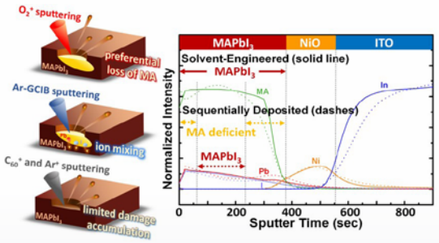
研究重點

Validated Analysis of Component Distribution Inside Perovskite Solar Cells and Its Utility in Unveiling Factors of Device Performance and Degradation

Cheng-Hung Hou, Shu-Han Hung, Li-Ji Jhang, Keh-Jiunh Chou, Yu-Kai Hu, Pi-Tai Chou, Wei-Fang Su, Feng-Yu Tsai, Jay Shieh, and Jing-Jong Shyue*

Academic Sinica, Research Center for Applied Sciences

ACS Applied Materials & Interfaces 12 [20] 22730-22740 (2020) DOI:10.1021/acsami.9b22492



Time-of-flight secondary-ion mass spectrometry (ToF-SIMS) has been used for gaining insights into perovskite solar cells (PSCs). However, the importance of selecting ion beam parameters to eliminate artifacts in the resulting depth profile is often overlooked. In this work, significant artifacts were identified with commonly applied sputter sources, i.e., an O_2^+ beam and an Ar-gas cluster ion beam (Ar-GCIB), which could lead to the misinterpretation of the PSC structure. On the other hand, polyatomic C_{60}^+ and Ar^+ ionbeams were found to be able to produce depth profiles that properly reflect the distribution of the components. Based on this validated method, differences in component distribution, depending on the fabrication processes, were identified and discussed. The solvent engineering process yielded a homogeneous film with higher device performance, but sequential deposition led to a perovskite layer sandwiched by methylammonium-deficient layers that impeded the performance. For device degradation, it was found that most components remained intact at their original position except for iodide. This result unambiguously indicated that iodide diffusion was one of the key factors governing the device lifetime. With the validated parameters provided, ToF-SIMS was demonstrated as a powerful tool to unveil the structure variation amid device performance and during degradation, which are crucial for the future development of PSCs.

Adsorption of Drug Guest Molecules in Metal-Organic Frameworks Studied by Quartz Crystal Microbalance with Dissipation (QCM-D)

Wen-Yi Yu and Jing-Jong Shyue*

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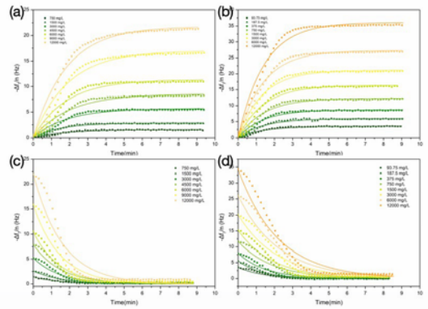

Guest molecules absorption and desorption processes in the aqueous phase were examined by QCM-D, and Acetaminophen, Caffeine and Aspirin were chosen for this study. The preparation of UiO-66-coated quartz crystal chip was via the spin-coating method. It was found that the absorption process was repeatable and reproducible. Furthermore, the degree of absorption varied by the guest molecule, and in descending order were aspirin, caffeine, acetaminophen due to electric charge, polarity and ϖ-ϖ stacking interaction.

In order to study the effect of environment on guest uptake in MOF, the absorption and desorption processes were observed under different pHs. As pH value went down, the absorption of acetaminophen decreased due to the failure to form hydrogen bond with UiO-66 which was surrounded by more protons at lower pH. However, the caffeine absorption slightly increased, owing to the enhance of the electrostatic interaction caused by the increase of UiO-66 zeta potential at lower pH. For aspirin, the absorption first raised and then descended at pH 3. The increase resulted from the zeta potential of uio-66 as well, while the decrease was caused by dissociated aspirin molecules getting back protons at lower pH. It led to molecular become neutral, and reduce the electrostatic interaction.

The drug absorption and desorption kinetics was also investigated, and the result showed that non-linear pseudo first order kinetic model was the most suitable one. There was good correlation between models and experiment data. Moreover, the interaction between MOF and guest would have an effect on absorption and desorption kinetics.

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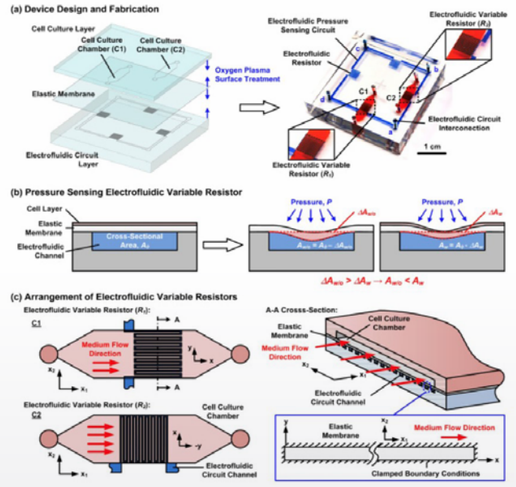
研究重點

Revealing anisotropic elasticity of endothelium under fluid shear stress

Ping-Liang Ko, Chien-Kai Wang, Heng-Hua Hsu, Tse-Ang Lee, and Yi-Chung Tung

Academic Sinica, Research Center for Applied Sciences
Acta Biomaterialia 2022, DOI: 10.1016/j.actbio.2022.03.040

Endothelium lining interior surface of blood vessels experiences various physical stimulations in vivo. Its physical properties, especially elasticity, play important roles in regulating the physiological functions of vascular systems. An integrated approach is developed to characterize the anisotropic elasticity of the endothelium under physiological-level fluid shear stress. A pressure sensor-embedded microfluidic device is developed to provide fluid shear stress on the perfusion-cultured endothelium and to measure transverse in-plane elasticities in the directions parallel and perpendicular to the flow direction. Biological atomic force microscopy (Bio-AFM) is further exploited to measure the vertical elasticity of the endothelium in its out-of-plane direction. The results show the highly anisotropic physical properties of the endothelium. The quantitative measurement of the endothelium anisotropic elasticity in different directions at the tissue level under the fluid shear stress provides biologists insightful information for the advanced vascular system studies from biophysical and biomaterial viewpoints.



Study 3D Endothelial Cell Network Formation under Various Oxygen Microenvironment and Hydrogel Composition Combinations Using Upside-Down Microfluidic Devices

Heng-Hua Hsu, Ping-Liang Ko, Hsiao-Mei Wu, Hsi-Chieh Lin, Chien-Kai Wang, and Yi-Chung Tung

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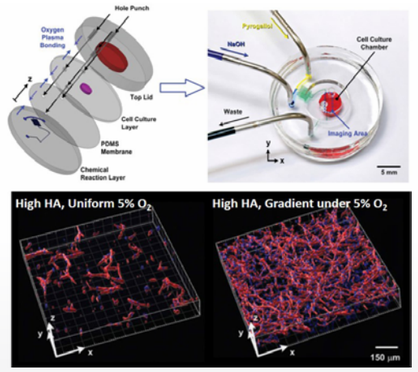
Formation of 3D networks is a crucial process for endothelial cells during development of primary blood vessels under both normal and pathological conditions. In order to investigate effects of oxygen microenvironment and matrix composition on the 3D network formation, an upside-down microfluidic cell culture device capable of generating oxygen gradients is developed. In cell experiments, network formation of human umbilical vein endothelial cells (HUVECs) within fibrinogen-based hydrogels with different concentrations of hyaluronic acid (HA) is systematically studied. In addition, five different oxygen microenvironments (uniform normoxia, 5%, and 1% O2; oxygen gradients under normoxia and 5% O2) are also applied for the cell culture. The experimental results show increased 3D cell network length when the cells are cultured under the oxygen gradients within the hydrogels with the HA addition suggesting their roles in promoting network formation. The developed upside-down microfluidic device can provide an advanced platform to investigate 3D cell culture under the controlled oxygen microenvironments for various biomedical studies *in vitro*.



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專長及研究重點

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研究重點

Application of statistical clustering to diagnose sub-zone activities in potential deep-seated landslide sites

Pi-Wen Tsai, Chih-Yu Kuo[1], Rou-Fei Chen

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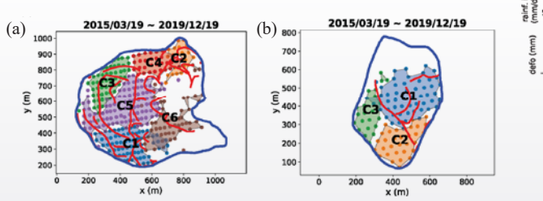
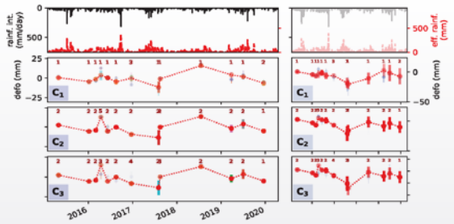
Multi-Temporal Interferometric Synthetic Radar (MTInSAR) is a remote sensing technology, which can provide high accuracy and wide coverage of transient surface deformation through analyzing a sequence of radar interferograms. It has been applied to hazard mitigation planning for potential deep-seated landslides and long-term monitoring of the slope activities in Taiwan. In this study, a Gaussian mixture model is proposed to perform statistical clustering for the surface deformation data points, associated clusters are defined to connect multitemporal deformation clusters, and the time series of the deformation clusters can be composed. These techniques enable investigations on the relations among the time series of the deformation clusters, precipitations or other influential factors of the landslide activities. The results indicate that the method can be further deployed for wider deep-seated landslide applications.



Clusters and their α-shapes of ALOS2 2014~2019 MTInSAR deformation rates of (a) D066 and (b) D077. The red solid lines indicate the surface cracks



2014~2019 upward ALOS2 multi-temporal InSAR deformation sequence of D077. The rainfall are taken from records of Meishan rainfall station. Other caption statements are referred to Fig. 8

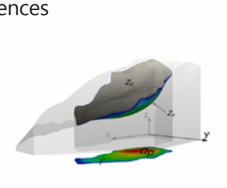
Application assessments of using scarp boundary-fitted, volume constrained, smooth minimal surfaces as failure interfaces of deep-seated landslides

Chih-Yu Kuo[1], P.W. Tsai, Y. C. Tai, Y. H. Chan, R. F. Chen, C. W. Lin

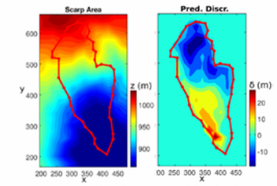
[1]Academic Sinica, Research Center for Applied Sciences

Front. In Earth Sci., 2020, DOI: 10.3389/feart.2020.00211

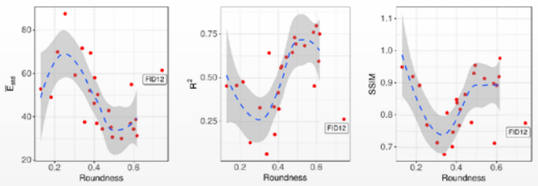
More than 9,000 potential deep-seated landslide sites in the mountain ranges of Taiwan have been identified by a series of governmental hazard mitigation initiatives after the 2009 Morakot typhoon. Among them, 186 sites have protection targets where thorough mitigation strategies are to be implemented. One of the important tasks is to estimate the volume, failure interface and related quantities of each landslide site. With this number of sites, an automated tool is needed to generate predictions at low operational costs. We propose to use volume-constrained smooth minimal surfaces to approximate the landslide failure interfaces. A volume-constrained smooth minimal surface in the current context is defined as a differentiable surface that encloses a given landslide volume with the minimal surface area. Although the stratigraphy and geological structures are omitted, the smooth minimal surface method is verified with 24 known landslides and is shown to be able to generate acceptable, approximated failure interfaces. A collection of assessment indices is employed to measure the fitness of the predictions.



The concept of minimal smooth surface



Application to FID18 landslide



Accuracy assessments of the minimal smooth surface predictions with 24 actual landslides. Three selected normalized assessment indices versus scarp roundness. The indices are the standard deviation, coefficients of determination, and structural similarity, calculated by comparing the predicted and actual landslide scarps.

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2015　美國科學促進會 (AAAS) 紐科姆·克利夫蘭獎 (Newcomb Cleveland Prize)
2020　第十八屆有庠科技論文獎一光電組
2021　中央研究院年輕學者研究成果獎

專長及研究重點

- 超分辨螢光影像技術
- 快速三維活體影像
- 發展高空間及時間解析之層光顯微鏡
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代表著作

1. W.-C. Tang, Y.-T. Liu, C.-H. Yeh, Y.-L. Lin, Y.-C. Lin, T.-L. Hsu, L. Gao, P. Chen*, and **B.-C. Chen***, "Optogenetic Manipulation of Cell Migration with High Spatiotemporal Resolution Using Lattice Lightsheet Microscopy" *Communications Biology*, 5, 879, DOI:10.1038/s42003-022-03835-6 (2022)
2. Fan, Y.-J.*; Hsieh, H.-Y.; Huang, Y.-R.; Tsao, C.; Lee, C.-M.; Tahara,H.; Wu,Y.-C.; Sheen, H.-J.*; **Chen, B.-C.***, "Development of a water refractive index-matched microneedle integrated into a light sheet microscopy system for continuous embryonic cell imaging", *Lab on a chip*, 22, 584-591 DOI:10.1039/D1LC00827G (2022)
3. Lin, M.-H., Chen, J.-C., Tian, X., Lee, C.-M., Yu,I-S., Lo, Y.-F., Uchida, S., Huang, C.-L., **Chen, B.-C.***; Cheng, C.-J.*, "Impairment in renal medulla development underlies salt wasting in Clc-k2 channel deficiency", *JCI Insight*, 9:151039 ; DOI:10.1172/jci.insight (2021) selected as the cover image
4. Fan, Y.-J.*, Hsieh, H.-Y., Tsai, S.-F., Wu, C.-H., Lee, C.-M., Liu, Y.-T., Lu, C.-H., Chang, S.-W.*, **Chen, B.-C.***, "Microfluidic channel integrated with a lattice lightsheet microscopic system for continuous cell imaging" *Lab on a chip*, 21, 344 DOI: 10.1039/d0lc01009j (2021)
5. Tsai, Y.-C.; Tang, W.-C.; Low, C. S. L.; Liu, Y.-T.; Wu, J.-S.; Lee, P.-Y.; Lin, Y.-L.; Kanchanawong, P.; Gao, L, and **Chen, B.-C.*** "Rapid High Resolution 3D Imaging of Expanded Biological Specimens with Lattice Lightsheet Microscopy", *Methods*, 174, 11-19 DOI:10.1016/j.ymeth.2019.04.006 (2020)
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7. Lu, C.-H.; Tang, W.-C.; Liu, Y.-T.; Wu, F. C. M.; Chen, C. Y.; Tsai, Y. C.; Yang, S.-M; Kuo, C.-W.; Okada, Y.; Hwu, Y.-K.; Chang, S.-W.; Chen, P. * and **Chen, B.-C.***, "Lightsheet localization microscopy enables fast, large-scale, and three-dimensional super-resolution imaging." *Communications Biology*, 2, 177 DOI:10.1038/s42003-019-0403-9 (2019)
8. Gao, L. *; Tang,W.-C.; Tsai, Y.-C.; **Chen, B.-C.*** "Lattice light sheet microscopy using tiling lattice light sheets" *Opt. Express*, 27 1497-1506 DOI:10.1364/OE.27.001497. (2019)

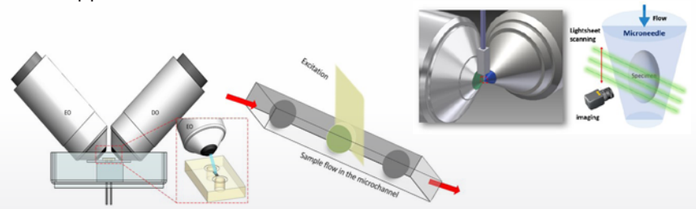
研究重點

Microfluidic channel integrated with lightsheet microscopic system for continuous live 3D imaging

Fan, Y.-J.* , Hsieh, H.-Y., Tsai, S.-F., Wu, C.-H., Lee, C.-M., Liu, Y.-T., Lu, C.-H., Chang, S.-W.* , Chen, B.-C.*

Academic Sinica, Research Center for Applied Sciences
Lab on a chip **21**, 344 (2021)
Lab on a chip **22**, 584 (2022)

A continuous live imaging system with subcellular resolution by integrating a water refractive index-matched microfluidic device was develop to achieve high spatiotemporal resolutions in 3D.

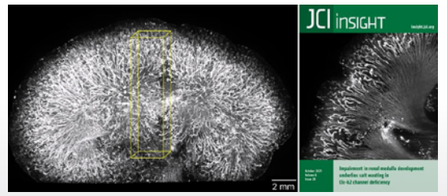


Lightsheet expansion microscopy for 3D super-resolution imaging in the organ

Lin, M.-H., Chen, J.-C., .., Chen, B.-C.*; Cheng, C.-J.*

JCI Insight, 9, 151039 (2021)

We have expanded isotropically the mouse kidney by 4x expansion microscopy and imaged such a centimeter sized sample at high speed by lightsheet microscopy to approach high spatial resolution of the immunolabeled thick ascending limb of Henle's loop within the whole organ.

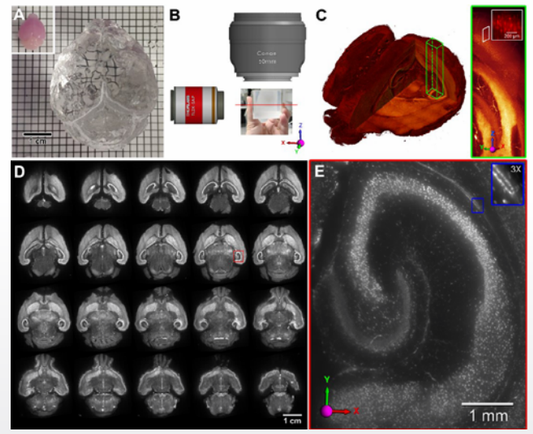


Macro Photography with Lightsheet Illumination Enables Whole Expanded Brain Imaging with Single-cell Resolution

Lee, C.-M., Tian, X., Tsao, C., Chen, P. Huang, T.-N., Hsueh,Y.-P., Chen, B.-C.*

Academic Sinica, Research Center for Applied Sciences
Discoveries Journals, Jul-Sep, **9(3)**:e133
DOI:10.15190/d.2021.12 (2021)

Macro photography allows direct visualization of enlarged whole mouse brain by a combination of lightsheet illumination and expansion microscopy with single-cell resolution. Taking advantage of the long working distance of a macro lens, we imaged a 3.7-cm thick, transparent, fluorescently-labeled expanded brain. In order to improve 3D sectioning capability, we used lightsheet excitation confined as the depth of field of the macro lens. Using 4x sample expansion and 5x optical magnification, macro photography enables imaging of expanded whole mouse brain with an effective resolution of 300 nm.



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2015-2020 國立清華大學化學工程學系 博士後研究員
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榮　譽

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2020 財團法人李昭仁教授生醫工程發展基金會 年輕學者獎
2019 國科會博士後研究人員學術著作獎

專長及研究重點

- 開發先進藥物遞送系統
- 開發治療性氣體生成系統

代表著作

1. Ruan, T., Fu, C. Y., Lin, C. H., Chou, K. C., **Lin, Y. J.*** Nanocontroller-mediated dissolving hydrogel that can sustainably release cold-mimetic menthol to induce adipocyte browning for treating obesity and its related metabolic disorders. *Biomaterials* 2023, 297, 122120.
2. Chou, C. W., Chia, W. T., Mac, C. H., Wu, C. Y., Chen, C. C., Song, H. L., Lin, Y. H., **Lin, Y. J.***, Sung, H. W.* Selective accumulation of ionic nanocrystal H2 storage system as an in situ H_2/boric acid nanogenerator fights against ethanol-induced gastric ulcers. *Chemical Engineering Journal* 2023, 463, 142373.
3. Nguyen, N., Lin, Z. H., Barman, S. R. Korupalli, C., Cheng, J. Y., Song, N. X., Chang, Y., Mi, F. L., Song, H. L., Sung, H. W.*, **Lin, Y. J.*** Engineering an integrated electroactive dressing to accelerate wound healing and monitor noninvasively progress of healing. *Nano Energy* 2022, 99, 107393.
4. Mac, C. H., Chan, H. Y., Lin, Y. H., Sharma, A. K., Song, H. L., Chan, Y. S., Lin, K. J.*, **Lin. Y. J.***, Sung, H. W.* Engineering a biomimetic bone scaffold that can regulate redox homeostasis and promote osteogenesis to repair large bone defects. *Biomaterials* 2022, 286, 121574.
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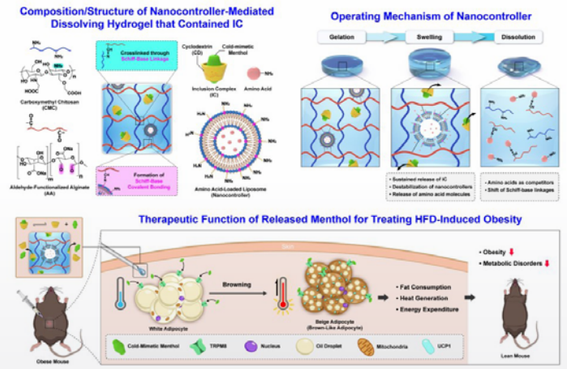
7. **Lin, Y. J.**, Chen, C. C., Nguyen, D., Su, H. R., Lin, K. J., Chen, H. L., Hu, Y. J., Lai, P. L., Sung, H. W. Biomimetic engineering of a scavenger-free nitric oxide-generating/delivering system to enhance radiation therapy. *Small* 2020, 16, e2000655. (Selected as Inside Cover)
8. **Lin, Y. J.**, Chen, C. C., Chi, N. W., Nguyen, T., Lu, H. Y., Nguyen, D., Lai, P. L., Sung, H. W. In situ self-assembling micellar depots that can actively trap and passively release NO with long-lasting activity to reverse osteoporosis. *Advanced Materials* 2018, 30, e1705605.

研究重點

Nanocontroller-Mediated Dissolving Hydrogel that Can Sustainably Release Cold-Mimetic Menthol to Induce Adipocyte Browning for Treating Obesity and Its Related Metabolic Disorders

Ting Ruan, Chih-Yu Fu, Chih-Hung Lin, Kun-Chi Chou, and Yu-Jung Lin*

Research Center for Applied Sciences, Academic Sinica
Biomaterials 2023, 297, 122120.

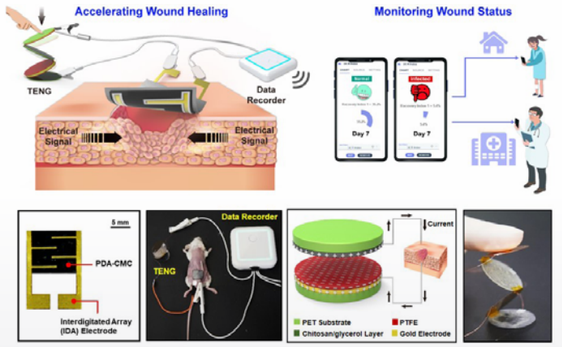


An injectable hydrogel is developed to sustainably deliver cold-mimetic menthol for adipocyte browning. It contains carboxymethyl chitosan and aldehyde-functionalized alginate crosslinked with dynamic Schiff-base linkages, loaded with menthol-cyclodextrin inclusion complexes. Amino acid-loaded liposomes, functioning as nanocontrollers, are grafted onto the hydrogel to make it soluble after the payload release. When injected into obese mice, the hydrogel gradually releases menthol to induce adipocyte browning and increase energy expenditure. The hydrogel networks expand, triggering the grafted liposomes to release amino acids that dissolve the hydrogel. This nanocontroller-mediated dissolving hydrogel is effective for treating obesity and related metabolic disorders without leaving exogenous hydrogel materials inside the body, and thereby preventing any undesired adverse effects.

Engineering an Integrated Electroactive Dressing to Accelerate Wound Healing and Monitor Noninvasively Progress of Healing

Nhien Nguyen, Zong-Hong Lin, Snigdha Roy Barman, Chiranjeevi Korupalli, Ji-Yen Cheng, Ni-Xuan Song, Yen Chang, Fwu-Long Mi, Hsiang-Lin Song, Hsing-Wen Sung*, and Yu-Jung Lin*

Research Center for Applied Sciences, Academic Sinica
Nano Energy 2022, 99, 107393.



This work develops an engineered electroactive dressing that comprises a layer of polydopamine-crosslinked carboxymethyl chitosan conductive hydrogel and an interdigitated array (IDA) electrode. The conductive hydrogel provides a channel that transmits endogenous bioelectrical signals to the wound; these stimulate electrical stimuli-responsive cells, and thereby accelerate the restoration of the wounded tissue. The IDA electrode detects the electrical resistance or output current across the wounded tissue for the noninvasive real-time monitoring of the overall healing process. This wound monitoring system is integrated with a WIFI-based system for wireless data collection and transmission using a personal smartphone. Such a real-time wound monitoring system can be worn by patients, to whom it issues early warnings of potential infections and it wirelessly sends data on the progression of healing to remote medical staff for dynamic intervention as required.

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2016　中央研究院應用科學研究中心研究副技師
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2005　國立聯合大學通識教育中心物理組助理教授
2002　國立台灣大學物理系博士後研究

榮　譽

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專長及研究重點

- 機器學習
- 生醫影像處理與訊號分析
- 計算物理
- 高效能計算系統建置與維護
- 格點量子場論計算

代表著作

1. Wei-Ru Lu, Wen-Tse Yang, Justin Chu, Tung-Han Hsieh, and Fu-Liang Yang, "Deduction learning for precise noninvasive measurements of blood glucose with a dozen rounds of data for model training", Sci. Rep. 12, 6506 (2022).
2. Wei-Che Huang, Chin-Dian Wei, Shimshon Belkin, Tung-Han Hsieh, and Ji-Yen Cheng, "Machine-learning assisted antibiotic detection and categorization using a bacterial sensor array", Sensors and Actuators B: Chemical, 355 (2022) 131257.
3. Justin Chu, Wen-Tse Yang, Wei-Ru Lu, Yao-Ting Chang, Tung-Han Hsieh, and Fu-Liang Yang, "90% Accuracy for Photoplethysmography-Based Non-Invasive Blood Glucose Prediction by Deep Learning with Cohort Arrangement and Quarterly Measured HbA1c", Sensors 2021, 21(23), 7815.
4. Bitewulign Kassa Mekonnen, Tung-Han Hsieh, Dian-Fu Tsai, Shien-Kuei Liaw, Fu-Liang Yang, and Sheng-Lung Huang, "Generation of Augmented Capillary Network Optical Coherence Tomography Image Data of Human Skin for Deep Learning and Capillary Segmentation", Diagnostics 2021, 11(4), 685.
5. Hsiao-Mei Wu, Tse-Ang Lee, Ping-Liang Ko, Wei-Hao Liao, Tung-Han Hsieh, and Yi-Chung Tung, "Widefield frequency domain fluorescence lifetime imaging microscopy (FD-FLIM) for accurate measurement of oxygen gradients within microfluidic devices", Analyst, 2019, 144, 3494.
6. Hsien-San Hou, Kuang-Li Lee, Chen-Hung Wang, Tung-Han Hsieh, Juan-Jie Sun, Pei-Kuen Wei, and Ji-Yen Cheng, "Simultaneous assessment of cell morphology and adhesion using aluminum nanoslit-based plasmonic biosensing chips", Sci. Rep. 9, 7204 (2019).
7. Wing Kiu Yeung, Huai-Yi Chen, Juan-Jie Sun, Tung-Han Hsieh, Mansoureh Z. Mousavi, Hsi-Hsien Chen, Kuang-Li Lee, Heng Lin, Pei-Kuen Wei, and Ji-Yen Cheng, "Multiplex detection of urinary miRNA biomarkers by transmission surface plasmon resonance", Analyst, 2018, 143, 4715.

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研究重點

PPG signal pattern analysis via deduction learning

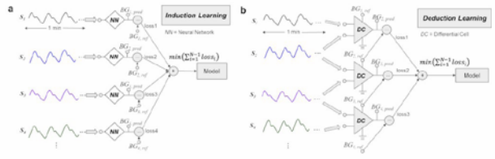
Wei-Ru Lu, Wen-Tse Yang, Justin Chu, Tung-Han Hsieh, Fu-Liang Yang

Research Center for Applied Sciences, Academia Sinica
(A part of work in *Scientific Report* (2022) **12**:6506)

Diabetes mellitus (DM) is a chronic condition of abnormally elevated blood glucose level (BGL), which leads to various complications. Currently, reliable BGL measurement utilize invasive methods.

In this work, an attempt of noninvasive blood glucose (NIBG) prediction via correlating photoplethysmo-graphy (PPG) to BGL using deduction learning (DL) was developed. Unlike the traditional induction learning (IL), DL has rules based on our domain knowledge being imposed in the model to guide the learning. For PPG based NIBG, the rule imposed is the assumption of the relation between predicted BGL with its precede BGL, and also the measured PPG signals.

$$DL \leftarrow \sum_{i=2}^{N} f(S_i, S_{i-1}, BG_{i-1})$$
$$BG_k \leftarrow DL(S_k, S_N, BG_N)$$



Methods	DL+S	DL	IL	RF w/o signal	RF w/ signal
Accuracy score (R_A)	93.50 ± 3.50	88.21 ± 8.82	81.47 ± 12.28	80.46 ± 14.21	82.13 ± 12.82
Mean absolute error (MAE) [mg/dl]	12.07	25.96	38.38	40.46	37.19
Root mean squared error (RMSE) [mg/dl]	13.93	36.25	46.51	53.18	48.88
Pearson correlation coefficient (R_P)	0.81	0.44	0.2	−0.08	−0.018
A-Zone ratio	100%	80%	55%	60%	60%

Using DL, we successfully trained our model with only a dozen of rounds (1 – 12) of training data, and gave good predictions on BGL for rounds 13 – 15.

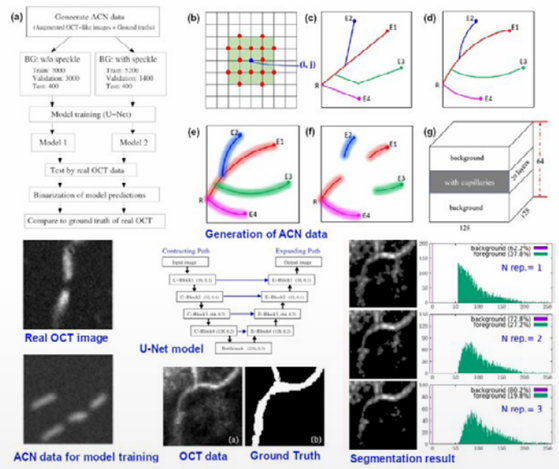
OCT skin image analysis for capillary network reconstruction

Bitewulign K. Mekonnen, Tung-Han Hsieh, Dian-Fu Tsai, Shien-Kuei Liaw, Fu-Liang Yang, Sheng-Lung Huang

Research Center for Applied Sciences, Academia Sinica
(Diagnostics **2021**, 11, 685)

Automated capillary segmentation plays an important role in computer vision and clinical application. Full-Field Optical Coherence Tomography (FF-OCT) provides a convenient tool for noninvasive in vivo visualization for dermatology, oncology, retinal, micro-angiography in intercellular resolution.

In this work, we developed a machine learning model for capillary segmentation from FF-OCT images of human skin. Due to lack of sufficient annotated data for model training, an algorithm was developed to generate a large set of augmented capillary network (ACN) data. Then the U-Net model was trained by the ACN data to perform the task of capillary segmentation from the real FF-OCT image volume. Finally, the more accurate segmentation from the predicted image volume was achieved by counting the number N of repeated appearance of signal for each pixel over the layers in the image volume. Setting N=1 as the binarization threshold, we attended accuracy 0.798, and F1 score 0.814.



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- Small Molecule Drug Development and Drug Delivery
- Biosensor Development and Applications

代表著作

1. S. H. Wang, S. C. Y. J. Tung, C. W. Kuo, Y. H. Tai, S. Y. Hsieh, K. L. Lee, S. R. Hsiao, J. F. Sheen, J. C. Hsu and P. K. Wei. "Multichannel Nanoplasmonic Platform for Imidacloprid and Fipronil Residues Rapid Screen Detection Biosensors and Bioelectronics or its open access mirror" *Biosens. Bioelectron*. **2020**, 170, 112677.
2. S. H. Wang, C. W. Lee, M. Y. Pan, S. Y. Hsieh, F. G. Tseng, and P. K. Wei. "Chromatogram analysis on revealing aggregated number and location of gold nanoparticles within living cells." *Plasmonics*, **2015**, *10*(4), 873-880.
3. W. H. Lin, T. K. Yeh, W. T. Jiaang, K. J. Yen, C. H. Chen, C. T. Huang, S. C. Yen, S. Y. Hsieh, L. H. Chou, C. P. Chen, C. H. Chiu, L. C. Kao, Y. S. Chao, C. T. Chen, and J. T. A. Hsu. & Chiu, C. H. "Evaluation of the antitumor effects of BPR1J-340, a potent and selective FLT3 inhibitor, alone or in combination with an HDAC inhibitor, vorinostat, in AML cancer." *PloS one*, **2014**, *9*(1), e83160.
4. S. H. Wu, S. Y. Hsieh, K. L. Lee, R. H. Weng, A. Chiou, and P. K. Wei, "Cell viability monitoring using Fano resonance in gold nanoslit array." *Applied Physics Letters*, **2013**, *103*(13), 133702.
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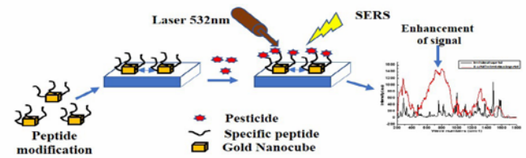
研究重點

Multiple Pesticides Detection by Integrating Synthetic Peptides and Gold Nanoparticles

Tran Thi Anh Hong,[1] Sheng-Hann Wang,[1] Ting-Wei Chang,[1] Pei-Kuen Wei, [1] Shu-Yi Hsieh [1]*

In this study, we attempt to develop a detection system by integrating self-synthesized peptides and gold nanoparticles (AuNPs) that is time-saving and enhances specificity as well as a simple technique. Principally, the surface-enhanced Raman scattering (SERS) technique is applied for pesticide detection, herein, AuNPs can be used as SERS substrate due to its roughened surfaces induces Raman signal enhancement. In addition, oligopeptide sequences CGGGRKRIRRMMPRPS (Cys-P1) and CGGGRNRHTHLRTRPR (Cys-P2) were found for specific binding with thiacloprid and imidacloprid, respectively, whereas the CGGG fragment helps to bind with AuNPs forming peptides-modified AuNPs. Therefore, Raman signal from the captured pesticides is enhanced, and an improved specificity is also achieved by decreasing non-specific signals. For oligopeptide Cys-P1 and Cys-P2, Rink amide resin was used for Fmoc solid phase peptide synthesis. The purity of Cys-P1-CONH2 and Cys-P2-CONH2 was estimated to be about 90% and 92% by reverse phase HPLC (RP-HPLC). Together, Matrix-assisted laser desorption/ ionization-time of flight (MALDI-TOF) mass spectrometry (MS) analysis shows the m/z value of Cys-P1-CONH2 to be 1857.14 and 1858.13; Cys-P2-CONH2 to be 1873.27 and 1874.26 which contained cis-Proline and trans- Proline isomers in sequence. In future work, we will continuously optimize the peptide-pesticides binding conditions in SERS analysis.

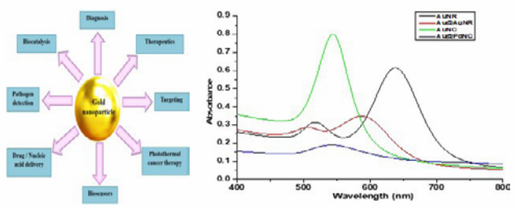


MALDI-TOF/MS spectra of oligopeptide　RP-HPLC analysis of oligopeptide

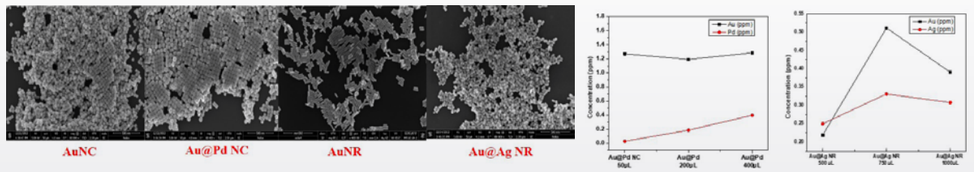
Various Gold Nanoparticles Synthesis: Property, Morphology and Applications

Tran Thi Anh Hong, [1] Shu-Yi Hsieh [1]*

Gold nanoparticles (NPs) have been used in a variety of applications such as diagnosis, therapeutics, targeting, photothermal cancer therapy, biosensors, drug delivery, pathogen detection, and biocatalysis. In RCAS, we synthesize the various AuNPs including AuNCs, Au@Pd NCs, AuNRs, and Au@Ag NRs and provide it to research. Furthermore, by employing the surface-enhanced Raman scattering technique, AuNCs and AuNRs are used as sensitive probes as well as an enhanced signal in SERS. Core-shell Au@Ag NRs with different shell thicknesses of silver will enhance the chemical interface damping (CID) effect. In addition, bimetallic core-shell Au@Pd nanoparticles were applied in enhanced catalytic activity. The particles of AuNPs were characterized by scanning electron microscopy (SEM) and UV–visible spectroscopy, and ICP-OES determined the Au/Ag/Pd mass concentration.



Application of AuNPs　UV-VIS spectrum of various AuNPs



SEM image of the AuNPs immobilized on Si wafer　ICP-OES measurement of Au@PdNC and Au@AgNR

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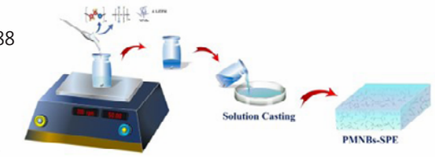
研究重點

Intimate Interaction of TFSI- Anions with MoO_3 Ionic Conductivity of Cathode-supported Solid Polymer Electrolyte

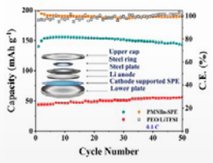
Rohan Paste, Chintam Hanmandlu, Po-Yu Su, Cheng-Hung Hou, Hsin-An Chen, Chun-Wei Pao, Jing-Jong Shyue, Kuei-Hsien Chen, Heng-Liang Wu, Hong-Cheu Lin, Chih Wei Chu

Academic Sinica, Research Center for Applied Sciences
Chemical Engineering Journal, 2023, DOI: 10.1016/j.cej.2022.139088

A solid-state electrolyte should display high ionic conductivity, low interfacial impedance, good mechanical properties, and stability. Although poly(ethylene oxide) (PEO) has been investigated extensively as a potential polymer host in solid polymer electrolytes (SPEs), it suffers from low ionic conductivity, flammability, Li dendrite growth, and poor mechanical strength. To tackle these issues, we have developed a composite cathode-supported SPE that incorporates oxygen-deficient MoO3–x nanobelts (MNBs) as passive nanofillers. The synthesis of MNB is easy, economical, and scalable, allowing for large-scale production of SPE. In comparison to the PEO-only SPE, the composite SPE with 5% MNBs (PMNBs-SPE) demonstrates higher ionic conductivity, improved mechanical strength, superior cycling performance, and reduced flammability. The enhanced ionic conductivity is attributed to the dissociation of LiTFSI in the presence of oxygen vacancies, which act as Lewis acid sites, as well as the shorter diffusion pathways created by the MNBs.



The process used for fabrication of the PMNBs-SPE



Cycling performance of PEO/ LiTFSI andPMNBs-SPE with an LFP cathode and Li anode at 0.1C and at 60˚C

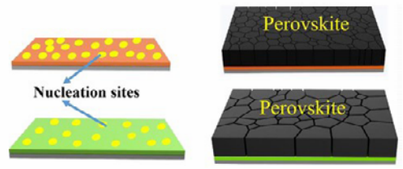
LED test and measured value of Voc of a CR2032 cell containing PMNBs-SPE

Few-layer fluorine-functionalized graphene hole-selective contacts for efficient inverted perovskite solar cells

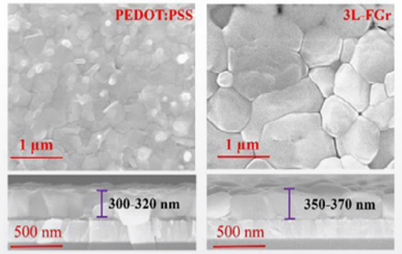
Chintam Hanmandlu, Mamina Sahoo, Chi-Ching Liu, Hsin-An Chen, Chun-Wei Pao, Yun-Chorng Chang, Chih Wei Chu, Chao-Sung Lai

Academic Sinica, Research Center for Applied Sciences
Chemical Engineering Journal, 2022, DOI: 10.1016/j.cej.2021.132831

Charge-selective contacts can play a critical role in enhancing the efficiency of perovskite solar cells (PSCs). We employed fluorine-functionalized graphene (FGr) layers as hole transport layers (HTLs) to improve the power conversion efficiency (PCE) and stability of inverted PSCs. The non-wetting surface of the FGr enhanced the crystallinity of organic–inorganic perovskites films with large aspect ratios, relative to that of poly(3,4-ethylenedioxythiophene): polystyrenesulfonate. Combining the high work function of the HTL interface with the enhanced crystallinity and limited grain boundary area dramatically decreased the charge recombination losses in organic–inorganic trihalide perovskite films. Thus, when incorporating FGr HTLs in inverted PSCs, the best PCE reached 19.34%—the highest efficiency reported to date for any PSC featuring a functionalized graphene HTL. Furthermore, we used this HTL to prepare flexible PSCs and obtained a highest efficiency of 17.50%. Therefore, this highly applicable and facile interface strategy using functionalized graphene HTLs provides stable PSCs displaying high PCEs.



Mechanism of large grain growth of perovskite on a non-wet



Top-view and cross-sectional surface morphologies of perovskites on various HTLs

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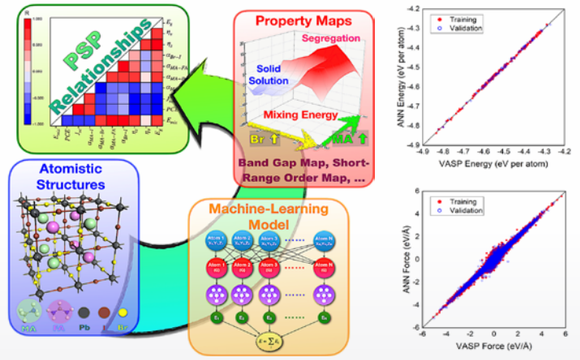
研究重點

Microstructure Maps of Complex Perovskite Materials from Extensive Monte Carlo Sampling Using Machine Learning Enabled Energy Model

Hsin-An Chen, Ping-Han Tang, Guan-Jie Chen, Chien-Cheng Chang*, Chun-Wei Pao*

Journal of Physical Chemistry Letters **12**, 3591 (2021)

In this work, we trained an artificial neural network (ANN) potential energy model of the $MA_yFA_{1-y}Pb(Br_xI_{1-x})_3$ complex perovskite material and investigated the microstructure over the composition space using extensive Monte Carlo simulations. We sampled around 8.1x105 structures of different site permutations and compositions, identified low energy structures and mapped the structural properties - the mixing energy, SRO parameters, and lattice distortion - over the composition space. Subsequent Pearson correlation analysis revealed the process-structure-property relationship of complex perovskite materials, indicating that the composition lowering the lattice distortion would yield better efficiency because of formation of single solid solution phase.



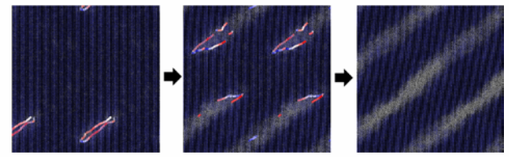
Extensive Monte Carlo samplings allows mapping of structural properties

High fidelity of the ANN model to DFT calculations

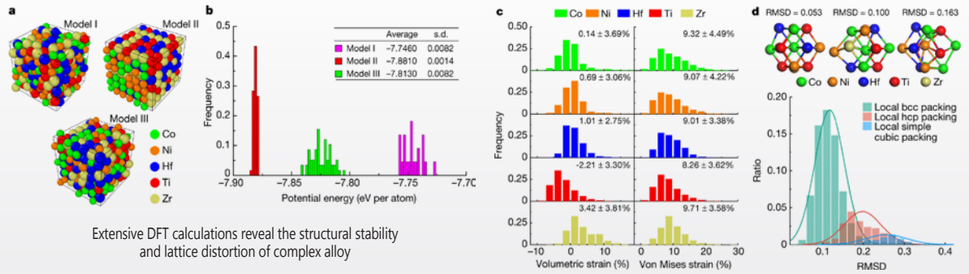
A Highly Distorted Ultra-Elastic Chemically Complex Elinvar Alloy

Quanfeng He, J.G. Wang, Hsin-An Chen, Z.Y. Ding, Z.Q. Zhou, L.H. Xiong, Junhua Luan, J.M. Pelletier, J.C. Qiao, Q. Wang, L.L. Fan, Yang Ren, Qiaoshi Zeng, Chain Liu, C.W. Pao*, David Srolovitz*, Yong Yang*

Nature 602, 251 (2022) In this work, we collaborated with our experimental collaborators in Hong Kong and decoded the atomistic structure of $Ni_{25}Co_{25}(HfTiZr)_{50}$ chemically complex alloy using extensive DFT calculations. From DFT calculations, we revealed the judicious chemical ordering at atomic scale helps retain the stability of crystalline material while undergoing a 11% of atomic size mismatch, which was also confirmed by STEM-EDS experiments. We performed extensive DFT calculations to examine the lattice distortion of the crystal, indicating that each constituent elements is subjected to ~9% of distortion, which is several times more severe than other high entropy alloys, and is the primary factor leading to the ultraelasticity and Elinvar effect of this extraordinary alloy. At this moment we have trained a machine learning energy model for large-scale molecular simulation to further examine its exceptional plastic deformation properties.



Plastic deformation from MLMD simulations (ongoing)



Extensive DFT calculations reveal the structural stability and lattice distortion of complex alloy

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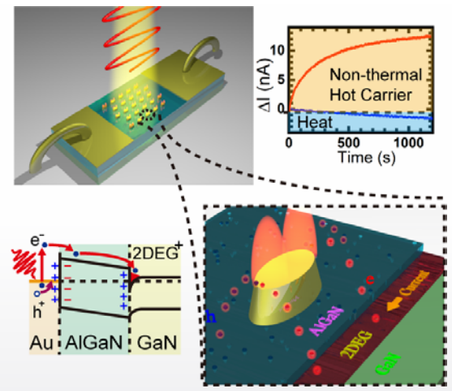
研究重點

Quantifying the Plasmonic Generation Rate of Non-Thermal Hot Carriers with an AlGaN/GaN High-Electron-Mobility Transistor

Chun-Yu Li, Chi-Ching Liu, Wei-Chih Lai, Yung-Chiang Lan*, and Yun-Chorng Chang*

Academic Sinica, Research Center for Applied Sciences
Advanced Sciences, 2021, DOI: 10.1002/advs.202100362

Plasmonic generation of hot carriers in metallic nanostructures has attracted much attention due to its great potential in several applications. However, it is highly debated whether the enhancement is due to the hot carriers or the thermal effect. Here, the ability to exclude the thermal effect and detect the generation of non-thermal hot carriers by surface plasmon is demonstrated using an AlGaN/GaN high-electron-mobility transistor. This ultrasensitive platform, which demonstrates at least two orders of magnitude more sensitivity compared to the previous reports, can detect the hot carriers generated from discrete nanostructures illuminated by a continuous wave light. The quantitative measurements of hot carrier generation also open a new way to optimize the plasmonic nanoantenna design in many applications.



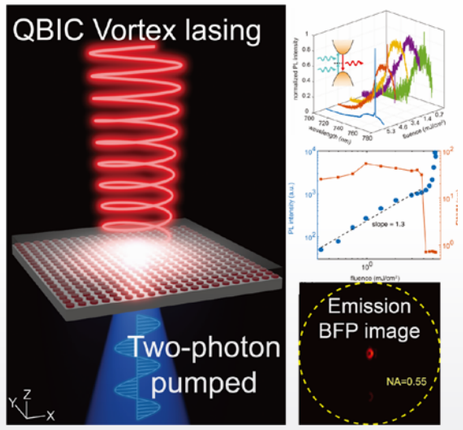
Schematical illustration of hot-electron generation and injection into the 2DEG of an AlGaN HEMT device

Nonlinear Two-photon Pumped Vortex Lasing Based on Quasi-Bound States in the Continuum from Perovskite Metasurface

Chi-Ching Liu, Hui-Hsin Hsiao and Yun-Chorng Chang*

Academic Sinica, Research Center for Applied Sciences
Science Advances, 2023, DOI: 10.1126/sciadv.adf6649

The experimental observation of nonlinear two-photon pumped vortex lasing from perovskite metasurfaces is demonstrated for the first time. The vortex lasing beam is based on symmetry-protected quasi-bound states in the continuum (QBIC). The topological charge is estimated to be +1 according to the simulation result. The quality factor and lasing threshold is around 1100 and 4.28 mJ/cm^2, respectively. Theoretical analysis reveals that the QBIC mode originates from the magnetic dipole mode. The lasing wavelength can be experimentally designed within a broad spectral range by changing the diameter and periodicity of the metasurface. The finite array size effect of QBIC can affect the quality factor of the lasing and be used to modulate the lasing. Results shown in this study can lead to more complex vortex beam lasing from a single chip and new ways to obtain ultrafast modulation of the QBIC lasing via finite array size effect.



Schematical illustration of two-photon pumped vortex lasing based on QBIC

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- 2D material epitaxy and optoelectronic devices.
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- Quantum photonic devices.

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2. Chi-Huang Chuang, Pei-Hao Kang, Yung-Yu Lai, Cheng-Hung Hou, and Yuh-Jen Cheng*, "Junction Engineering in Si Photoanode for Efficient Photoelectrochemical Water Splitting," ACS Appl. Energy Mater. 5, 7, 8483–8491 (2022).
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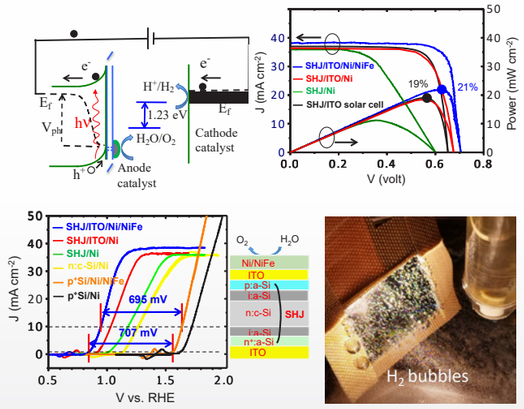
研究重點

Junction Engineering in Si Photoanode for Efficient Photoelectrochemical Water Splitting

Chi-Huang Chuang, Pei-Hao Kang, Yung-Yu Lai, Cheng-Hung Hou, and Yuh-Jen Cheng

ACS Appl. Energy Mater. 2022, doi.org/10.1021/acsaem.2c00974

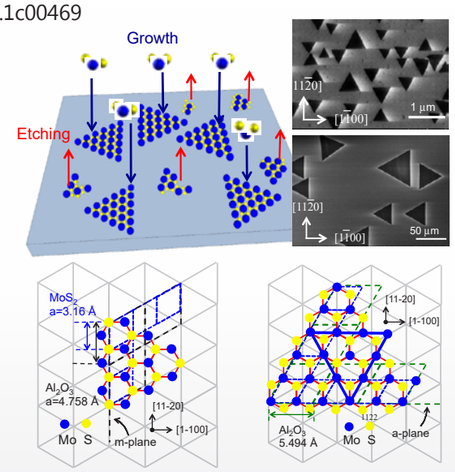


Hydrogen is a potential sustainable green energy fuel to tackle global warming problems caused by the use of fossil fuel. Its high-energy density and zero CO2 emission in combustion and the ability to be converted back electricity make it an attractive alternative fuel of the future. One attractive approach to produce green hydrogen is to integrate electrolysis catalyst with Si solar cell semiconductor to generate electricity from sunlight to drive water-spitting reaction. Through careful design of Si heterojunction (SHJ), the use of highly active nonprecious NiFe catalyst, and introducing a charge transport and passivation ITO interlayer, this SHJ photoanode exhibits a record high photovoltage of 707 mV to drive water splitting reaction. The integrated photoelectrode increases the underlying Si SHJ solar cell efficiency from 19 to 21 % and exhibits a high solar to hydrogen conversion efficiency of 15 %, demonstrating the promising potential of solar cell/catalyst integration.

Substrate Lattice Guided MoS_2 Crystal Growth

Yung-Yu Lai, Chi-Huang Chuang, Cheng-Hung Hou, and Yuh-Jen Cheng

ACS Appl. Nano Mater. 2021, doi.org/10.1021/acsanm.1c00469



Two-dimensional (2D) monolayer molybdenum disulfide (MoS_2) semiconductor is an emerging material with interesting device applications. 2D crystals grown on a substrate often show random orientations due to the weak van der Waals (vdW) interaction with the underlying substrate, leading to multiple defective grain boundaries when random orientated crystals coalesce together. By introducing a carefully adjusted oxygen flow in the growth environment, it can selectively etch away and prohibit the growth of unstable and defective MoS_2, while allowing energetically stable crystal structure to grow. Under a proper flow condition, single crystals are found to grow in two preferential orientations with triangle crystal edges aligned to two sapphire crystal directions, corresponding to a superlattice of (3x3) MoS_2 on (2x2) sapphire and (5x5) MoS_2 on (3x3) sapphire. The commeasure of MoS_2 crystal with sapphire lattice in superlattice lowers the surface energy of MoS_2 on sapphire lattice, thereby becoming the preferred stable growth orientation. This study demonstrates the use of etching-growth competition to realize a substrate lattice guided 2D material growth, paving the way for the future development of vdW single crystal epitaxy.

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- Plasmonics, nanophotonics, and metamaterials
- Plasmonic transition metal nitride materials and the green photonics
- Atom-scale light-matter interaction
- Ultrafast charge-carrier dynamics

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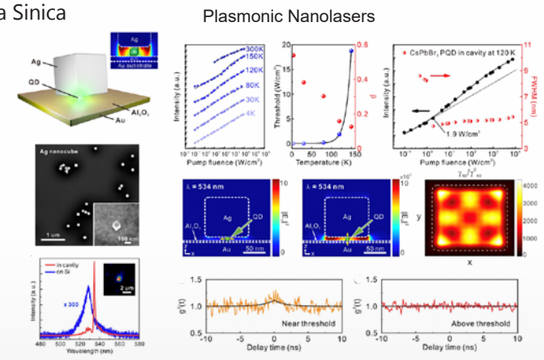
Perovskite Quantum Dot Lasing in a Gap-Plasmon Nanocavity with Ultralow Threshold

Yu-Hung Hsieh, Bo-Wei Hsu, Kang-Ning Peng, Kuan-Wei Lee, Chih Wei Chu, Shu-Wei Chang, Hao-Wu Lin*, Ta-Jen Yen*, and Yu-Jung Lu*

Research Center for Applied Sciences, Academia Sinica
ACS Nano **14**, 11670–11676 (2020).



Lasing signatures and the lasing mechanism of a single perovskite quantum dot (PQD) in a localized gap plasmon cavity at 120 K. The temporal coherence signature of the PQD nanolasing under 120 K was determined.

Lead halide perovskite materials have recently received considerable attention for achieving an economic and tunable laser owing to their solution-processable feature and promising optical properties. However, most reported perovskite-based lasers operate with a large lasing-mode volume, resulting in a high lasing threshold due to the inefficient coupling between the optical gain medium and cavity. Here, we demonstrate a novel continuous-wave (CW) nanolasing from a single lead halide perovskite ($CsPbBr_3$) quantum dot (PQD) in a plasmonic gap-mode nanocavity with an ultralow threshold of 1.9 Wcm^{-2} under 120 K. The calculated ultrasmall mode volume (~0.002 λ^3) with a z-polarized dipole and the significantly large Purcell enhancement at the corner of the nanocavity dramatically enhance the light-matter interaction in the nanocavity, thus facilitating lasing. The demonstration of PQD nanolasing with an ultralow-threshold provides a new approach for realizing on-chip electrically driven lasing and integration into on-chip plasmonic circuitry for ultrafast optical communication and quantum information processing.

Gate-Tunable Plasmon-Enhanced Photodetection in a Monolayer MoS_2 Phototransistor with Ultrahigh Photoresponsivity

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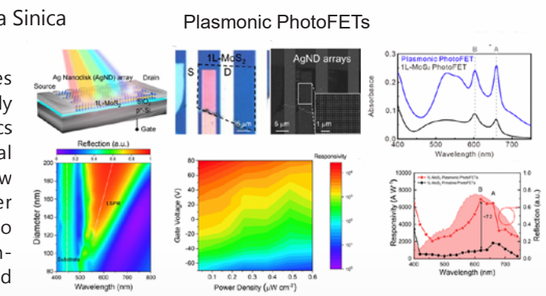
Nano Letters **21**, 3083–3091 (2021)



Monolayer MoS_2 plasmonic phototransistors (photoFETs) that consist of a monolayer MoS_2 and a 2D plasmonic crystal with square arrays of Ag nanodisks (AgND). Photoresponsivity of the plasmonic photoFETs and pristine photoFETs as a function of illumination wavelength reveals the working principle of the ultrahigh photoresponsivity in monolayer MoS_2 plasmonic photoFETs.

Monolayer transition metal dichalcogenides (TMDs)—direct bandgap materials with an atomically thin nature—are promising materials for electronics and photonics, especially at highly scaled lateral dimensions. However, the characteristically low total absorption of photons in the monolayer TMD has become a challenge in the access to and realization of monolayer TMD-based high-performance optoelectronic functionalities and devices. Here, we demonstrate gate-tunable plasmonic phototransistors (photoFETs) that consist of monolayer molybdenum disulfide (MoS_2) photoFETs integrated with the two-dimensional plasmonic crystals. The plasmonic photoFET has an ultrahigh photoresponsivity of $2.7x10^4$ AW^{-1}, achieving a 7.2-fold enhancement in the photocurrent compared to pristine photoFETs. This benefits predominately from the combination of the enhancement of the photon-absorption-rate via the strongly localized-electromagnetic-field and the gate-tunable plasmon-induced photocarrier-generation-rate in the monolayer MoS_2. These results demonstrate a systematic methodology for designing ultrathin plasmon-enhanced photodetectors based on monolayer TMDs for next-generation ultra-compact optoelectronic devices in the trans-Moore era.

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專長及研究重點

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- Energy Materials
- Solid-state Materials

代表著作

1. Hsu, J.-Y.; Chung, R.-J.; Kuo, Y.-L.; Lin, C. C. Majewska, N.; Kreft, D.; Mahlik, S.*; **Fang, M. H.*** Concentration-Induced Hetero-Valent Partial-Inverse Occupation of Infrared Phosphor. *Adv. Optical Mater.* **2023**, 11, 2300121.
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3. Hsu, J.-Y.; Chung, R.-J.; Majewska, N.; Kreft, D.; Sheu, H.-S.; Lee, J.-F.; Mahlik, S.; **Fang, M. H.*** Probing Local Structural Change by Sharp Luminescent Infrared Nano-Phosphor for Application in Light-Emitting Diodes. *Chem. Mater.* **2022**, 34, 11093–11100.
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8. **Fang, M. H.**; Yang, T. H.; Lesniewski, T.; Lee, C.; Mahlik, S.; Grinberg, M.; Peterson, V. K.; Didier, C.; Pang, W. K.; Su, C.*; Liu, R. S.* Hydrogen-Containing $Na_3HTi_{1-x}Mn_xF_8$ Narrow-Band Phosphor for Light-Emitting Diodes. *ACS Energy Lett.* **2019**, 4, 527–533.
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研究重點

Sharp Emission Infrared Phosphors for the Application in Light-Emitting Diodes

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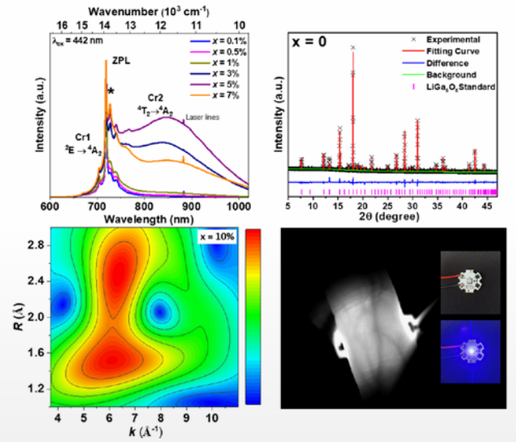
Chem. Mater. **2022**, 34, 11093–11100.
Adv. Optical Mater. **2023**, 11, 2300121.



Infrared (IR) luminescent materials have elicited much attention due to their diverse applications. However, most studies focus on broadband Cr^{3+}-doped phosphors, and the control mechanism of Cr^{3+}-doped phosphors with sharp line emission remains ambiguous. Here, we report systematic research on $LiGa_5O_8:Cr^{3+}$ phosphors by tuning the local structure via the incorporation of Al^{3+} ions and controlling the concentration of the activators. The unexpected two-site emission is explained and well-resolved by the synchrotron techniques and Raman spectra. Furthermore, the morphologies of phosphors with high aluminum concentration demonstrate their great potential for mini-LED applications. Finally, the LED package is conducted and reveals the potential for angiographic applications. This study opens up a new understanding and perspective for the Cr^{3+}-doped sharp emission phosphor and reveals their potential for LED applications.

Quantum Dot–vitrimer Composites: An Approach for Reprocessable, Self-healable, and Sustainable Luminescent Materials

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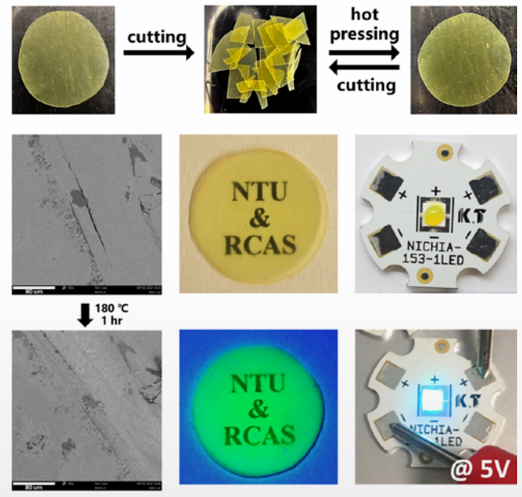
ChemSusChem **2023**, 16, 202300227e.



Quantum dots (QDs) are of great concern in many fields. However, they suffer from high toxicity and may lead to environmental pollution. We report the development of a QD–vitrimer composite with reprocessable, self-healable, and sustainable properties. Our QD–vitrimer composite reveals fine transparency and highly uniform QDs distribution without significant aggregation. The photoluminescence quantum yield (PLQY) is basically about 3–4 times higher than the commercial QD films. The QD–vitrimer composites can be recycled at least for three times without any significant lost in structure and luminescence efficiency. A prototype light-emitting diode device is fabricated to demonstrate the promising potential of QD–vitrimer composites in real application. This research sheds light on developing environmentally friendly luminescent materials and opens up an avenue for designing advanced nanomaterials–vitrimer composites.

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專長及研究重點

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研究重點

Remarkably Deep Moiré Potential for Intralayer Excitons in $MoSe_2/MoS_2$ Twisted Heterobilayers

Bo-Han Lin, Yung-Chun Chao, I-Ta Hsieh, Chih-Piao Chuu, Chien-Ju Lee, Fu-Hsien Chu, Li-Syuan Lu, Wei-Ting Hsu, Chun-Wei Pao, Chih-Kang Shih, Jung-Jung Su, and Wen-Hao Chang

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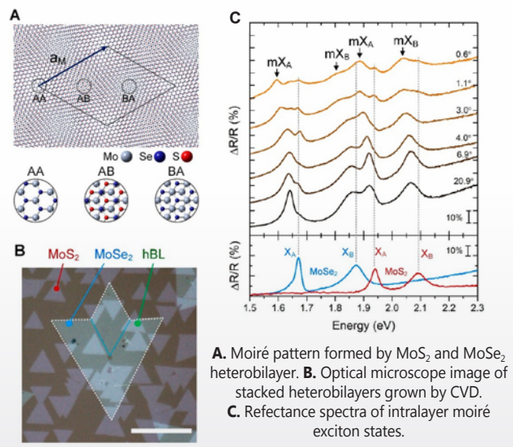
Department of Electrophysics, National Yang Ming Chiao Tung University

Nano Letters 2023, DOI:10.1021/acs.nanolett.2c04524

A moiré superlattice formed in twisted van der Waals bilayers can be a new tuning knob for creating new electronic and excitonic states in 2D materials. However, quantifying the moiré potential for excitons is nontrivial. By creating a large ensemble of $MoSe_2/MoS_2$ heterobilayers with a systematic variation of twist angles, we map out the minibands of interlayer and intralayer excitons as a function of twist angles, from which we determine the moiré potential for excitons. Surprisingly, the moiré potential depth for intralayer excitons is up to ~130 meV, comparable to that for interlayer excitons. The remarkably deep intralayer moiré potential is understood within the framework of structural reconstruction within the moiré unit cell.



A. Moiré pattern formed by MoS_2 and $MoSe_2$ heterobilayer. **B.** Optical microscope image of stacked heterobilayers grown by CVD. **C.** Refectance spectra of intralayer moiré exciton states.

Moiré Potential Impedes Interlayer Exciton Diffusion in Van der Waals Heterostructures

Junho Choi, Wei-Ting Hsu, Li-Syuan Lu, Liuyang Sun, Hui-Yu Cheng, Ming-Hao Lee, Jiamin Quan, Kha Tran, Chun-Yuan Wang, Matthew Staab, Kayleigh Jones, Takashi Taniguchi, Kenji Watanabe, Ming-Wen Chu, Shangjr Gwo, Suenne Kim, Chih-Kang Shih, Xiaoqin Li, Wen-Hao Chang

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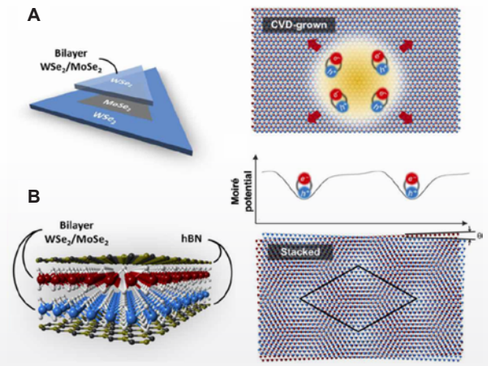
Science Advances 2020, DOI: 10.1126/sciadv.aba8866

In a moiré crystal with a large supercell and deep potential, interlayer excitons may be completely localized. As the moiré period reduces at a larger twist angle, excitons can tunnel between supercells and diffuse over a longer lifetime. The diffusion should be the longest in commensurate heterostructures where the moiré superlattice is completely absent. Here, we experimentally demonstrate the rich phenomena of interlayer exciton diffusion in $WSe_2/MoSe_2$ heterostructures by comparing several samples prepared with chemical vapor deposition (CVD) and mechanical stacking with accurately controlled twist angles.



A. Commensurate $WSe_2/MoSe_2$ heterobilayer without moiré potential formed by direct CVD growth. **B.** Mechanically stacked twisted $WSe_2/MoSe_2$ heterobilayer with moiré potential formed by direct CVD growth.

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研究重點

Boost lasing performances of 2-D semiconductor in A hybrid tungsten diselenide monolayer / cadmium selenide quantum dots microcavity laser

Hsiang-Ting Lin, Chiao-Yun Chang, Cheng-Li Yu, Andrew Boyi Lee, Shih-Yu Gu, Li-Syuan Lu, Yu-Wei Zhang, Shih-Yen Lin, Wen-Hao Chang, Shu-Wei Chang, and Min-Hsiung Shih*

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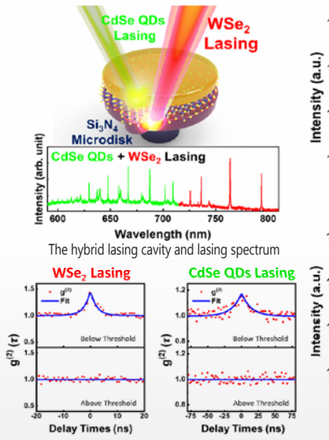
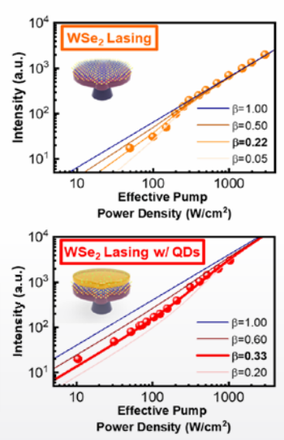
Advanced Optical Materials, 2022, DOI: 10.1002/adom.202200799

We investigated dual-color continuous-wave microcavity lasers by integrating a tungsten diselenide (WSe_2) monolayer and cadmium selenide (CdSe) quantum dots (QDs) into a single microdisk cavity. The hybrid WSe_2/QDs microcavity device not only provides the lasing action in two distinct wavelength regions, but also boost the lasing performances of WSe_2 monolayer because of the energy conversion between two gain materials. The results indicate the lasing threshold of the 2-D WSe_2 monolayer cavity with the CdSe QDs reduces more than 2.5 times, compared to the WSe2 cavity without the QDs. Our findings both expand the wavelength range of TMDC-based compact lasers at room temperature and support their implementation in such applications as photonic integrated circuits, broad-band LEDs, and quantum display systems.



The hybrid lasing cavity and lasing spectrum

Both WSe_2 and QDs lasing confirmed the coherent light emission



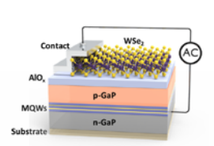
WSe_2 lasing performance is boosting with lower lasing threshold in hybrid cavity

AC-driven multicolor electroluminescence from a hybrid WSe_2 monolayer/AlGaInP quantum well light-emitting device

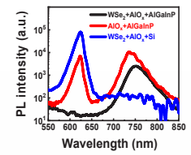
Ya-Hui Chang, Yen-Shou Lin, Konthoujam James Singh, Hsiang-Ting Lin, Chiao-Yun Chang, Zheng-Zhe Chen, Yu-Wei Zhang, Shih-Yen Lin, Hao-Chung Kuo and Min-Hsiung Shih*

Academic Sinica, Research Center for Applied Sciences
Nanoscale, 2023, https://doi.org/10.1039/D2NR03725D

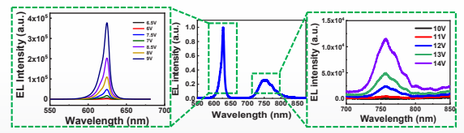
A multicolor AC-driven light-emitting device is developed by integrating a WSe_2 monolayer and AlGaInP–GaInP multiple quantum well (MQW) structures. The CVD-grown WSe_2 monolayer was placed on the top of an AlGaInP-based light-emitting diode (LED) wafer to create a two-dimensional/three-dimensional heterostructure. More than 20% energy conversion from the AlGaInP MQWs to the WSe_2 monolayer was observed to boost the WSe_2 monolayer emissions. Electroluminescence intensity–voltage characteristic curves indicated that thermionic emission was the mechanism underlying carrier injection across the potential barrier at the Ag–WSe_2 monolayer interface at low voltage, whereas Fowler–Nordheim emission was the mechanism at voltages higher than approximately 8.0 V. These multi-color hybrid light-emitting devices both expand the wavelength range of 2-D TMDC-based light emitters and support their implementation in applications such as chip-scale optoelectronic integrated systems, broad-band LEDs, and quantum display systems.



Device structur



Color conversion phenomena associated with the AlGaInP QWs and the WSe_2 monolayer



EL spectra of the device at various voltages and fixed frequency (AlGaInP-based MQW (left) and WSe_2 emissions (right))

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- Emerging materials for sustainable energy

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代表著作

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研究重點

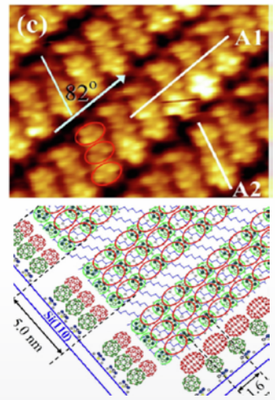
Self-organized C_{70}/C_{60} heterojunction nanowire arrays on Si(110) for Si-based molecular negative differential resistance nanodevices

Ie-Hong Hong, Chai-Jung Gao, Kuan-Bo Lin, and Chao-Cheng Kaun

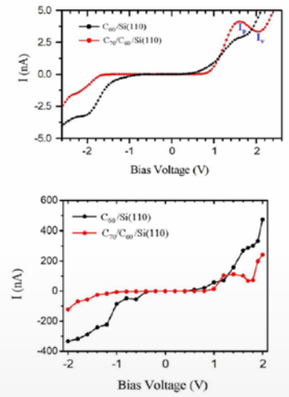
Academic Sinica, Research Center for Applied Sciences

Applied Surface Science, 2020, DOI:10.1016/j.apsusc.2020.147338

The parallel-aligned C_{70}-triplet/C_{60}-triplet heterojunction nanowires over a large area on Si(1 1 0) were successfully constructed through self-assembly. Scanning tunneling spectroscopy results show that these C_{70}/C_{60} heterojunction nanowires on Si(1 1 0) exhibit obvious negative differential resistance (NDR) at room temperature. Using first-principles calculations, we suggest that the observed NDR of C_{70}/C_{60} heterojunction nanowires on Si(1 1 0) is due to the relatively weak interaction between C_{70} molecules and Si(1 1 0) via the spacers of C_{60} molecules. This controlled organic heterojunction nanowire array on Si(1 1 0) provides a feasible way for applications in nanoelectronics.



Topographic STM images of a nanowire array and the corresponding structural model.



The measured and calculated I-V curves of the systems.

Hydrogen Evolution Driven by Photoexcited Entangled Skyrmion on Perovskite $Ca_2Nan_{-3}Nb_nO_{3n+1}$ Nanosheet

Miladina R. Aziza, Chia-Wei Chang, Chao-Cheng Kaun, and Yen-Hsun Su

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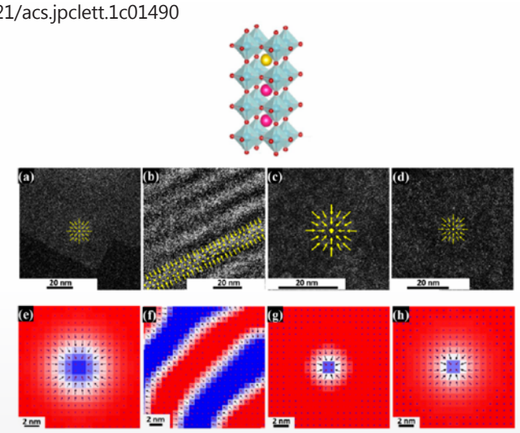
Journal of Physical Chemistry Letters, 2021, DOI:10.1021/acs.jpclett.1c01490

We demonstrate the real-space observation of skyrmions in Dion–Jacobson phase perovskite, Ca2Nan–3NbnO3n+1– (CNNO), nanosheets by using optical injection. The CNNO4 and CNNO6 nanosheets exhibit weak ferromagnetics, while the CNNO5 nanosheet is superparamagnetic. The magnetic skyrmion can be clearly observed in those 2D nanosheets in the absence of the external magnetic field. First-principles calculations and micromagnetic simulations predict that the magnetic skyrmions in CNNO nanosheets is Néel-type with a diameter of 11–15 nm, in corresponding to the experiments. Our findings provide insights for developing room-temperature skyrmions in CNNO nanosheets for skyrmionic water-splitting performance in future energy generation and quantum computing devices.



The structure, HAADF-STEM images and micromagnetic simulations of CNNO nanosheets.

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代表著作

1. **Shih-Yen Lin***, Wei-Hsun Lin, Chi-Che Tseng, Kuang-Ping Chao, and Shu-Cheng Mai, "Voltage-Tunable Two-Color Quantum-Dot Infrared Photodetectors", Appl. Phys. Lett., vol. 95, no. 12, pp. 123504, September 2009.
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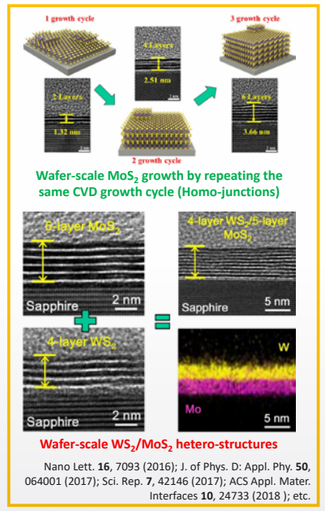
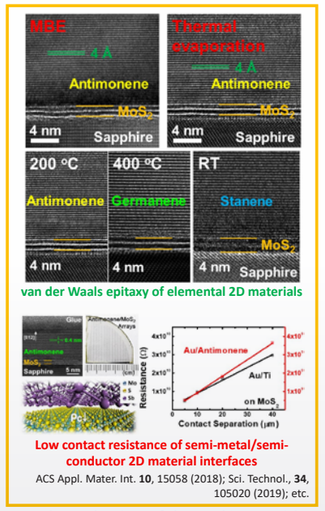
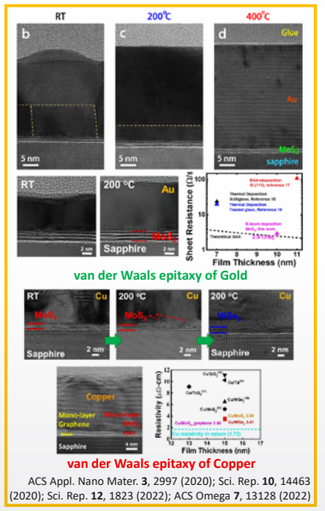
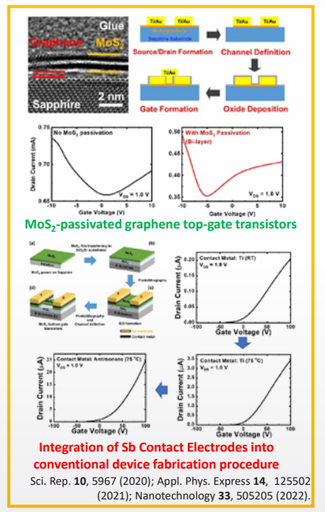
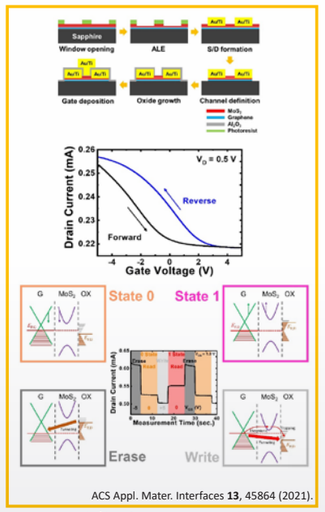
研究重點

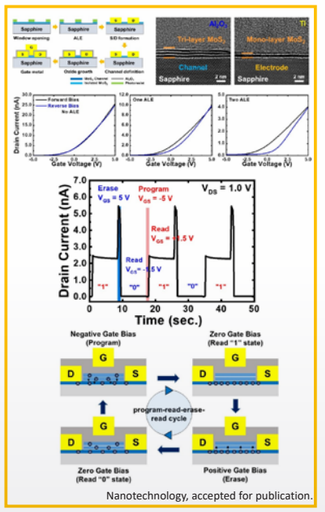












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- Semiconductor Photonics
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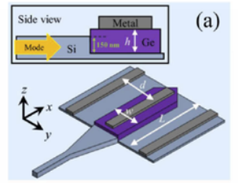
研究重點

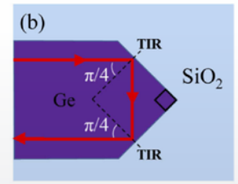
Increasing responsivity-bandwidth margin of germanium waveguide photodetector with simple corner reflector

Chih-Hsien Lin, Ding-Wei Huang, Tien-Tsorng Shih, Hao-Chung Kuo, and Shu-Wei Chang

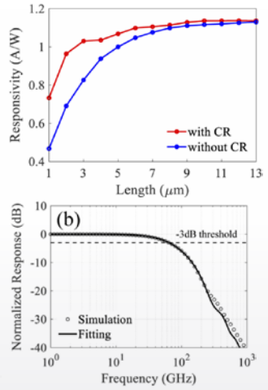
Academic Sinica, Research Center for Applied Sciences
Opt. Express, 2021, DOI: 10.1364/OE.414691

The external bandwidth of germanium waveguide photodetectors (PDs) decreases with the device length due to the load and parasitic effects even if the internal one is less affected. Shortening PDs raises the external bandwidth but lowers the responsivity, introducing a trade-off between the two figures of merits. We present a scheme of waveguide PDs based on total internal reflections of corner reflectors. The reflector can be easily fabricated with the standard photolithography at the end of PDs to efficiently reflect optical power back to germanium for additional absorption, allowing for further size reduction. The structure may render the optimization of PDs more flexible.





Device scheme and total internal reflection at corner mirror



Increment of responsivity due to corner mirror and bandwidth of the device

Spinning Mode with Maximum Chirality in Photonic Crystal Defect Cavity at Exceptional Point

Chao-Chieh Cheng, Pi-Ju Cheng, Tzu-Wei Huang, Wei-Ting Wang, Jui-Tse Tsai, Min-Hsiung Shih, and Shu-Wei Chang

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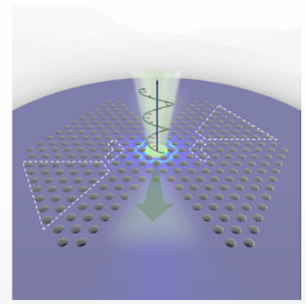
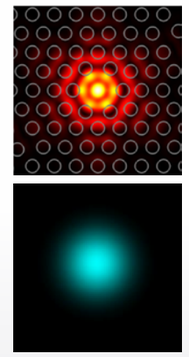
Optica, 2023, DOI: 10.1364/OPTICA. 481825

Optical modes spinning with maximum chirality in cavities at chip level are essential for quantum and biomedical applications. The coalescent chiral mode at the exceptional point (EP) due to non-hermicity is the one in demand. In this work, we realize circularly-polarized-like lasing modes with maximum chirality at the EP of photonic-crystal one-hole cavities. We adopt the in-plane tunneling loss that is well controlled with the layer number of air holes in photonic-crystal slab. By removing and relocating holes in blocks, we systematically elevate the chirality of radiation field. The collective variations of holes render the EP robust against the uncertainty in fabrications. Without auxiliary non-Hermitian and chiral structures, our works promote coherent chiral light sources at chip level.



The schematic of non-Hermitian but chiral H_1 cavity. Some of air holes are collectively removed or relocated (enclosed in white dashed lines) when approaching the EP.



The near-field and far-field patterns of modes at the chiral exceptional point.

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專長及研究重點

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- Low-dimensional materials and mesoscopic assembly.

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代表著作

1. P.-W. Tang, S.-Y. Shiau, H.-C. Chou, J.-R. Yu, X.-Q. Zhang, C.-T. Sung, Y.-H. Lee*, and C. Chen*, Visualization of bandgap evolution and bilayer coupling in WxMo1-xS2 alloy by near-field broadband absorption microscopy. *ACS Nano*, 16, 7503 (2022)
2. H.-C. Chou, X.-Q. Zhang, S.-Y. Shiau, C.-H. Chien, P.-W. Tang, C.-T. Sung, Y.-C. Chang, Y.-H. Lee*, and C. Chen*, Near-field spectroscopic imaging of exciton quenching at the atomically sharp MoS_2/WS_2 lateral heterojunction. *Nanoscale* 14, 6323 (2022)
3. S. Luo, P. P. Lin, L.-Y. Nieh, G.-B. Liao, P.-W. Tang, C. Chen, and J. C. Liao*, A cell-free self-replenishing CO_2 fixing system. *Nature Catalysis* 5, 154 (2022)
4. H.-C. Chou, C.-K. Fang, P.-Y. Chung, J.-R. Yu, W.-S. Liao, S.-H. Chen, P. Chen, I.-S. Hwang, J.-T. Chen*, and C. Chen*, Structural and optical identification of planar side-chains stacking P3HT nanowires. *Macromolecules* 54, 23, 10750 (2021)
5. H.-C. Chou, W.-C. Hsu, Y. Yang, K. S. Schanze*, S.-C Luo *, C. Chen*, "Real-time spectral evolution of interchain coupling and assembling during solvent vapor annealing of dispersed conjugated polymers", *Macromolecular Chemistry and Physics*, 222, 2100125 (2021)
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7. J.-R. Yu, H.-C. Chou, C.-W. Yang, W.-S. Liao, I.-S. Hwang, and C. Chen*, A horizontal-type scanning near- field optical microscope with torsional mode operation toward high-resolution and non-destructive imaging of soft materials. *Review of Scientific Instruments* 91, 073703 (2020)
8. K.-C. Chen, S.-M. Lai, B.-Y. Wu, C. Chen*, and S.-Y. Lin*, Van der Waals epitaxy of large-area and single-crystalline gold films on MoS2 for low contact-resistance 2D–3D interfaces. *ACS Applied Nano Materials* 3, 2997 (2020)
9. V. M. Balois, N. Hayazawa*, C. Chen*, E. Kazuma, Y. Yasuyuki, Y. Kim, T. Tanaka*, Development of tip-enhanced Raman spectroscopy based on a scanning tunneling microscope in a controlled ambient environment, *Japanese Journal of Applied Physics*, 58, SI0801 (2019)

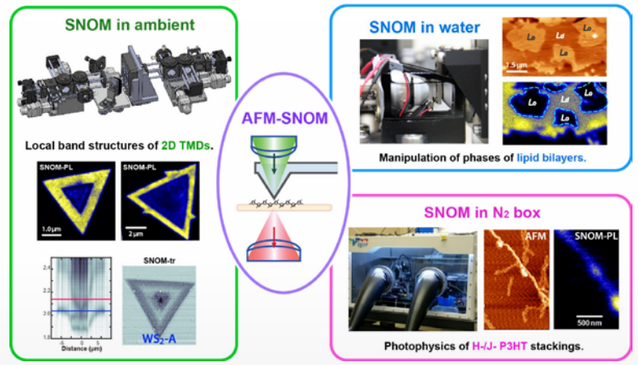
研究重點

Scanning Near-Field Optical Microscopy in Various Environments for Nanoscale Molecular and 2D Material Assemblies

J.-R. Yu, S.-Y. Weng, S.-M. Lai, H.-C. Chou, P.-W. Tang, and Chi Chen*

The primary tool developed in my lab is the home-built AFM-based scanning near-field optical microscopy (SNOM) with spectroscopic readout. Three horizontal-type aperture SNOM instruments in different environments have been successfully constructed and operated to investigate the stacking of 2D materials as well as soft molecular assemblies including polymer nanowires and lipid bilayers.

The SNOM instruments are highly-stable for reproducible topographic scan and optical signaling, which realized high-quality near-field absorption and PL microscopy. We also achieved small amplitude (< 2 nm) tapping mode in glove box and in water to avoid sample damages and to regulate tip-sample interaction. In addition, we have the full control of the near-field tip, including its design, fabrication, and operation.



P.-W. Tang *et al*., ACS Nano, 16, 5, 7503 (2022)
H.-C. Chou *et al*., Nanoscale 14, 6323 (2022)
H.-C. Chou *et al*., Macromolecules 54, 10750 (2021)
J.-R. Yu *et al*., Rev. Sci. Instrum. 91, 073703(2020)

Revealing the Local Band Structures of WS_2/MoS_2 Heterojunction $W_xMo_{1-x}S_2$ Alloy by Near-Field Optical Imaging

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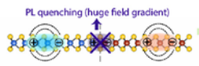
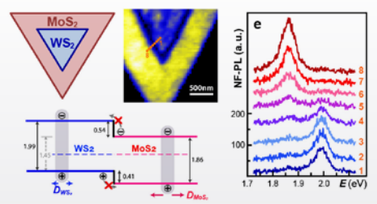
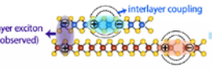
Lateral Heterojunction



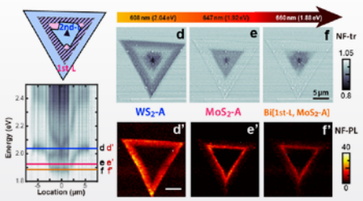
We employed near-field photoluminescence (NF-PL) imaging to study the atomically sharp 1D interfaces between WS_2 and MoS_2 heterojunction with an optical resolution of 68 nm. Our NF-PL imaging resolved the narrowest quenching width (105 nm) and sharpest strain mapping because of the superior spatial resolution and stability of our home-built SNOM.



Vertical Stacking



We further developed a near-field broadband transmission, (NF-tr) imaging method for low-quantum-yield materials. The energy contour maps present the bandgap evolution in the $W_xMo_{1-x}S_2$ alloy and reveal the interlayer coupling in bilayer $W_xMo_{1-x}S_2$. The NF-tr technique provides abbreviation-free and nanoscale-resolution imaging capability of the entire conduction band over highly lateral inhomogeneity.



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- Manipulation of spin states

代表著作

1. N. Chejanovsky, A. Mukherjee*, J. Geng, **Y. C. Chen**, Y. Kim, A. Denisenko. A. Finkler, T. Taniguchi, K. Watanabe, D. B. R. Dasari*. P. Auburger, A. Gali, J. H. Smet, and J. Wrachtrup. Single-spin resonance in a van der Waals embedded paramagnetic defect. Nature Materials 20, 1079-1084 (2021).
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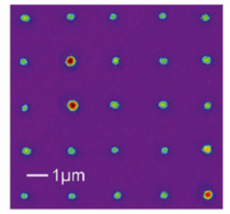
研究重點

Laser writing of individual nitrogen-vacancy defects in diamond with near-unity yield

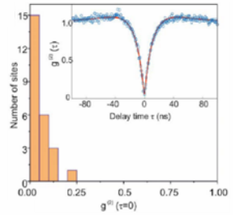
Yu-Chen Chen

Optica 6 (2019): 662-667

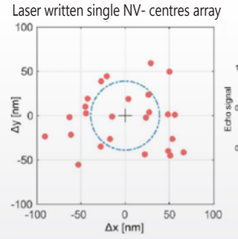
Spin defects in wide band gap materials show a great potential for various quantum applications. Nitrogen-vacancy (NV-) centre in diamond is one of the most promising spin defect. In order to realise quantum applications, it is important to engineer the NV- centre at desired location with high positioning accuracy and yield. Although the traditional single NV- centre generation method can provide high position accuracy, the yield is lower than 50%. We developed a method which using femtosecond laser pulse sequence combined with fluorescence feedback to generate single NV- centres array with yield of 96%. The positioning accuracy of single NV- centres in the image plane is measured to be about 40 nm. Moreover, the laser written single NV- centres still possess good spin coherence properties and the T_2 coherence time was measured up to 170 μs by standard Hahn echo measurements.



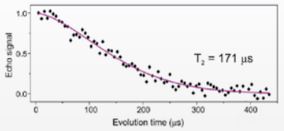
Laser written single NV- centres array



$g^{(2)}(0)$ values histogram



The position of NV- centres relative to target grid



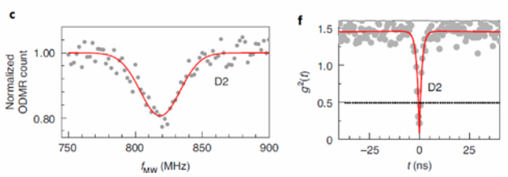
T2 coherence time measured by Hahn echo pulse sequence

Spin readout and manipulation of single defect in hBN 2D material

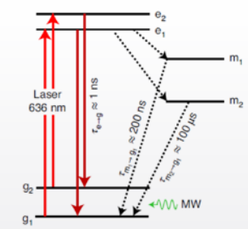
Yu-Chen Chen

Nature Materials 20 (2021): 1079-1084

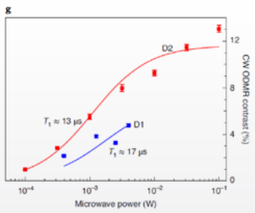
Single photon emitters in hexagonal boron nitride (hBN) have attracted many researchers' attentions, because it can be easily coupled into photonic structures. Moreover, some single photon emitters' zero-phonon line (ZPL) have been found to be Fourier transformed limited linewidth at room temperature. This property pave a way to realise the quantum repeater and quantum communication at room temperature. However, single spin defects was not discovered in the hBN. We have successfully found that some single defects show optically detected magnetic resonance (ODMR). Various laser and microwave pulse sequences were used to investigate the spin dynamics and we built a simple model to describe the results. We concluded that the magnetic resonance locates at the ground state. The g-factor of the defect was measured to be 2.06. The T1 spin coherence time of the spin defects were estimated to be around 13~17 μs.



ODMR signal and $g^{(2)}(t)$ result of a defect in hBN



Model of the level diagram



Estimation of T1 spin coherence time

量子電腦專題中心

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- 奈米材料的電子傳輸特性
- 超導及磁性單電子電晶體的基礎研究及應用
- 超導量子位元晶片與系統

代表著作

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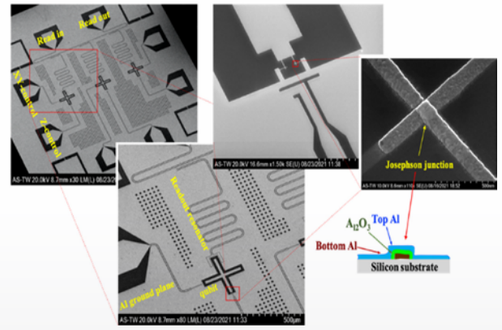
研究重點

Superconducting qubit fabrication using one-step all electron beam lithography lift-off process

Yen-Yu Chiang, Cheng-Chen Huang, Kun-Ying Lu, Lan-Hsuan Lee, Xiao-Cheng Lu, Luo-Uei Liang, Jun-Yi Tsai, Chung-Ting Ke, Cen-Shawn Wu, Yen-Chun Chen, Chii-dong Chen

Our ongoing project is centered on developing a rapid and dependable fabrication technique for superconducting qubit chips. This approach proves invaluable in evaluating various qubit and resonator designs, all within a turnaround time of just two weeks. To achieve this, we've introduced an all-electron-beam-lithography method for the one-step fabrication of superconducting qubits. This encompasses electron resist application, electron beam exposure, development, metal deposition, and lift-off processes, all completed in a single operation. This approach not only enhances fabrication efficiency and quality but also resolves the issue of electrical contacts between base electrodes produced through photolithography and counter electrode fabrication via e-beam lithography. Figure 1 presents SEM images of a fabricated device, depicted at different magnifications.

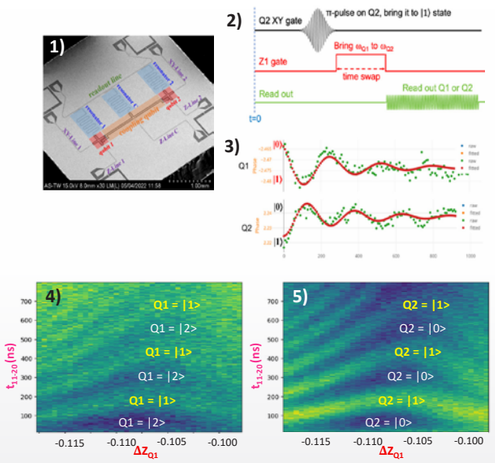


SEM images of a 3-qubit device crafted through a single-step, all-electron-beam lithography lift-off procedure are displayed. Josephson junctions are fashioned using the widely employed tilt-angle evaporation technique, and the lower-right panel exhibits a cross-sectional view of the setup.

Two qubit SWAP gate and CZ gate

Li-Chieh Hsiao, Li-Wei Chang, Dai-Jia Wu, Zong-Yen Zhu, Myrron Albert C. Aguila, David T. Lee, Jyh-Yang Wang, Chung-Ting Ke, Watson Kuo, Chii-dong Chen

Two-qubit gates are foundational for constructing a universal quantum computer, and we have successfully demonstrated the state-swap process between two interconnected qubits, a crucial step in enabling 2Q gate operations. Fig. 1 displays the design of the 2Q circuit featuring a tunable coupling qubit, Qc, while Fig. 2 illustrates the operational procedure. Initially, we raise Q2 to its excited state using a π-pulse. During the idle period, the Z gate for Q1 (Z1) is adjusted to detune it from Q2, effectively separating them. In the subsequent swap process, Z1 is redirected to Q2, allowing the two qubits to become coupled. As portrayed in Fig. 3, this coupling facilitates the exchange of states between |01⟩ and |10⟩ at a frequency corresponding to the Q1-Q2 coupling strength. Similarly, we fine-tuned the CZ gate by bringing $Q1_{1\text{-}2}$ and $Q2_{0\text{-}1}$ into resonance. This resulted in the coherent exchange of energy between |20⟩ and |11⟩, as observed in the correlated Rabi oscillations of both Q1 (Fig. 4) and Q2 (Fig. 5). State readout can be performed on either Q1 or Q2, and the outcomes should reveal opposite states.



重要獎項榮譽

2023	方牧懷	中央研究院前瞻計畫
	包淳偉	有庠科技論文獎
2022	包淳偉	中研院深耕計畫
	朱治偉	全球頂尖 2% 科學家
	朱治偉	國際光學工程（SPIE）資深會員
	林鈺容	國科會補助 2030 跨世代年輕學者方案－新秀學者計畫
	陳　祺	中央研究院前瞻計畫
	楊富量	第十九屆國家新創獎
	謝東翰	第十九屆國家新創獎
	關肇正	國科會未來科技獎
2021	呂宥蓉	國際光電工程學會 SPIE Women in Optics Planner, USA
	施閔雄	2021 International Electron Devices & Materials Symposium (IEDMS), 論文獎
	施閔雄	2021 Optics & Photonics Taiwan International Conference (OPTIC), 論文獎
	陳培菱	中研院深耕計畫
	陳壁彰	中央研究院年輕學者研究成果獎
	魏培坤	中研院特優學術研究獎
	關肇正	科技部未來科技獎
2020	呂宥蓉	中華民國光電學會青年光電工程獎
	林鈺容	財團法人李昭仁教授生醫工程發展基金會年輕學者獎
	陳壁彰	2020 第十八屆有庠科技論文獎－光電組
	郭志禹	中華水土保持學會論文獎
	楊富量	第十七屆國家新創獎
2019	朱治偉	亞太材料學院副院士
	朱治偉	亞太材料青年學者表率
	林榮信	中央研究院深耕計畫
	陳培菱	英國皇家化學學會會士
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2014	張允崇	國際光電學會（SPIE）資深會員
2012	楊富量	第九屆國家新創獎

中心核心設施

本中心核心設施是為提供本中心及本院研究同仁進行研究使用，分布在跨領域大樓六樓、四樓及地下二樓，目前中心內核心設施依功能可分為三大類型：高解析顯微鏡、樣品分析及微奈米製程（如下圖表一）。

表一、核心設施資訊

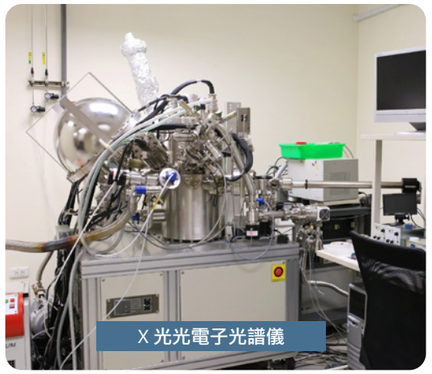
類型	儀器	功能	廠牌	位置
高解析顯微鏡	原子力顯微鏡	材料表面分析	Bruker DM-CAFM	交大田家炳中心 506 室
	快速雷射掃描共軛焦分光光譜顯微鏡	生物暨螢光樣品量測	Leica TCS-SP5	跨領域 4B20
	液相原子力顯微鏡	奈米材料或元件液態檢測	JPK Nano Wizard II & III	跨領域 B2 公用實驗室
	顯微拉曼光譜儀	材料螢光及結晶特性分析	Jobin Yvon HR800	跨領域 6B08
	場發射高低真空高解析度掃描式電子顯微鏡	表面結構與元素分析	Nova 200 NPE 44/ D8187	跨領域 4C05
樣品分析	X 光光電子光譜儀	表面與縱深元素分析	ULVAC-PHI PHI-5000 Versaprobe	跨領域 4C05
	掃描式離子顯微鏡	表面與縱深元素與分子分析	ULVAC-PAI TRIFTV	跨領域 4C05
	皮秒時間相關單分子螢光顯微光譜儀	多通道的時間解析光譜系統	PicoQuant Micro Time 2000	跨領域 6B10
	可變角度橢圓儀	材料膜厚及折射率分析	VUV-VASE,Gen-II	跨領域 6A02
	奈米級雷射非接觸式 3D 表面量測儀	奈米級表面輪廓 / 粗糙度量測	Keyence VK9710K S/ N 2190011	跨領域 4C01
	桌上型直寫曝光系統	元件光阻圖樣製作	Heidelberg uPG501	跨領域 B2 微製程室
微米製程	試片準備機一套	表面薄膜製程與蝕刻	Gated Sted SKE104005	跨領域 6A02
	高解析高精密雙束聚焦離子系統	奈米元件結構製作	FEI NanoLab660	跨領域 4B19
	電感耦合電漿蝕刻機	奈米元件乾溼蝕刻	OXFORD ICP65	跨領域 B2 微製程室

行政人員

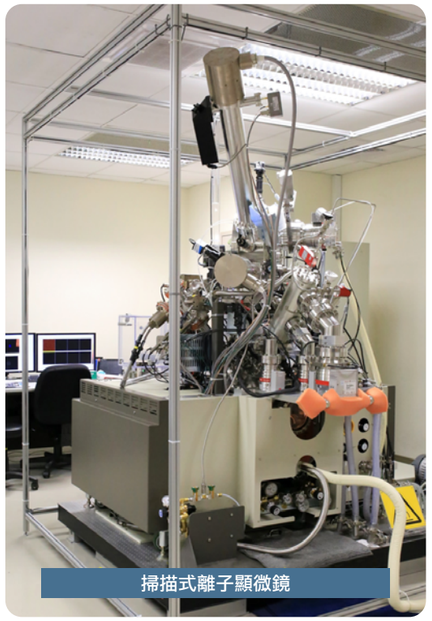
本中心的核心設備主要能協助同仁進行生醫影像觀測、材料表面分析、元件結構製作及精密樣品製程等研究；除了核心設施，中心在六樓、四樓及地下二樓都有公用實驗室，配合同仁進行相關製程、影像、細胞及蛋白質研究。

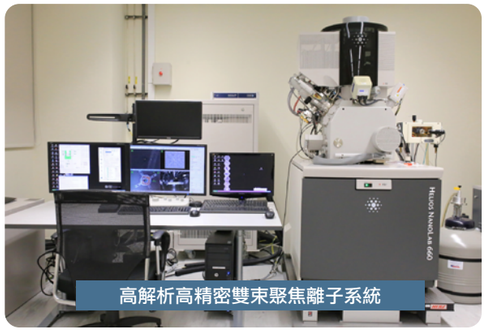
使用者具備本院實驗安全認證後，皆可經由儀器訓練取得核心設施的使用權限，不過具有毒性、揮發性、爆炸性的化學物質不得使用，生物樣品則須於使用記錄備註，磁性及粉體樣品則由管理人員同意才能進行；所有設施使用皆須經由預約 (http://scheduler.rcas.sinica.edu.tw./)，並且填寫使用記錄。

所有設施每年都會進行例行性維護保養，本中心也會視情況進行設施升級及相關實驗室配置改善，為了讓同仁安全地進行研究，中心對於各實驗室及設施都有相對應的安全規劃及管理。


X 光光電子光譜儀


快速雷射掃描共軛焦分光光譜顯微鏡


掃描式離子顯微鏡


高解析高精密雙束聚焦離子系統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