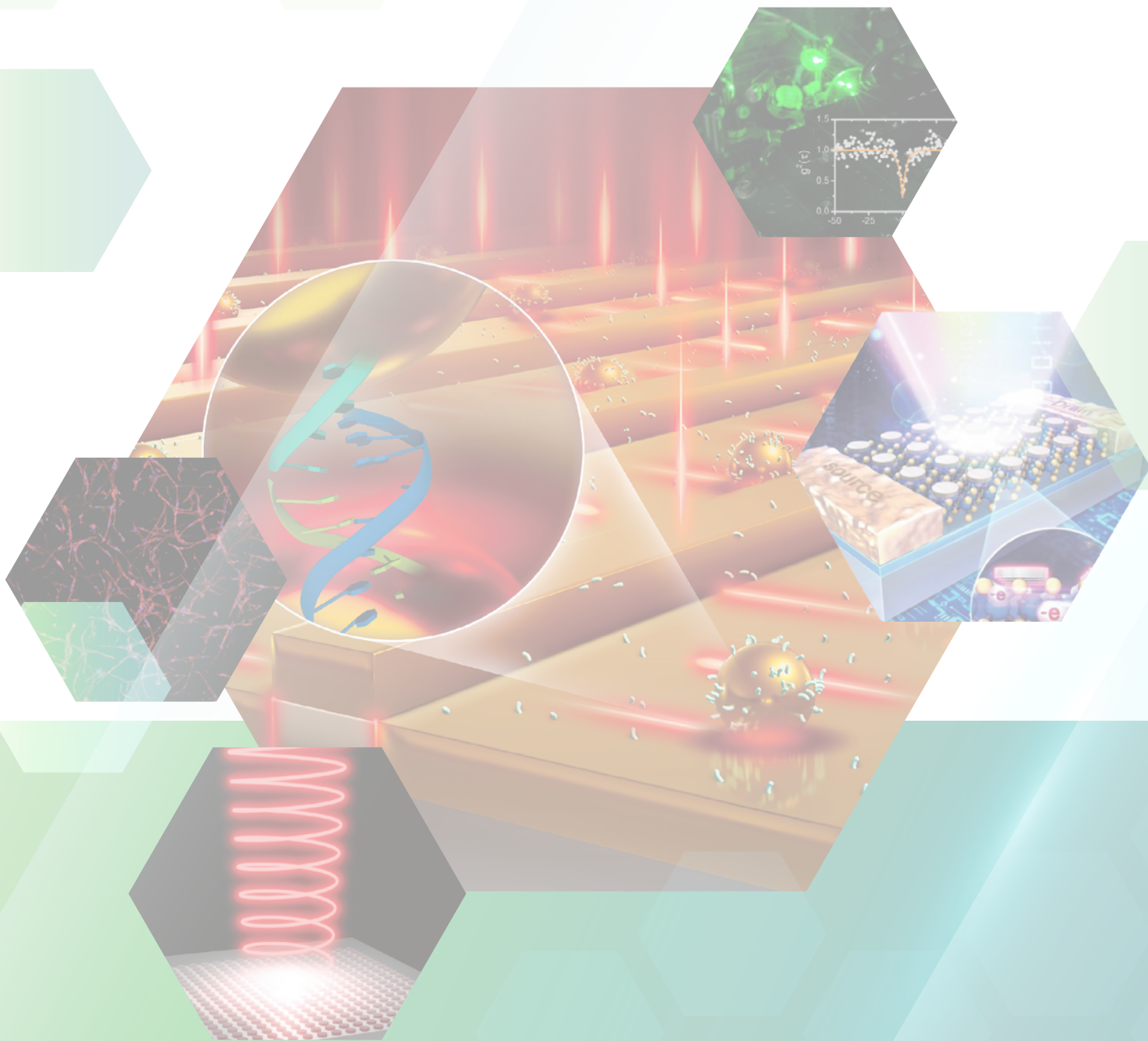




*Academia Sinica*

# Research Center for Applied Sciences



Research Center for Applied Sciences Academia Sinica

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## Mission

RCAS employs cutting-edge science and technology to conduct interdisciplinary applied science research for achieving local impact and global excellence.

RCAS has four thematic centers: Intelligence BioEngineering, Green Technology, Quantum Photonics, and Quantum Computer.

## Cooperation outside Academia Sinica (MOU)

<i>January 1<sup>st</sup>, 2012</i>	National Chiao Tung University (Academic Cooperation Agreement on Optoelectronic Technology)
<i>December 3<sup>rd</sup>, 2012</i>	Department of Materials Science and Engineering, National Dong Hwa University
<i>December 3<sup>rd</sup>, 2012</i>	Department of Physics, National Dong Hwa University
<i>July 31<sup>st</sup>, 2012</i>	The Hebrew University of Jerusalem in Israel
<i>January 24<sup>th</sup>, 2013</i>	Molecular Biomedical Imaging Center, National Taiwan University
<i>August 14<sup>th</sup>, 2013</i>	Department of Photonics/ Materials and Optoelectronic Science/ Physics/ Mechanical and Electromechanical Engineering, National Sun Yat-sen University
<i>February 18<sup>th</sup>, 2014</i>	College of Engineering, Chang Gung University
<i>February 18<sup>th</sup>, 2014</i>	College of Biomedical Science and Engineering, National Yang Ming University
<i>December 22<sup>nd</sup>, 2014</i>	Research Institute of Electronic Science, Hokkaido University, Japan
<i>July 17<sup>th</sup>, 2014</i>	Graduate Institute of Applied Physics and Department of Physics, National Taiwan University
<i>May 1<sup>st</sup>, 2015</i>	Department of Photonics, National Cheng Kung University
<i>August 26<sup>th</sup>, 2016</i>	Department of Materials Science and Engineering, National Tsing Hua University
<i>March 25<sup>th</sup>, 2020</i>	Department of Applied Science, National Taitung University
<i>July 27<sup>th</sup>, 2020</i>	School of Engineering, The University of Tokyo, Japan
<i>August 1<sup>st</sup>, 2020</i>	Abbe Center of Photonics, Friedrich Schiller University Jena
<i>January 1<sup>st</sup>, 2021</i>	Leibniz Institute of Photonic Technology e. V.

## Elite Scholarship Program MOU

- Department of Photonics, National Yang Ming Chiao Tung University
- Department of Electrophysics, National Yang Ming Chiao Tung University
- College of Photonics, National Yang Ming Chiao Tung University
- Department Of Materials Science and Engineering, National Yang Ming Chiao Tung University
- College of Biological Science and Technology, National Yang Ming Chiao Tung University
- Brain Research Center, National Tsing Hua University
- Department of Life Science, National Tsing Hua University
- Department of Materials Science and Engineering, National Tsing Hua University
- Department of Chemical Engineering, National Tsing Hua University
- Institute of Biophotonics, National Yang-Ming University
- Department of Photonics, National Cheng Kung University
- College of Engineering, Chang Gung University
- Ph.D. Program of Green Materials and Precision Devices, National Taiwan University
- Department of Chemistry, National Taiwan University

### Prof. Li-Chyong Chen



Distinguished Research Fellow, Center for Condensed Matter Sciences, National Taiwan University, Taiwan

國立臺灣大學凝態中心特聘研究員

### Prof. Tai Chang Chiang



Research Professor, Department of Physics, University of Illinois, USA

美國伊利諾伊大學香檳分校物理系名譽教授及研究教授

### Prof. Hiroaki MISAWA



(Specially Appointed) Professor, RIES – Research Institute for Electronic Science, Hokkaido University, Japan

北海道大學電子科學研究所特任教授

### Prof. Chung-Yuan Mou (Chair)



Professor Emeritus, Distinguished Chair Professor for Research, Department of Chemistry, National Taiwan University, Taiwan

國立臺灣大學化學系名譽教授

### Prof. Yu-Chong Tai



Anna L. Rosen Professor of Electrical Engineering and Mechanical Engineering, California Institute of Technology (Caltech), USA

加州理工學院電機及機械工程系 Anna L. Rosen講座教授

### Prof. Nai-Chang Yeh



Professor of Physics, California Institute of Technology (Caltech), USA

加州理工學院物理系教授

### 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

The mission of the Thematic Center for Intelligence Bioengineering is to advance biomedical applications through the development of innovative sensing, imaging, characterization, and fabrication technologies. Our focus is on topics that have the potential for industrial value in biotechnology or high-impact clinical applications. The center is comprised of eleven principal investigators (PIs): Dr. Peilin Chen, Dr. Pei-Kuen Wei, Dr. Ji-Yen Cheng, Dr. Fu-Liang Yang, Dr. Chau-Hwang Lee, Dr. Jung-Hsin Lin, Dr. Jing-Jong Shyue, Dr. Yi-Chung Tung, Dr. Chih-Yu Kuo, Dr. Bi-Chang Chen and Dr. Yu-Jung Lin, as well as two research specialists, Dr. Tung-Han Hsieh and Dr. Shu-Yi Hsieh. Collaboration with the research institutes of the Life Science Division in Academia Sinica and medical institutes of universities in Taiwan is a key aspect of this thematic center.

The major research fields of the Thematic Center for Intelligence Bioengineering include 1) the development of ultra-resolution microscopic and spectroscopic tools to investigate the chemistry, physics, mechanics, and genetics in cells and cell-cell microenvironment interactions; 2) the fabrication of nano-biosensors and nanoparticles for drug delivery or labeling; and 3) the study of intelligence computation for bio-molecular interactions and biomedical applications.

Our thematic center has made significant progress in research over the past few years, primarily in three key areas: developing sophisticated imaging and sensing technologies, integrating artificial intelligence into traditional experimental and theoretical tools, and advancing drug delivery systems. In the realm of imaging and sensing, we've made groundbreaking progress. We've successfully innovated lightsheet expansion microscopy to match the resolution of electron microscopes. We've applied cluster ion beams and secondary ion mass spectrometry to investigate organic-inorganic composites. We've created a high-throughput drug screening platform that utilizes cellular traction forces. Additionally, we've developed a surface plasmon resonance (SPR)-based digital nanoplasmonmetry (DiNM) method for the sensitive detection of biomolecules, eliminating the need for labeling. We've also employed a 3D cell co-culture system to evaluate the synergistic effects of anti-fibrotic and anti-cancer drugs on lung cancer cells and cancer-associated fibroblasts. Through this research, we've identified four genes in fibroblasts that could potentially be suppressed by the anti-fibrotic drug nintedanib.

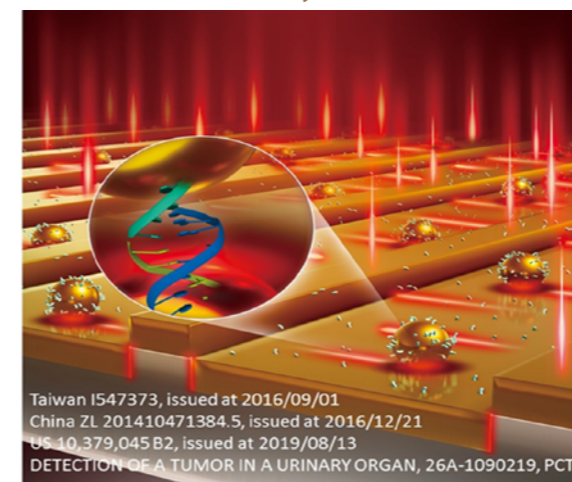
With respect to artificial intelligence integration, we've made considerable advancements. Our AI Deduction Learning Non-Invasive Blood Glucose Meter earned us the National Innovation Award. Furthermore, we've introduced a unique computational approach to calculate the standard free energy of binding based on the statistical mechanics of biomolecular interactions in an all-atom explicit solvent description. This method has proven useful in protein-protein, protein-peptide, and protein-small molecule systems. We've also successfully applied machine learning to Raman image spectra categorization for illicit drug detection. To aid in the development of biomedical sensors for pesticide molecules, we've synthesized various oligopeptide fragments and composite metal nanostructures.

Finally, in the drug delivery sector, we've made recent breakthroughs in creating delivery systems for cold-mimetic and heat-mimetic compounds. We've designed a dissolving hydrogel system to release the cold-mimetic compound menthol gradually. This release mechanism triggers adipocyte browning, presenting a potential solution for obesity and associated metabolic disorders. Our thematic center has also developed in vitro cell culture models

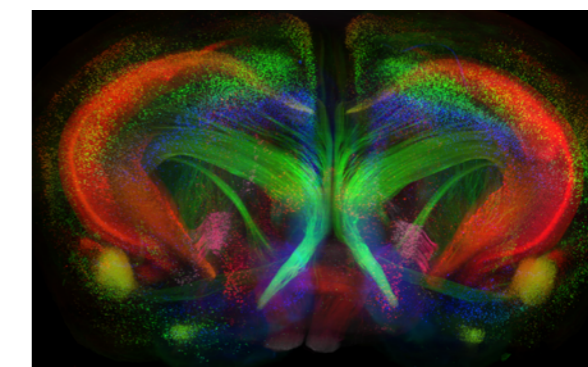
based on microfluidics to examine blood vessel formation processes, like vasculogenesis and angiogenesis, in more lifelike microenvironments.

To encourage collaboration between PIs, we have established several focusing projects that serve as seed funds to exchange ideas, refine thinking, and demonstrate preliminary results for applying integrated projects both in Academia Sinica and the National Council of Science and Technology. With the support of the focusing project, several integrated projects were funded, including the development of nanoforce sensors for drug screening, a microRNA detection system for diagnosis, and cellular memory devices. Additionally, we are conducting several pilot projects in spatial biology as a new direction of this thematic center, such as the development of expansion microscopy for large samples, single-cell analysis systems using integrated microfluidic devices and 3D cellular imaging using focused ion beam scanning electron microscopy (FIB/SEM). Currently, we are running two focusing projects. In the first project, we have undertaken concentrates on creating an integrated platform for high-performance drug discovery. This platform encompasses intelligent computation, efficient chemical synthesis, digital biosensing, and patient-derived organoid models for drug testing. In an era where personalized medicine is rapidly gaining traction, this project is both timely and significant. The marriage of cloud computing and artificial intelligence can expedite drug discovery, potentially enabling new treatments to reach patients more rapidly. Meanwhile, the development of patient-derived organoid models aligns with global regulatory efforts to reduce animal testing, contributing to more ethical and accurate drug testing methods. Our second focusing project aims to revolutionize optical microscopy by achieving a level of spatial resolution comparable to electron microscopy (EM), while retaining chemical information and the capacity for 3D imaging. This endeavor could fundamentally change our understanding of biological structures like synapses, a key area of focus in neurology and related fields. By enhancing the resolution and capabilities of optical microscopy, we can facilitate more comprehensive research into synaptic connectivity and advance our understanding of how information flows within the brain.

## 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.



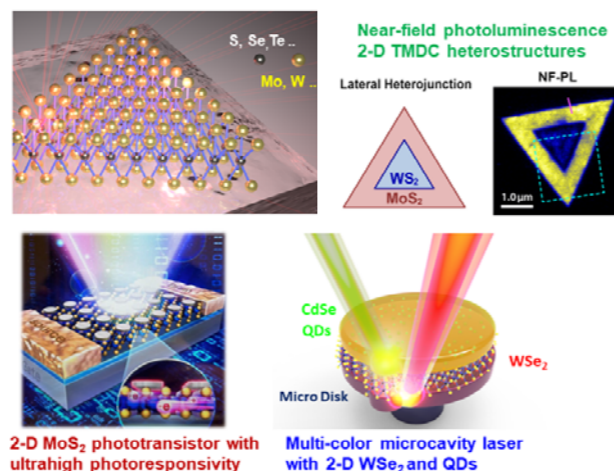
Cleared Thy1-eYFP mouse brain imaged by lightsheet microscopy

The objective of this thematic center is to explore innovative manufacturing and emerging materials in order to expedite the development and implementation of sustainability technologies: The key research interests include: (1) Energy-Efficient and Energy Generation Devices, (2) Solid state Lithium batteries, and (3) Advanced Materials Simulation. Currently, the thematic center is comprised of five principal investigators (PIs): Yun-Chorng Chang, Yuh-Jen Cheng, Chih Wei Chu, Chun-Wei Pao, and Mu-Huai Fang.

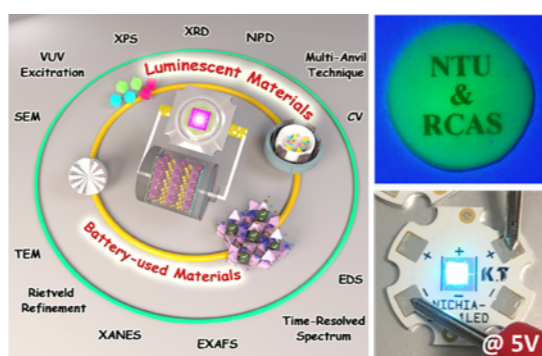
## Focusing Project

We are performing two focusing projects in this thematic center:

The First focusing direction is to study two-dimensional materials for ultra-thin, high efficient optoelectronics. The epitaxial growth techniques for the wafer-scale, high quality 2-D materials such as graphene, (TMDCs) and related heterostructures are well established and developed in RCAS. Beside the fundamental studies on the new material properties, the PIs in RCAS are also working on the novel optoelectronic devices with 2-D semiconductors such as LEDs, lasers and phototransistors.



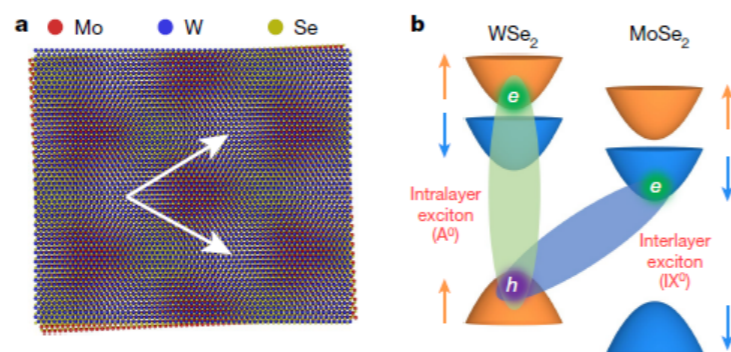
The second focusing project is on the development of battery-used materials and luminescent materials. The PIs in RCAS are working on the solid-state battery, flexible solar cells, and light-emitting diodes with novel perovskite materials.



## Research Achievements

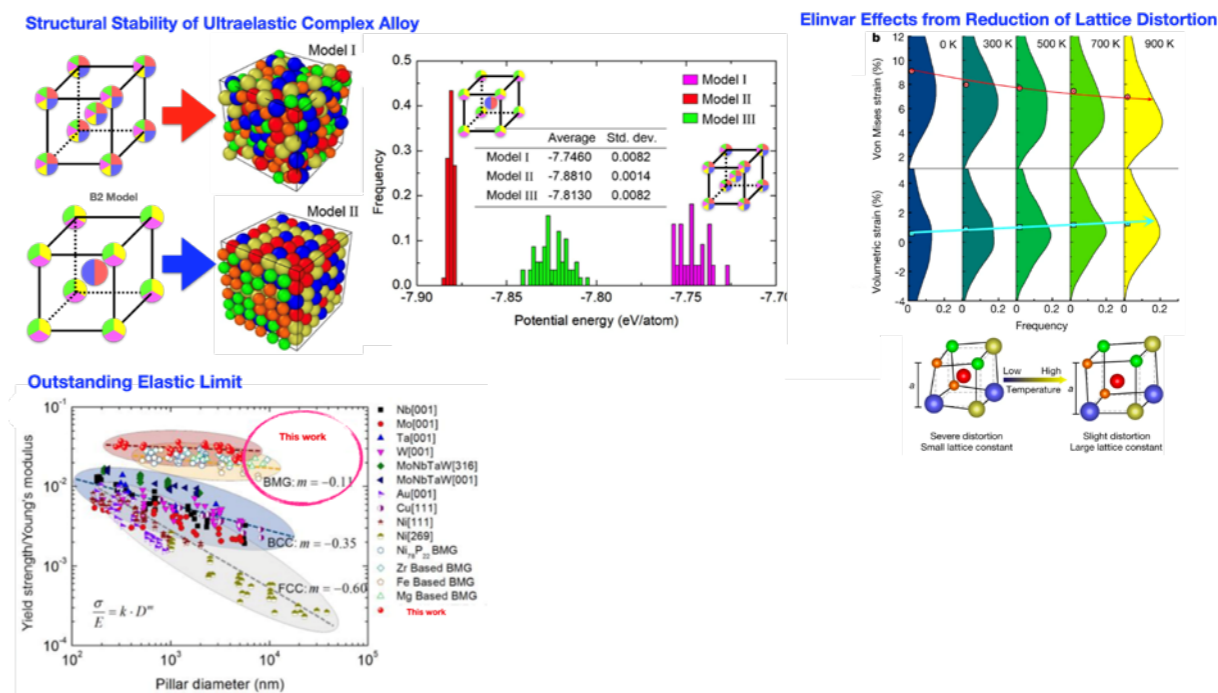
**Signatures of Moire triions in WSe<sub>2</sub>/MoSe<sub>2</sub> heterobilayers** (*Nature* 594, 46–50 (2021))

We report significant coupling between triions and Moiré potential of Moiré superlattices in TMDCs. These findings will facilitate the future development for probing many-body phenomena and quantum device applications.



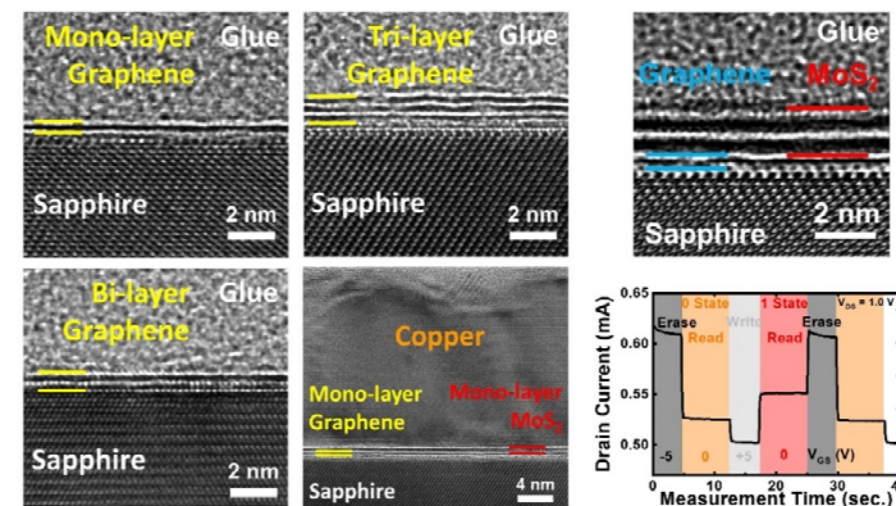
**New opportunity from microscale ordering under high entropy: ultra-elastic high entropy Elinvar alloy** (*Nature* 602, 251–257 (2022))

By performing a series of large-scale density functional theory calculations, we successfully reveal the atomistic structure of Co<sub>25</sub>Ni<sub>25</sub>(HfTiZr)<sub>50</sub> chemically complex alloy. The large atomic size mismatch of 11% could be accommodated by judicious arrangement of atomic sites. Our atomistic simulations indicate that the large atomic size misfit and induced strong lattice distortion (9%) are responsible for the outstanding elastic limit as well as the Elinvar effects of this complex alloy.



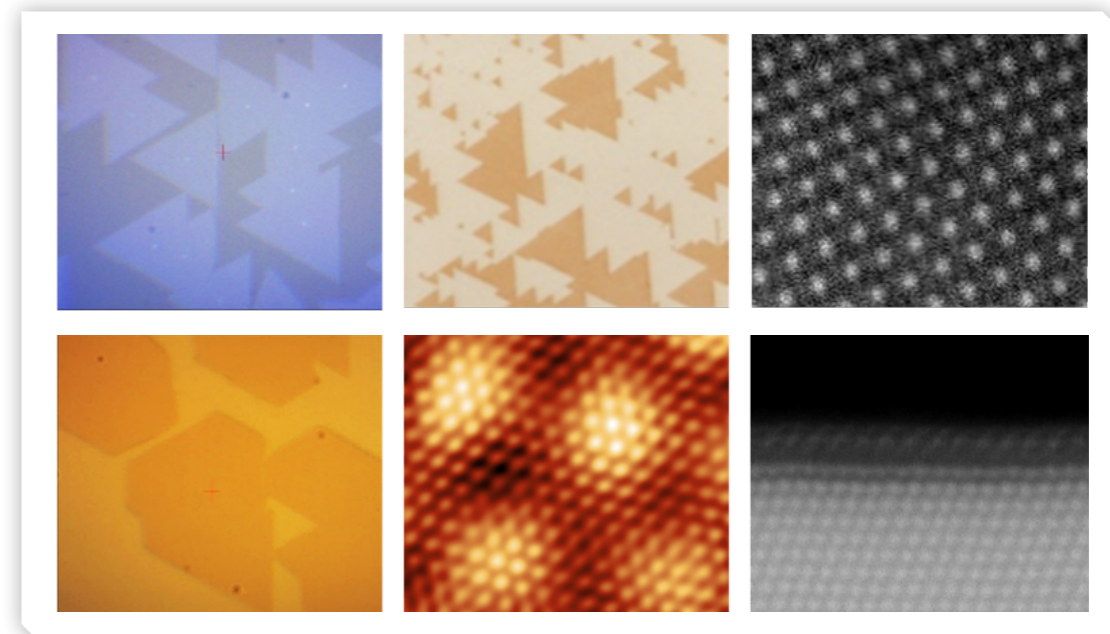
**Two dimensional (2D) material for next-generation memory technologies**

We have demonstrated that through sequential CVD growth cycles, wafer-scale and uniform graphene films can be grown layer-by-layer on sapphire substrates. By using mono-layer MoS<sub>2</sub> and mono-layer graphene as the liner/barrier stacks, nanometer Cu films with record-low resistivity can be grown on MoS<sub>2</sub> surfaces. By using MoS<sub>2</sub> as the charge storage and graphene as the channel layers, the first all 2D material memories, which exhibit long retention and high operation cycles, are demonstrated through the use of a top-gate transistor architecture.



The main objective of the Thematic Center for Quantum Photonics is to develop key materials and devices for applications in photonic quantum technologies. We synergize the existing research strengths in RCAS, including material growth, spectroscopy measurements, device fabrications, and theoretical analysis. Collaborations with domestic and overseas leading research teams have also been established in order to leverage state-of-the-art techniques for tackling the technical barriers in materials and devices for applications in quantum photonics technologies.

In the short and midterm, the Thematic Center aims at developing new material growth and device fabrication technologies for quantum light sources, single-photon detectors, and quantum photonic chips. We hope in the long term can make breakthroughs in photonic quantum computations and communications.



The research goal of this thematic center is to construct a superconducting quantum computer. Through this endeavor, we not only aim to study and develop the hardware architecture of quantum computers, but also to provide researchers with a collaborative platform for optimizing control mechanisms of quantum gates and offering users a means to test algorithms. Our focus lies in the design and fabrication of superconducting quantum bit chips, as well as continuous refinement of mechanisms for controlling and reading qubits. We are also collaborating with partners to develop a system architecture that advances towards cloud-based services. The thematic center has been actively recruiting researchers from both domestic and international backgrounds, working together towards the construction of a superconducting quantum computer.

## Key Areas of Focus

To construct a superconducting quantum computer, the key areas of focus include

1. Chip Design: Providing optimal control and readout circuitry for quantum bits (qubits), along with connectivity characteristics, while mitigating the effects of electromagnetic radiation.
2. Chip Fabrication: Refining processes for high yield, incorporating precise parameter control to ensure the manufacturing of high-quality chips.
3. System Architecture: Creating a low-temperature environment with minimal electromagnetic interference. Constructing control systems, programming, and advanced user interfaces.

## Achievements

**A. Chip Design:** Through ongoing refinement, we present a comprehensive set of parameters for chip components based on the theory and practical systems of qubit operations. Leveraging prior chip testing outcomes alongside numerical simulations, we generate the design blueprint for the actual chips. Our designs encompass Purcell filters and two-qubit circuits with tunable-frequency coupling (Figure 1c), featuring various arrangements of symmetrical, asymmetrical, suspended, and grounded qubits (Figure 1c). We also engineer circuits with five tunable-frequency qubits in various configurations (Figure 1a).

**B. Chip Fabrication:** Employing all-electron-beam lithography techniques, we circumvent the complexities arising from electrical contacts between the lower and upper electrodes of qubits. With this approach, the T1 relaxation time of qubits reaches 26 microseconds (Figure 1b). This quality empowers swift testing of novel design circuits. Concurrently, we collaborate with the Industrial Technology Research Institute (ITRI) and Taiwan Semiconductor Research Institute (TSRI) to develop Josephson junction devices utilizing niobium as the bottom electrode of qubit capacitive plates, along with air bridges (Figure 1c).

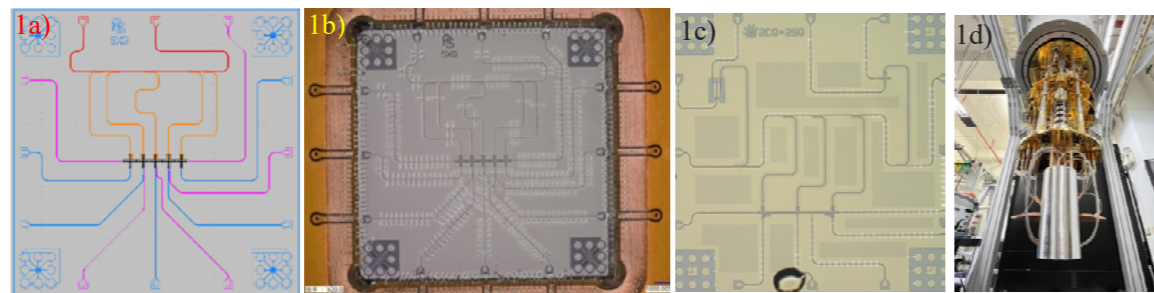


Figure 1: Figure 1a illustrates the design of a one-dimensional array with 5Q circuits. The orange lines represent readout resonators, blue lines indicate Z-gates, magenta lines depict XY-gates, and red lines correspond to readout lines. In Figure 1b, the completed chip is wire-bonded onto the chip holder PCB board. The chip is fabricated with an aluminum structure on a silicon substrate using all-electron-beam lithography processes. Aluminum wire bonding is utilized to suppress slotline mode and reduce XY and Z crosstalk between qubits. Figure 1c showcases a two-qubit circuit with a tunable-frequency coupler (located in the lower half of the chip), with floating and grounded qubits in the upper left and upper right corners, respectively. This chip also features aluminum air bridges with underneath silicon dioxide. In Figure 1d, a mu-metal cylindrical sample holder is suspended from the 10mK stage of the dilution refrigerator.

**C. System Architecture:** The photon shielding, magnetic field isolation, and low-temperature environment of the chip enclosure are all crucial factors for achieving high fidelity in logic gates. To this end, we are continuously enhancing the chip enclosure and simultaneously evaluating solutions provided by vendors. Additionally, we are developing measurement protocols and data processing systems within the laboratory, collaborating with instrumentation manufacturers to advance measurement techniques and user interfaces.

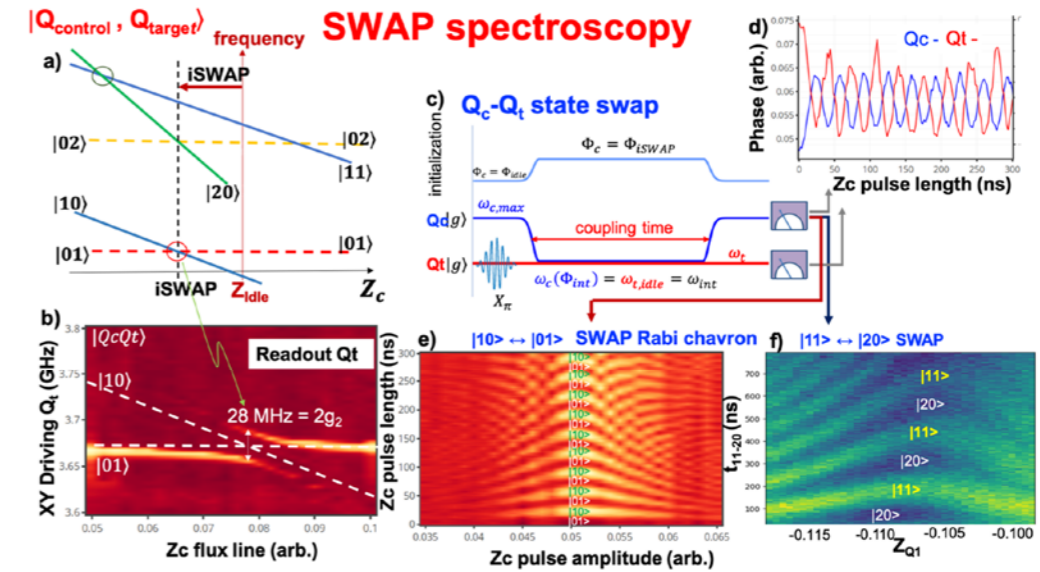


Figure 2: In Figure 2a, the response of the control-qubit Z-gate (Zc) applied to a pair of directly coupled control qubit and target qubit is depicted. After eliminating cross-talk, the target qubit does not respond to Zc. This allows aligning the control qubit's frequency to that of the target qubit at a designed Zc value and to induce coupling between the two qubits. Figure 2b shows a coupling strength of 14 MHz observed at the intersection of |10> and |01>. At this crossing, a state swap between |10> and |01> (seen in Figure 2e) can be executed. Figure 2c illustrates the execution method: within the coupling time, a z-gate is utilized to bring the frequencies of both qubits into alignment. During this period, the rate of state exchange between the two qubits is determined by the coupling strength (as shown in Figure 2d). Figure 2f captures the state exchange behavior of qubits at the intersection of |11> and |20>.

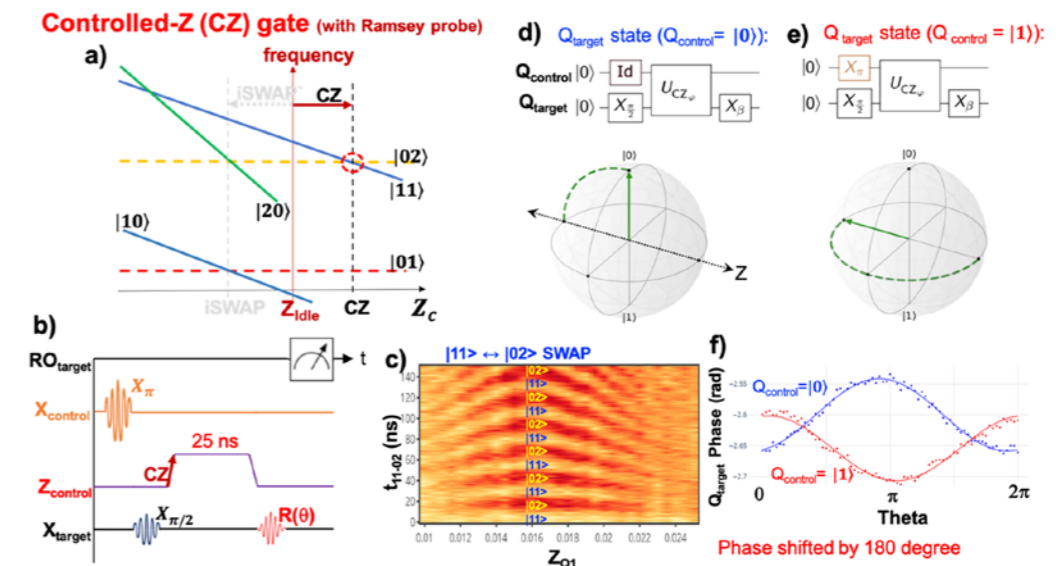


Figure 3: In Figure 3a, the same operation as in Figure 2a is performed, but the operating point is shifted to the intersection of |11> and |02>, enabling the operation of the CZ gate. In Figure 3b, the CZ operation involves bringing the control qubit's frequency close to the target qubit's frequency. Depending on the state of the control qubit, changes can be induced in the target qubit. The roles of these two qubits can also be interchanged. Figure 3c displays a state swap between |11> and |02>, at the operating point. The control qubit can be in the ground state (Figure 3d) or the excited state (Figure 3e). During the CZ operation, this leads to different phase angle rotations in the target qubit, achieving control over the relative phase of the two-qubit system. Figure 3f shows that an appropriate operating time (e.g., 25 ns) can create a phase difference of 180 degrees between the two-qubit states.

# Peilin Chen

Executive Officer of the TCIB and Research Fellow

**Education** | Education: Ph.D. Chemistry, University of California, Irvine (1998)

## Selected Publications

- Chi-Shan Li, et al., "Cytosolic galectin-4 enchains bacteria, restricts their motility and promotes inflammasome activation in intestinal epithelial cells" *Proc. Natl. Acad. Sci. U.S.A.*, 2023, **12**, e2207091120.
- Yuan-Yuan Cheng, et al., "Metabolic changes associated with cardiomyocyte dedifferentiation enable adult mammalian cardiac regeneration." *Circulation*, 2022, **146**, 1950.
- Wei-Chun Tang, et.al., "Optogenetic Manipulation of Cell Migration with High Spatiotemporal Resolution Using Lattice Lightsheet Microscopy" *Communications Biology*, 2022, **5**, 879.
- Chiung Wen Kuo, Feby Wijaya Pratiwi, Yen-Ting Liu, Di-Yen Chueh and Peilin Chen\* "Revealing the nanometric structural changes in myocardial infarction models by time-lapse intravital imaging" *Frontiers in Bioengineering and Biotechnology*, 2022, **10**, 935415.
- San-Shan Huang, et al., "Immune cell shuttle for precise delivery of nanotherapeutics for heart disease and cancer" *Science Advances*, 2021, **7**, eabf2400.
- Hung-Lin Chen, et. al., "Galectin-7 downregulation in lesional keratinocytes contributes to enhanced IL-17A signaling and skin pathology in psoriasis" (2020) *J. Clin. Invest.* **131**, e130704.
- Rong-Lin Chang, Feby Wijaya Pratiwi, Bi-Chang Chen, Peilin Chen,\* Si-Han Wu,\* Chung-Yuan Mou\* "Simultaneous Single-particle Tracking and Dynamic pH Sensing Reveal Lysosome-targetable Mesoporous Silica Nanoparticles Pathways", *ACS Applied Materials & Interfaces*, 2020, **12**, 42472.
- Yi-Ping Chen, Chien-Tsu Chen, Tsang-Pai Liu, Fan-Ching Chien, Si-Han Wu\*, Peilin Chen\*, Chung-Yuan Mou\* "Catcher in the rel: Nanoparticles-antibody conjugate as NF- $\kappa$ B nuclear translocation blocker" *Biomaterials*. 2020, **246**, 119997.
- Li-An Chu, et. al., "Rapid single-wavelength lightsheet localization microscopy for clarified tissue" *Nature Communications*, 2019, **10**, 4762.
- Chieh-Han Lu, et. al., "Lightsheet localization microscopy enables fast, large-scale, and three-dimensional super-resolution imaging" *Communications Biology*, 2019, **2**, 177.
- Tony WH Tang, et. al., "Loss of Gut Microbiota Alters Immune System Composition and Cripples Post-Infarction Cardiac Repair" *Circulation*, 2019, **139**, 647.

## Positions and Career

- Research Fellow, RCAS, Academia Sinica, 2010-present
- Chief Executive Officer, Thematic Center for Intelligence Bioengineering, RCAS, 2023-present
- Joint Research Fellow, Institute of Physics, Academia Sinica, 2021-present
- Visiting Professor, Kyoto University, Kyoto, Japan, 2015
- Visiting Professor, RIKEN, Wako, Japan, 2012
- Chief Executive Officer, Thematic Center for Optoelectronic, RCAS, 2012
- Deputy Director, RCAS, Academia Sinica (2010 -2012)
- Associate Research Fellow, RCAS, Academia Sinica (2005-2010)
- Assistant Research Fellow, RCAS, Academia Sinica (2001-2005)
- Postdoctoral Fellow, University of California, Berkeley (1999-2001)
- Postdoctoral Fellow, University of California, Irvine (1998)

## Honors and Awards

- Research Award for Junior Research Investigators, Academia Sinica, Taiwan (2007)
- Ta-You Wu Memorial Award, National Research Council, Taiwan (2007)
- Career Development Award, Academia Sinica, Taiwan (2009)
- Fellow, the Royal Society of Chemistry (2019)
- Investigator Award, Academia Sinica, Taiwan (2021)

## Research Interests

- Advanced imaging: super-resolution, single molecules, intravital
- Bioelectronic and biomedical devices
- Multifunctional materials for Nanomedicine

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[https://www.rcas.sinica.edu.tw/pi\\_web/peilin.php](https://www.rcas.sinica.edu.tw/pi_web/peilin.php)

- Chiung Wen Kuo, Di-Yen Chueh, Peilin Chen\*, "Real-Time in vivo Imaging of Subpopulations of Circulating Tumor Cells Using Antibody Conjugated Quantum Dots" *J. Nanobiotech*, 2019, **17**, 26.
- Po-Kai Chuang, et al., "Signaling pathway of globo-series glycosphingolipids and  $\beta$ 1,3-galactosyltransferase V ( $\beta$ 3GalT5) in breast cancer" *Proc Natl Acad Sci USA* 2019, **116**, 3518-3523.

## Research Focus

### The Applications of Real-time Intravital Imaging

Chiung Wen Kuo, Di-Yen Chueh, Peilin Chen

Academic Sinica, Research Center for Applied Sciences

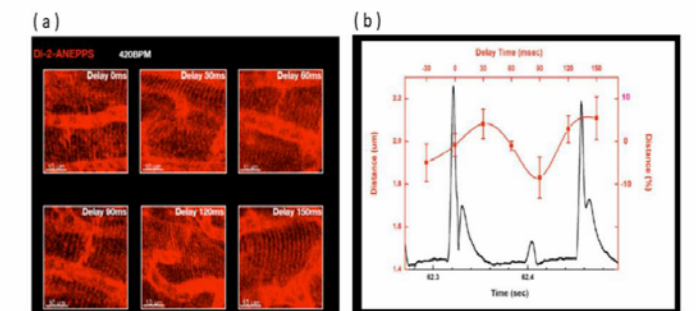
- Frontiers in Bioengineering and Biotechnology, 2022, **10**, 935415
- Circulation, 2022, **146**, 1950
- Science Advances, 2021, **7**, eabf2400
- Circulation, 2019, **139**, 647
- Science Translational Medicine 2016, **8**, 365ra160
- J. Nanobiotech 2019, **17**, 26
- J. Clin. Invest. 2021, **131**,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

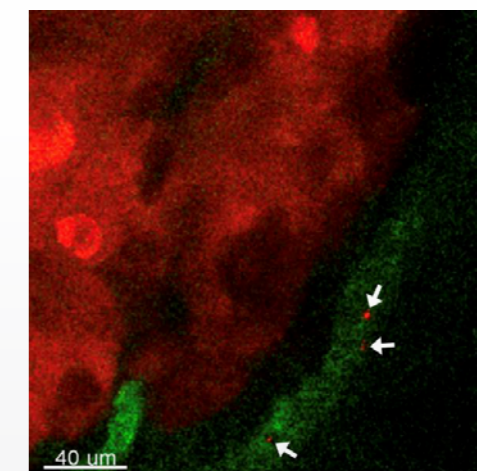
In the case of tumor imaging, we are interested in the real-time imaging of the circulating tumor cells (CTCs). The detection of circulating tumor cells (CTCs) is very important for cancer diagnosis. CTCs can travel from primary tumors through the circulation to form secondary tumor colonies via bloodstream 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.

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.



(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 length displacement in one complete cardiac cycle



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.



# Pei-Kuen Wei

Director and Research Fellow

## Education

Ph.D. Electrical Engineering, National Taiwan University (1994)

## Selected Publications

- Shu-cheng Lo, Chia-wei Lee, Ruey-lin Chern, and Pei-kuen Wei, "Hybrid modes in gold nanoslit arrays on Bragg nanostructures and their application for sensitive biosensors," *Opt. Express* 30, 30494-30506 (2022)
- Shu-Cheng Lo, Sheng-Hann Wang, Ting-Wei Chang, Kuang-Li Lee, Ruey-Lin Chern, and Pei-Kuen Wei\*, "Dual Gold-Nanoslit Electrodes for Ultrasensitive Detection of Antigen–Antibody Reactions in Electrochemical Surface Plasmon Resonance", *ACS Sensors* 2022 7 (9), 2597-2605
- Yi-Ru Li, Kuang-Li Lee, Kuan-Ming Chen, Yun Cheng Lu, Pin Chieh Wu, Sy-Hann Chen, Jiun-Haw Lee, and Pei-Kuen Wei\*, "Direct detection of virus-like particles using color images of plasmonic nanostructures," *Opt. Express* 30, 22233-22246 (2022)
- Chia-Wen Kuo, Sheng-Hann Wang, Shu-Cheng Lo, Wei-Han Yong, Ya-Lun Ho, Jean-Jacques Delaunay, Wan-Shao Tsai, and Pei-Kuen Wei\*, "Sensitive Oligonucleotide Detection Using Resonant Coupling between Fano Resonance and Image Dipoles of Gold Nanoparticles", *ACS Applied Materials & Interfaces* Article 2022
- 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)
- Shu-Cheng Lo, Chun-Wei Yeh, Sheng-Hann Wang, Chia-Wen Kuo, Kuang-Li Lee, Ruey-Lin Chern, Pei-Kuen Wei\*, "Self-Referencing Biosensors Using Fano Resonance in Periodic Aluminium Nanostructures", *Nanoscale*, 2021, 13, 17775-17783
- Sheng-Hann Wang, Shu-Cheng Lo, Yung-Ju Tung, Chia-Wen Kuo, Yi-Hsin Tai, Shu-Yi Hsieh, Kuang-Li Lee, Shune-Rung Hsiao, Jenn-Feng Shenn, Ju-Chun Hsu, and Pei-Kuen Wei\*, "Multichannel Nanoplasmonic Platform for Imidacloprid and Fipronil Residues Rapid Screen Detection", *Biosensors and Bioelectronics* 170 (2020) 112677
- Lee, Kuang-Li; Hou, Hsien-San; Cheng, Ji-Yen; Wei, Pei-Kuei Wei\*, "High-throughput and dynamic study of drug and cells interactions using contrast images in aluminum-based nanoslit arrays", *Analytical Chemistry*, 92 (2020), 14, 9674–9681

## Positions and Career

- Director, Research Center for Applied Sciences, Academia Sinica (2023 - )
- Acting Director, Research Center for Applied Sciences, Academia Sinica (2022 – 2023)
- Deputy Director, Research Center for Applied Sciences, Academia Sinica (2012 – 2019)
- Adjunct Professor, Department of Photonics, National Sun Yat-sen University (2015 - )
- Adjunct Professor, Institute of Biophotonics Engineering, National Yang-Ming Chia-Tung University, (2011 - )
- Acting Executive Officer of the thematic center for Mechanics and Engineering Science, Academia Sinica (2009 – 2014)
- Research Fellow, Research Center for Applied Sciences, Academia Sinica (2009- )
- Adjunct Professor, Institute of Optoelectronic Sciences, National Taiwan Ocean University (2006 - 2021)
- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica (2004 – 2008)
- Assistant Research Fellow, Institute of Applied Science and Engineering research (preparatory house), Academia Sinica (2000 – 2004)
- Postdoctoral Research, Institute of Atomic and Molecular Sciences, Academia Sinica (1995 – 2000)

## Honors and Awards

- 2021 Presidential scholars, Academia Sinica
- 2018 Industrial paper award (Champion), International Conference on Smart Sensors
- 2017 SPIE Senior Member
- 2016 OSA Senior Member
- 2015 Investigator Award, Academia Sinica
- 1994 Doctoral Thesis Award, Optical Society of Taiwan

## Research Interests

- Nano-Fabrication & Measurement
- Nano-Photonics & Plasmonics
- Biosensors & Bioelectronics

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## Research Focus

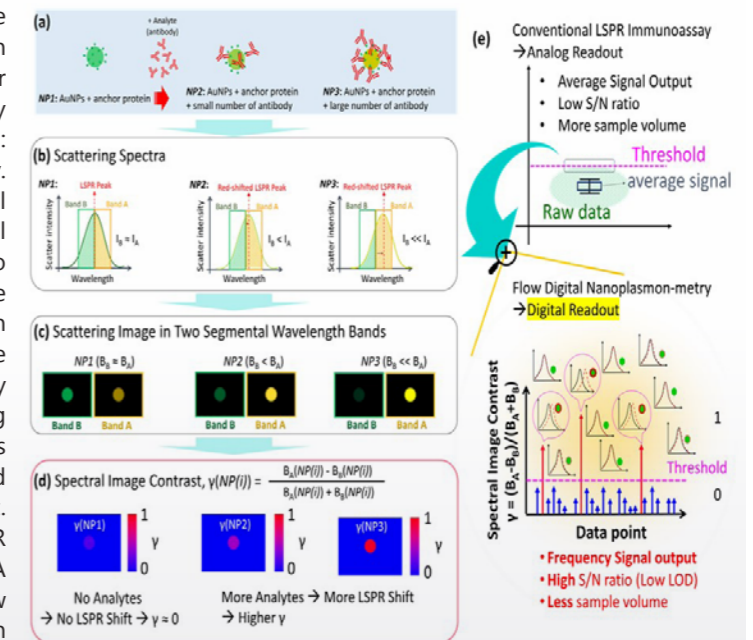
### Spectral Image Contrast-Based Flow Digital Nanoplasmon-metry for Ultrasensitive Antibody Detection

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

Academic Sinica, Research Center for Applied Sciences

*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<sup>-1</sup> within only a 15-min detection time and 500 μL sample volume.



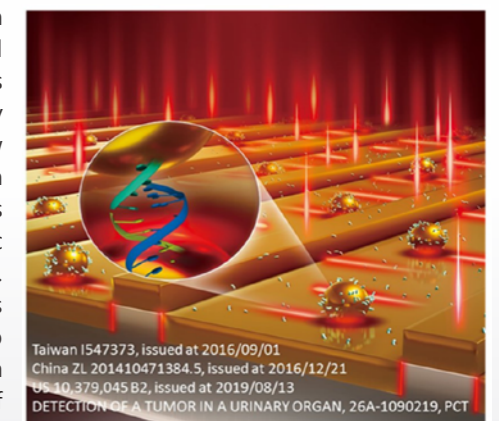
### Sensitive Oligonucleotide Detection Using Resonant Coupling between Fano Resonance and Image Dipoles of Gold Nanoparticles

Chia-Wen Kuo, Sheng-Hann Wang, Shu-Cheng Lo, Wei-Han Yong, Ya-Lun Ho, Jean-Jacques Delaunay, Wan-Shao Tsai, and Pei-Kuen Wei

Academic Sinica, Research Center for Applied Sciences

*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/μm<sup>2</sup>. 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.



# Fu-Liang Yang

Distinguished Research Fellow / Professor

## Education

Ph.D., Materials Science and Metallurgy,  
University of Cambridge, UK

## Selected Publications

- 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>
- 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>
- 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>
- 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
- 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
- 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>
- 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
- 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%)

## Positions and Career

- Distinguished Research Fellow/Professor Research Center for Applied Sciences, Academia Sinica (2013.08-Present)
- Director, Division of Intellectual Property and Technology Transfer, Academia Sinica (2013.08-2016.09)
- Distinguished Research Fellow, National Nano Device Laboratories(NDL), National Applied Research Laboratories(Narlabs) (2008.08-2013.08)
- Director General, National Nano Device Laboratories (2008.08-2013.05)
- TSMC, all in R&D Organization. Deputy Director, 2008; Department Manager, 2002; TSMC Academician, TSMC Academy, 2004; Section Manager, 2000 (2000.03-2008.07)
- Vanguard International Semiconductor Corporation (VIS) Section Manager, Dept. of Device Development, 1998 Principal Integration Engineer, 1996 Senior Process Engineer, 1994 (1994.12-2000.03)

## Honors and Awards

- 2022, "AI Deduction Learning Non-Invasive Blood Glucose Meter" awarded National Innovation Award.
- 2020, "Helix External Counter Pulsation System" awarded National Innovation Award.
- 2012, "A Label-Free Method for the Rapid Identification of Rare-Pathogens from Human Blood (<5min)" awarded National Innovation Award.
- 2004, Outstanding Young Engineer Award from the Chinese Institute of Engineering
- 2004, TSMC Academician of TSMC Academy.
- 2004, TSMC Innovation Award (for <100> boosted PMOS)
- 2006, TSMC Best Invention Disclosures Award(for an outstanding transistor structure invention)

## Research Interests

- Wearable Devices, Pulsation Waveform Characterization and Modulation
- Noninvasive Blood Glucose Measurements via AI Deduction Learning

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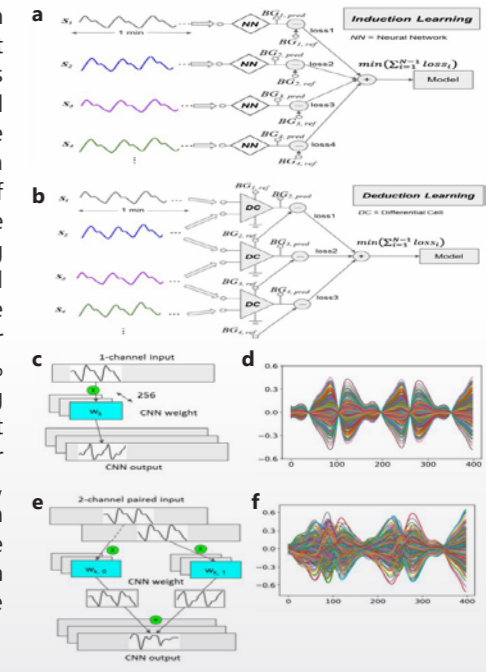
<http://www.rcas.sinica.edu.tw/faculty/flyang.html>

## Research Focus

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

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

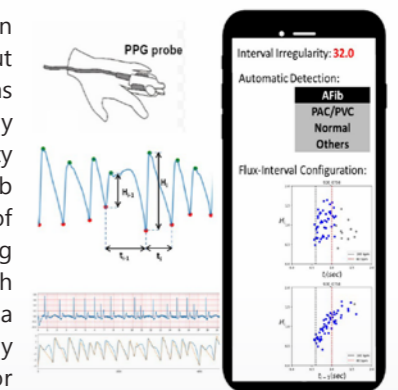
Personalized modeling has long been anticipated to approach precise noninvasive blood glucose (NIBG) measurements, but challenged by limited data for training personal model and its unavoidable outlier predictions. We recently significantly enhanced the training efficiency with the limited personal data 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.





# Ji-Yen Cheng

Deputy Director and Researcher

## Education

Ph.D. Chemistry, National Taiwan University, Taipei, TAIWAN.(1998)

## Positions and Career

- Deputy Director, RCAS, Academia Sinica Taiwan, 2023
- Executive Officer of the TCBMA (Thematic Center of Bio & Medical Applications) 2021 ~
- Executive Officer of the TCMES (Thematic Center of Mechanics and Engineering Sciences) 2015 ~
- Research Fellow, RCAS, Academia Sinica Taiwan, 2013
- Associate Research Fellow, RCAS, Academia Sinica Taiwan, 2007
- Assistant Research Fellow, RCAS, Academia Sinica Taiwan, 2001
- Postdoctoral Fellow, Institute of Biomedical Sciences, Academia Sinica Taiwan, 1998
- Adjunct Professor, National Taiwan Ocean University
- Adjunct Professor, National Yang Ming Chiao Tung University

## Honors and Awards

- 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.

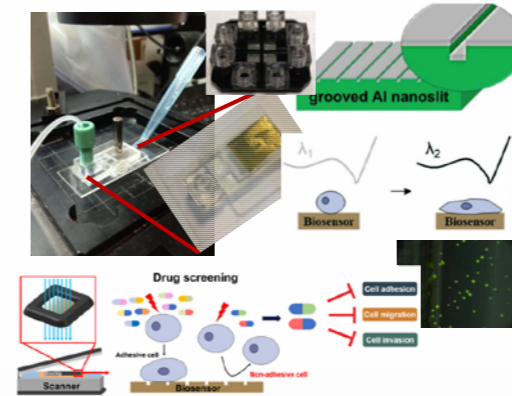
## Selected Publications

- 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.
- 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.
- 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.
- 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*.
- 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.
- 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.
- 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.
- Yeung, W.K., Chen, H.-Y., Sun, J.-J., Hsieh, T.-H., Mousavi, M.Z., Chen, H.-H., Lee, K.-L., Lin, H., Wei, P.-K. and Cheng, J.-Y. (2018) Multiplex detection of urinary miRNA biomarkers by transmission surface plasmon resonance. *Analyst*, 143, 4715-4722.
- Tsai, H.-F., Tsai, Y.-C., Yagur-Kroll, S., Palevsky, N., Belkin, S. and Cheng, J.-Y. (2015) Water pollutant monitoring by a whole cell array through lens-free detection on CCD. *Lab Chip*, 15, 1472-1480.
- Wang, C.-C., Ka, Y.-C., Chi, P.-Y., Huang, C.-W., Lin, J.-Y., Chou, C.-F., Cheng, J.-Y. and Lee, C.-H. (2011) Asymmetric cancer-cell filopodium growth induced by electric-fields in a microfluidic culture chip. *Lab Chip*, 11, 695-699.

## Research Focus

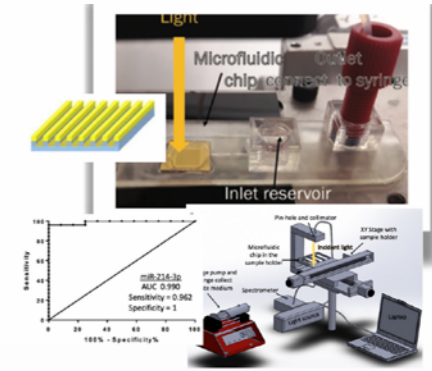
### Research Highlight -1/2

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

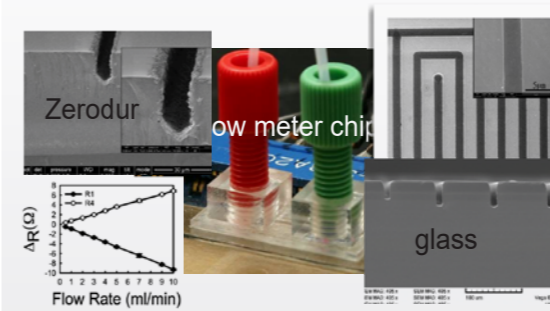


**Urinary cancer biomarker detection using nanostructure SPR**  
*Analyst 2013, 2015, 2018, 2021; SnB 2020*

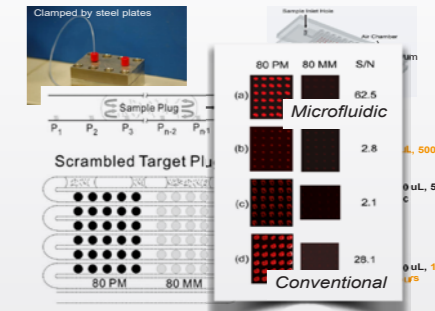
*Analyst 2013, 2015, 2018, 2021; SnB 2020*



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



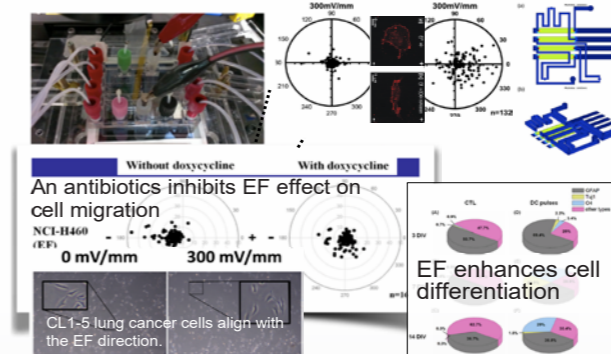
**10 min DNA hybridization in microfluidic chip**  
*Nucl. Acid. Res. 2005; Biotech. Bioeng. 2009*



### Research Highlight -2/2

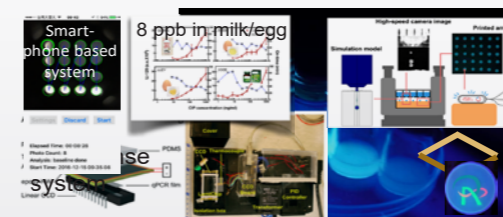
**Migration and differentiation of adherent cells in EF**

*Biomicrofluidics, 2008, 2009, 2012, 2014, 2015; Lab-on-a-chip 2009; PlosOne 2011, 2013; Sci. Rpt. 2019, JoVE 2015, 2016, 2021*



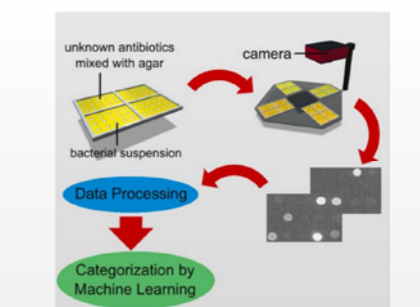
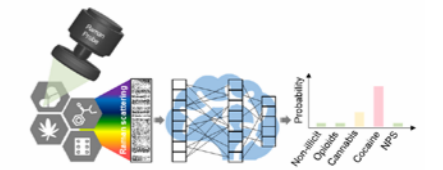
**Antibiotics detection and characterization using whole-cell biosensor,**

*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.

# Chau-Hwang Lee

Research Fellow

**Education** | Ph.D. Electrical Engineering, National Taiwan University (1997)

## Selected Publications

- 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).
- 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).
- 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).
- Y.-C. Kao, Z.-H. Chen, W.-Y. Wang, C.-H. Lee, and P.-L. Kuo, "Hydrostatic pressure promotes migration and filamin-A activation in fibroblasts with increased p38 phosphorylation and TGF- $\beta$  production," *Biochemical and Biophysical Research Communications* **568**, 15-22 (2021).
- 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).
- Y.-C. Kao, Y.-C. Liao, P.-L. Cheng, and C.-H. Lee, "Neurite regrowth stimulation by a red-light spot focused on the neuronal cell soma following blue light-induced retraction," *Scientific Reports* **9**, 18210 (2019).
- 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).
- 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).
- C.-H. Chang, H.-H. Lee\*, and C.-H. Lee, "Substrate properties modulate cell membrane roughness by way of actin filaments," *Scientific Reports* **7**, 9068 (2017).
- C.-W. Lee, C.-C. Wang, and C.-H. Lee, "Mechanoprofiling on membranes of living cells with atomic force microscopy and optical nano-profilometry," *Advances in Physics: X* **2**, 608-621 (2017).

## Positions and Career

- Deputy Executive Secretary, Central Academic Advisory Committee, Academia Sinica (2016–Present)
- Deputy Director, Research Center for Applied Sciences, Academia Sinica (2014–2016)
- Chairman, Institute of Biophotonics, National Yang-Ming University (2011–2014)
- Joint-appointment Professor, Institute of Biophotonics, National Yang Ming Chiao Tung University (2011–Present)
- Research Fellow, Research Center for Applied Sciences, Academia Sinica (2010–Present)
- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica (2004–2010)
- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica (2000–2004)
- Postdoctoral Research Associate, Institute of Atomic and Molecular Sciences, Academia Sinica (1997–2000)

## Honors and Awards

- 2012 Academia Sinica Junior Investigator Award.
- 2010 Dr. Ta-You Wu Memorial Award, National Science Council, Taiwan

## Research Interests

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

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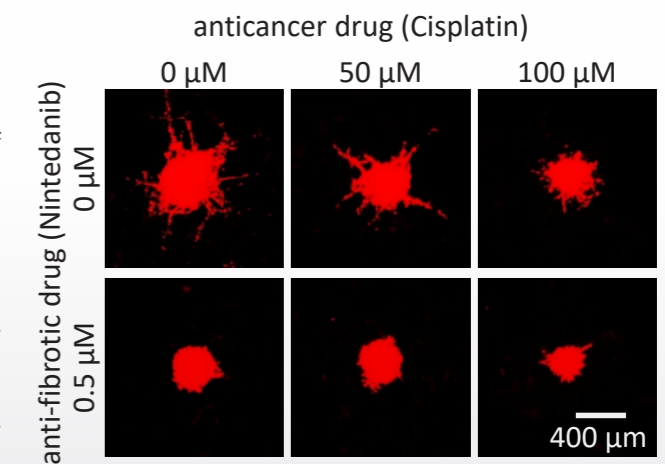
## Research Focus

### 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.

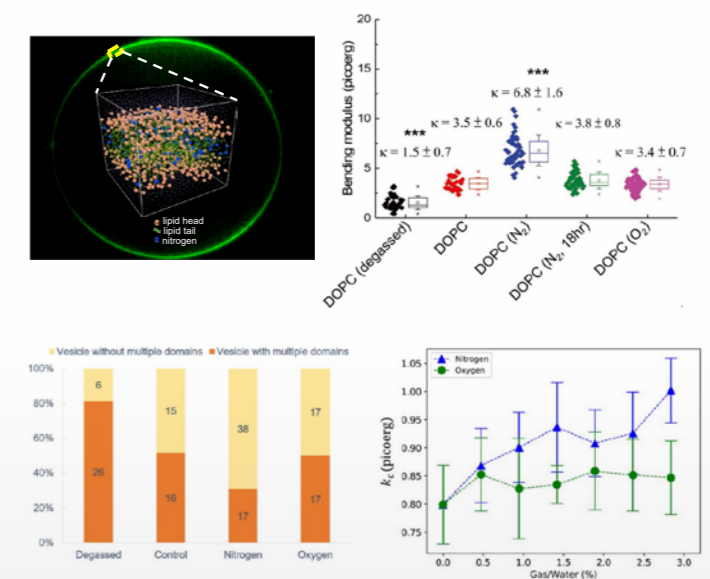


### Emerging roles of air gases in lipid bilayers

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/sml.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  $N_2$  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.



# Jung-Hsin Lin

Research Fellow

Education | Ph.D. Physics, University of Duisburg, Germany (2000)

## Selected Publications

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.
2. Dhananjay C. Joshi and Jung-Hsin Lin\*, "Delineating protein-protein curvilinear dissociation pathways and energetics with naïve multiple-walker umbrella sampling simulations", *J. Comput. Chem.* 40: 1652-1663 (2019) DOI:10.1002/jcc.25821
3. Yu-Hsuan Chen and Jung-Hsin Lin\*, "Can ligands of different functional types induce distinct dynamics in G protein-coupled receptors?" *Curr. Top. Med. Chem.* 17: 2370-2380 (2017)
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)

## Positions and Career

- Chief Executive Officer, Thematic Center for Intelligence Medicine, Biomedical Translation Research Center, Academia Sinica (2021 - )
- Deputy Director, Biomedical Translation Research Center, Academia Sinica (2020 - )
- Editorial Board, *ChungHwa Pharmacopoeia*, Ministry of Health and Welfare, (2019 - )
- Review Panel, Division of Physics, Department of Natural Sciences and Sustainable Development, Ministry of Science and Technology (2019 - 2022)
- Delegate of Division of Mathematical and Physical Sciences, General Assembly of Academia Sinica (2017-2021)
- Deputy Director, Research Center for Applied Sciences, Academia Sinica (2019-2020)
- Chief Executive Officer, Thematic Center for Biomedical Applications, Research Center for Applied Sciences, Academia Sinica (2015-2020)
- Joint Appointment, College of Engineering Science, Chang Gung University (2015- )
- Research Fellow, Research Center for Applied Sciences, Academia Sinica (2014- )
- Joint Appointment, School of Pharmacy, College of Medicine, National Taiwan University (2006 - )
- Joint Appointment, Institute of Biomedical Sciences, Academia Sinica (2004 - )
- Assistant Professor, School of Pharmacy, College of Medicine, National Taiwan University (2003 - 2006 )
- Bioinformatics Specialist, Howard Hughes Medical Institute, University of California at San Diego, U.S.A. (2000 - 2002)
- Postdoctoral Research, John von Neuman Institute of Computing, Forschungszentrum Jülich, Germany (2000 - 2000)

## Honors and Awards

- 2019 Investigator Award, Academia Sinica

## Research Interests

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

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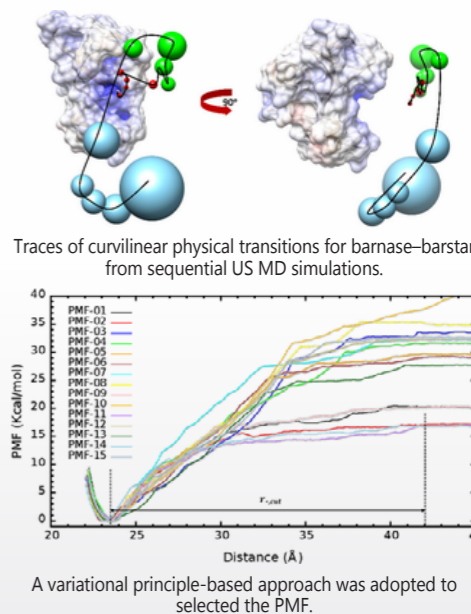
## Research Focus

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

Dhananjay C. Joshi, Jung-Hsin Lin\*

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

The protein-protein interaction 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.

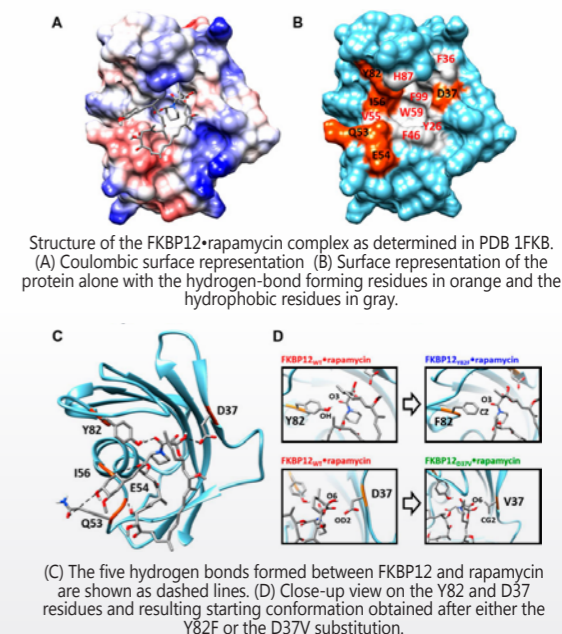


### A Curvilinear-Path Umbrella Sampling Approach to Characterizing the Interactions Between Rapamycin and Three FKBP12 Variants

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

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



# Jing-Jong Shyue

Research Fellow

## Education

Ph.D. Materials Science and Engineering, Case Western Reserve University, Ohio, U.S.A. (2004)

## Selected Publications

- JY Li, YZ Qian, W Li\*, SC Yu, YX Ke, HW Qian, YH Lin, CH Hou\*, **JJ Shyue**, J Zhou, Y Chen, JP Xu, JY Zhu, MF Yi\* and W Huang\* "Polymeric Memristor Based Artificial Synapses with Ultra-Wide Operating Temperature" *Adv. Mater.* 35 [23] 2209728 (2023).
- PH Ho\*, JR Chang, CH Chen, CH Hou, CH Chiang, MC Shih, HC Hsu, WH Chang, **JJ Shyue**, YP Chiu\* and CW Chen\* "Hysteresis-Free Contact Doping for High-Performance Two-Dimensional Electronics" *ACS Nano* 17 [3] 2653-2660 (2023).
- P Chen, Y Xiao, L Li, LC Zhao\*, MT Yu, SD Li, JT Hu, B Liu, YG Yang, DY Luo, CH Hou, XG Guo, **JJ Shyue**, ZH Lu, QH Gong, HJ Snaith\* and R Zhu\* "Efficient Inverted Perovskite Solar Cells via Improved Sequential Deposition" *Adv. Mater.* 35 [5] 2206345 (2023).
- CH Kuan, JM Chih, YC Chen, BH Liu, CH Wang, CH Hou, **JJ Shyue** and EWG Diau\* *ACS Energy Lett.* 7 4436-4442 (2022).
- KW Tsai, G Madhaiyan, LH Lai, YT Hsiao, JL Wu, CY Liao, CH Hou\*, **JJ Shyue\*** and YM Chang\* *ACS Appl. Mater. Interfaces* 14 [33] 38004-38012 (2022).
- S Shrestha, XX Li, HH Tsai, CH Hou, HH Huang, D Ghosh, **JJ Shyue**, LY Wang, S Tretiak, XD Ma and WY Nie\* *Chem* 8 [4] 1107-1120 (2022).
- LC Zhao, QY Li, CH Hou, SD Li, XY Yang, J Wu, SY Zhang, Q Hu, YJ Wang, YH Zhang, YF Jiang, SA Jia, **JJ Shyue**, TP Russell, QH Gong, XY Hu and R Zhu\* *J. Am. Chem. Soc.* 144 [4] 1700-1708 (2022).
- YZ Zhang, YJ Wang, LC Zhao\*, XY Yang, CH Hou\*, J Wu, R Su, S Jia, **JJ Shyue**, DY Luo, P Chen, MT Yu, QY Li, L Li, QH Gong, and R Zhu\* *Energy Environ. Sci.* 14 [12] 6526-6535 (2021).
- HH Huang, HH Tsai, R Raja, SL Lin, D Ghosh, CH Hou, **JJ Shyue**, S Tretiak, W Chen, KF Lin, WY Nie\* and LY Wang\* *ACS Energy Lett.* 6 [9] 3376-3385 (2021).
- WL Li, CH Hou\*, CM Yang, KW Tsai, JL Wu, YT Hsiao, C Hanmandlu, CW Chu, CH Tsai, CY Liao, **JJ Shyue\*** and YM Chang\* *J. Mater. Chem. A* 9 [33] 17967-17977 (2021).
- JT Lin, YK Hu, CH Hou, CC Liao, WT Chuang, CW Chiu\*, MK Tsai\*, **JJ Shyue\*** and PT Chou\* *Small* 16 [19] 2000903 (2020).
- CH Hou, SH Hung, LJ Jhang, KJ Chou, YK Hu, PT Chou, WF Su, FY Tsai, J Shieh and **JJ Shyue\*** *ACS Appl. Mater. Interfaces* 12 [20] 22730-22740 (2020).

## Positions and Career

- Research Fellow, Research Center for Applied Sciences, Academia Sinica (2015–Present)
- Professor, Department of Materials Science and Engineering, National Taiwan University (2015–Present)
- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica (2010–2015)
- Associate Professor, Department of Materials Science and Engineering, National Taiwan University (2011–2015)
- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica (2006–2010)
- Assistant Professor, Department of Materials Science and Engineering, National Taiwan University (2007–2011)
- Adjunct Assistant Professor, Department of Chemistry, National Taiwan University (2006–2007)

## Honors and Awards

- Research Project of Outstanding Young Scholar (優秀年輕學者研究計劃), Ministry of Science and Technology, 2014.
- Ta-You Wu Memorial Award (吳大猶先生紀念獎), National Science Council, 2013.
- Career Development Award (前瞻計劃), Academia Sinica, 2012-2016.

## Research Interests

- Functional materials (for electronic, chemical and biomedical applications).
- Synthesis and processing of materials (self-assembly, interface chemistry).
- Microcharacterization (surface analysis, electron/ion spectroscopy/microscopy).
- Computer programming, numerical simulation and scientific modeling.

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## Research Focus

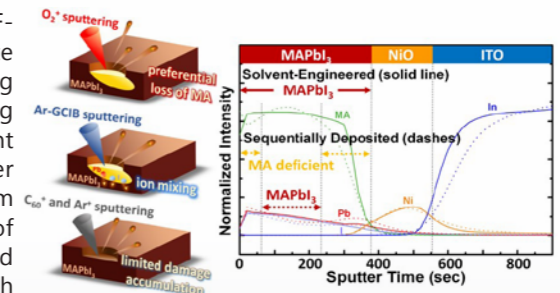
### Validated Analysis of Component Distribution Inside Perovskite Solar Cells and Its Utility in Unveiling Factors of Device Performance and Degradation

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)

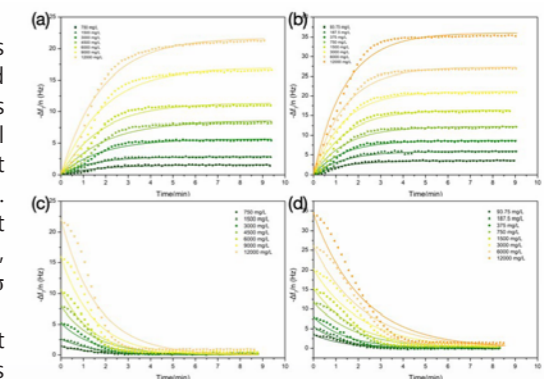
Wen-Yi Yu and Jing-Jong Shyue\*

Academic Sinica, Research Center for Applied Sciences

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  $\pi$ - $\pi$  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.





# Yi-Chung Tung

Research Fellow

## Education

Ph.D. Mechanical Engineering, University of Michigan, Ann Arbor, USA (2005)

## Selected Publications

1. C.-W. Chang, H.-C. Shih, M. Cortes-Medina, P. E. Beshay, A. Avendano, A. J. Seibel, W.-H. Liao, Y.-C. Tung\*, and J. W. Song\*, "ECM-Derived Biophysical Cues Mediate Interstitial Flow-Induced Sprouting Angiogenesis," *ACS Applied Materials & Interfaces*, Vol. 15, pp. 15047-15088, March 2023.
2. P.-L. Ko, C.-K. Wang, H.-H. Hsu, T.-A. Lee, and Y.-C. Tung\*, "Revealing Anisotropic Elasticity of Endothelium under Fluid Shear Stress," *Acta Biomaterialia*, Vol. 145, pp. 316-328, June 2022.
3. Y.-C. Tung, C.-K. Wang, Y.-K. Huang, C.-K. Huang, C.-C. Peng, B. Patra, H.-K. Chen, P.-N. Tsao\*, and T.-Y. Ling\*, "Identifying Distinct Oxygen Diffusivity through Type I Pneumocyte-Like Cell Layers Using Microfluidic Device," *Talanta*, Vol. 236, 122882, January 2022.
4. Y.-C. Chen, J.-J. Chen, Y.-J. Hsiao, C.-Z. Xie, C.-C. Peng, Y.-C. Tung\*, and Y.-F. Chen\*, "Plasmonic Gel Films for Time-Lapse LSPR Detection of Hydrogen Peroxide Secreted from Living Cells," *Sensors and Actuators B: Chemical*, Vol. 336, 129725, June 2021.
5. H.-H. Hsu, P.-L. Ko, H.-M. Wu, H.-C. Line, C.-K. Wang, and Y.-C. Tung\*, "Study Formation of Three-Dimensional Endothelial Cell Network under Various Oxygen Microenvironment and Hydrogel Composition Combinations Using Upside-Down Microfluidic Device," *Small*, Vol. 17, Issue 15, 2006091, April 2021. **(Featured as the inside back cover image)**
6. H.-C. Shih, T.-A. Lee, H.-M. Wu, P.-L. Ko, W.-H. Liao, and Y.-C. Tung\*, "Microfluidic Collective Cell Migration Assay for Study of Endothelial Cell Proliferation and Migration under Combinations of Oxygen Gradients, Tensions, and Drug Treatments," *Scientific Reports*, Vol. 9, 8234, June 2019.
7. H.-M. Wu, T.-A. Lee, P.-L. Ko, W.-H. Liao, T.-H. Hsieh, and Y.-C. Tung\*, "Widefield Frequency Domain Fluorescence Lifetime Imaging Microscopy (FD-FLIM) for Accurate Measurement of Oxygen Gradients within Microfluidic Devices," *Analyst*, Vol. 144, Issue 11, pp. 3494-3504, June 2019. **(Featured as the inside back cover image)**
8. T.-A. Lee, W.-H. Liao, Y.-F. Wu, Y.-L. Chen, and Y.-C. Tung\*, "Electrofluidic Circuit-Based Microfluidic Viscometer for Analysis of Newtonian and Non-Newtonian Liquids under Different Temperatures," *Analytical Chemistry*, Vol. 90, No. 3, pp. 2317-2325, February 2018.
9. B. Patra, C.-C. Peng, W.-H. Liao, C.-H. Lee, and Y.-C. Tung\*, "Drug Testing and Flow Cytometry Analysis on a Large Number of Uniform Sized Tumor Spheroids Using a Microfluidic Device," *Scientific Reports*, Vol. 6, 21061 (12 pages), February 2016.

## Positions and Career

- Research Fellow, Research Center for Applied Sciences, Academia Sinica (2018 - )
- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica (2013 - 2018)
- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica (2009 - 2013)
- Postdoctoral Research Fellow, Department of Biomedical Engineering, University of Michigan, Ann Arbor, USA (2006 - 2009)

## Honors and Awards

- 2018 Project for Excellent Junior Research Investigators, Taiwan Ministry of Science and Technology (MOST)
- 2016 Career Development Award, Academia Sinica
- 2016 Top 10% Highly Cited Author, Analytical Portfolio of Royal Society of Chemistry (RSC) Journals
- 2014 Ta-You Wu Memorial Award, Taiwan Ministry of Science and Technology (MOST)

## Research Interests

- Microfluidic Cell Culture and Analysis
- Biomedical Instruments
- Advanced Micro/Nano Fabrication Techniques

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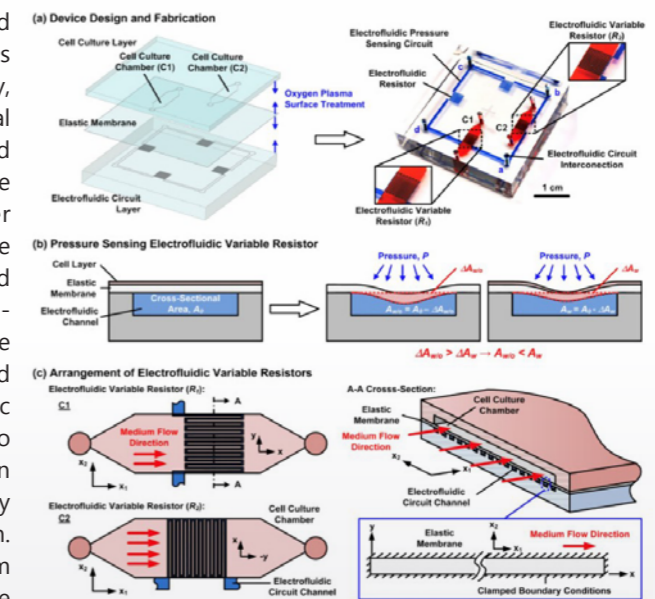
## Research Focus

### 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.

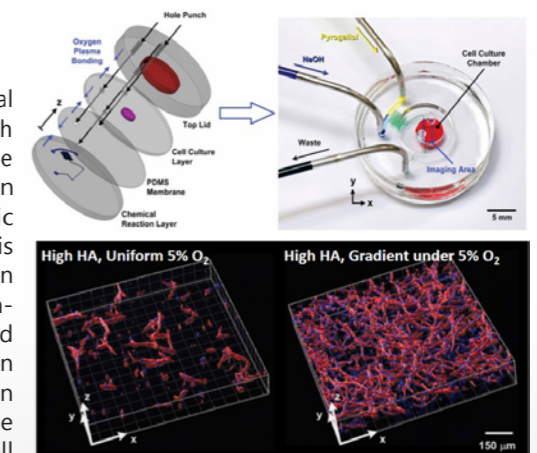


### Study 3D Endothelial Cell Network Formation under Various Oxygen Microenvironment and Hydrogel Composition Combinations Using Upside-Down Microfluidic Devices

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

Academic Sinica, Research Center for Applied Sciences  
*Small* 2021, DOI: 10.1002/smll.202006091

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% O<sub>2</sub>; oxygen gradients under normoxia and 5% O<sub>2</sub>) 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*.



# Chih-Yu Kuo

Research Fellow

Education | Ph.D. Engineering, Cambridge University, UK (1998)

## Positions and Career

- Adjunct Professor, Department of Civil Engineering, National Taiwan University, (2021 – )
- Research Fellow, Research Center for Applied Sciences, Academia Sinica (20017 – )
- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica (2013 – 2017)
- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica (2006 – 2013)
- Senior RD Engineer, Synopsys Co. (2005 – 2006)
- Senior RD Engineer, Nassda Co. (2000 – 2005)
- Research Associate, Department of Engineering, Cambridge University, UK (1998 – 2000)

## Honors and Awards

- 2020 research paper award, Journal of Chinese Soil Water Conservation
- 2018 research paper award, Journal of Chinese Soil Water Conservation
- 2013 research paper award, Journal of Mechanics

## Research Interests

- Slope stability monitoring
- Failure surface analysis and inversion
- Debris flow, fluid mechanics, granular flows, plasticity
- Wind resource assessments, Acoustics

## Selected Publications

1. Y. T. Lai, P. K. Wei, Chih-Yu Kuo, J. Y. Chen (2023) Inference detection and classification of illicit drugs by a modest Raman spectrometer with a convolutional neural network analyzer, *Sensors Actuators B: Chem.* **375**, 132923.
2. S. Alexandrov, Y.-R. Jeng, Chih-Yu Kuo, C.-Y. Chen, (2022). Towards the theoretical/experimental description of the evolution of material properties at frictional interfaces in metal forming processes. *Trib. Intl.*, 171, 107518.
3. Chih-Yu Kuo, S.-E. Lin, R.-F. Chen, Y.-J. Hsu, K.-J. Chang, S.-P. Lee, R.-Y. Wu, C.-W. Lin and Y.-H. Chan (2021). Occurrences of Deep-Seated Creeping Landslides in Accordance with Hydrological Water Storage in Catchments. *Front. in Earth Sci.*, **9**, doi:10.3389/feart.2021.743669.
4. Chih-Yu Kuo, P.-W. Tsai, Y.-C. Tai, Y.-H. Chan, R.-F. Chen, C.-W. Lin (2020). Application assessments of using scarp boundary-fitted, volume constrained, smooth minimal surfaces as failure interfaces of deep-seated landslides. *Front. in Earth Sci.*, **8**, doi:10.3389/feart.2020.00211
5. Y. C. Chung, C.-W. Wu, Chih-Yu Kuo, S. S. Hsiao, (2019). A rapid granular chute avalanche impinging on a small fixed obstacle: DEM modeling, experimental validation and exploration of granular stress. *Appl. Math. Model.*, **70**, 540-568.
6. S. Alexandrov, Chih-Yu Kuo, Y. R. Jeng (2018). An accurate numerical solution for the singular velocity field near the maximum friction surface in plane strain extrusion. *Int. J. Solids and Struct.*, **150**, 107-116.
7. I. Luca, Y. C. Tai, Chih-Yu Kuo. *Shallow geophysical mass flows down arbitrary topography*. Switzerland: Springer, 2016.
8. Chih-Yu Kuo, K.-J. Chang, P.-W. Tsai, S.-K. Wei, R.-F. Chen, J.-J. Dong, C.-M. Yang, Y.-C. Chan, Y.-C. Tai (2015). Identification of co-seismic ground motion due to fracturing and impact of the Tsaoing landslide, Taiwan. *Eng. Geo.*, **196**, 268-279.
9. S. Alexandrov, Chih-Yu Kuo, Y.-R. Jeng (2015). A numerical method for determining the strain rate intensity factor under plane strain conditions, *Conti. Mech. Thermodyn.*, **28**, 977-992.
10. Chih-Yu Kuo, L.-T. Sheng, S.-Y. Chiu, Y.-Z. Yang, Y.-C. Tai, S.-S. Hsiao (2015). Measurement and discrete element simulation of a fixed-obstacle disturbed rapid granular chute flow. *Phys. Fluids*, **27**, 013305.
11. W. C. Chen, Chih-Yu Kuo, K.-M. Shyue, Y.-C. Tai (2013). Gas kinetic scheme for anisotropic Savage-Hutter model. *Comm. Comput. Phys.*, **13**, 1432-1454.

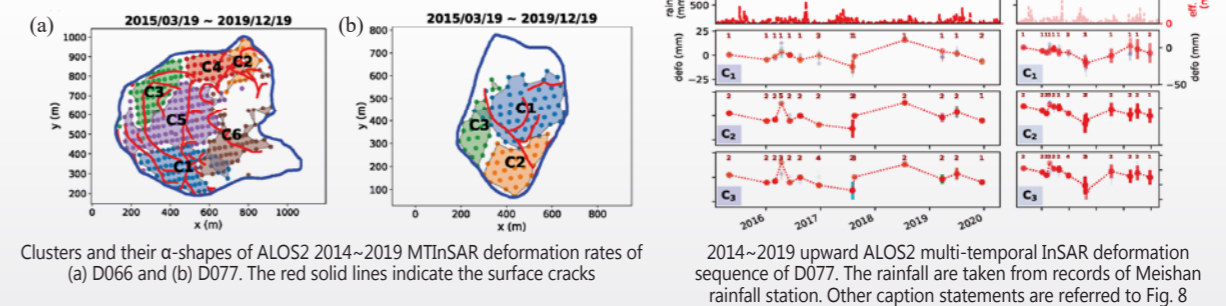
## Research Focus

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

Pi-Wen Tsai, Chih-Yu Kuo<sup>1</sup>, Rou-Fei Chen

<sup>1</sup>Academic Sinica, Research Center for Applied Sciences

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.



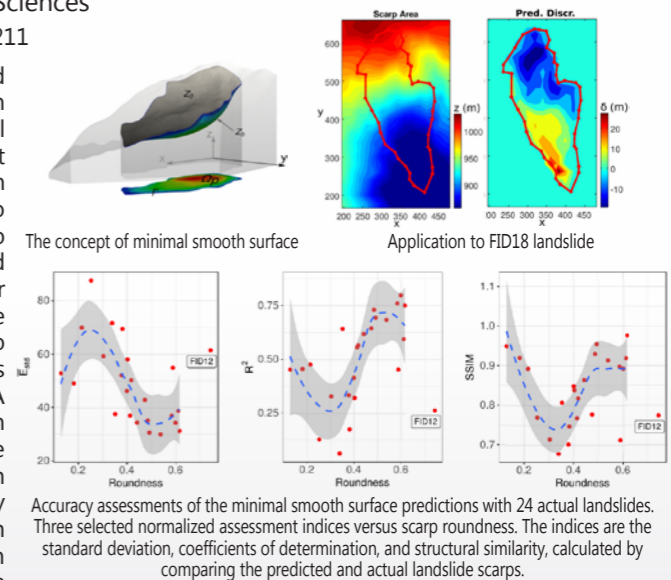
### Application assessments of using scarp boundary-fitted, volume constrained, smooth minimal surfaces as failure interfaces of deep-seated landslides

Chih-Yu Kuo<sup>1</sup>, P.W. Tsai, Y. C. Tai, Y. H. Chan, R. F. Chen, C. W. Lin

<sup>1</sup>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.





# Bi-Chang Chen

Associate Research Fellow

## Education

Ph.D. Chemistry and Biochemistry, The University of Texas at Austin, Texas, U.S.A.(2011)

## Selected Publications

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.jymeth.2019.04.006 (2020)
6. Chu, L.-A., Lu, C.-H., Yang, S.-M., Liu, Y.-T., Feng, K.-L., Tsai, Y.-C., Chang, W.-K., Wang, W.-C., Chang, S.-W., Chen, P.; Lee, T.-K., Hwu, Y.-K., Chiang, A.-S.\*; and **Chen, B.-C.\***, "Rapid single-wavelength lightsheet localization microscopy for clarified tissue" *Nature Communications*, 10, 4762, DOI: 10.1038/s41467-019-12715-3 (2019)
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)

## Positions and Career

- Associate Research Fellow, Research Center for Applied Sciences Academia Sinica (2020–Present)
- Assistant Research Fellow, Research Center for Applied Sciences Academia Sinica (2014–2020)
- Postdoctoral Associate, Howard Hughes Medical Institute/Janelia Research Campus, USA (2011–2014)

## Honors and Awards

- The 2015 AAAS Newcomb Cleveland Prize
- 2020 18th Y. Z. Hsu Science Paper Award, Optoelectronics Science & Technology Category
- 2021 Academia Sinica Early-Career Investigator Research Achievement Award

## Research Interests

- Super-resolution fluorescence imaging
- Fast 3D live imaging
- Developing Lightsheet microscopy technique
- Imaging on the expanded clarified tissue

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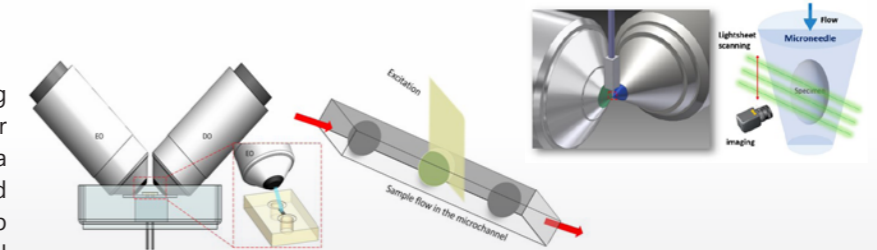
## Research Focus

### 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 developed to achieve high spatiotemporal resolutions in 3D.

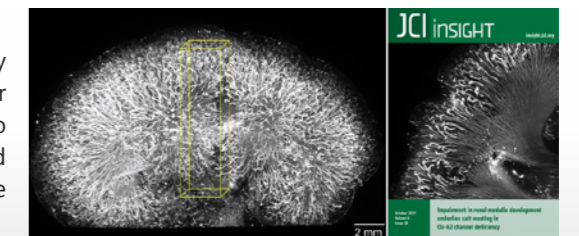


### Lightsheet expansion microscopy for 3D super-resolution imaging in the organ

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.

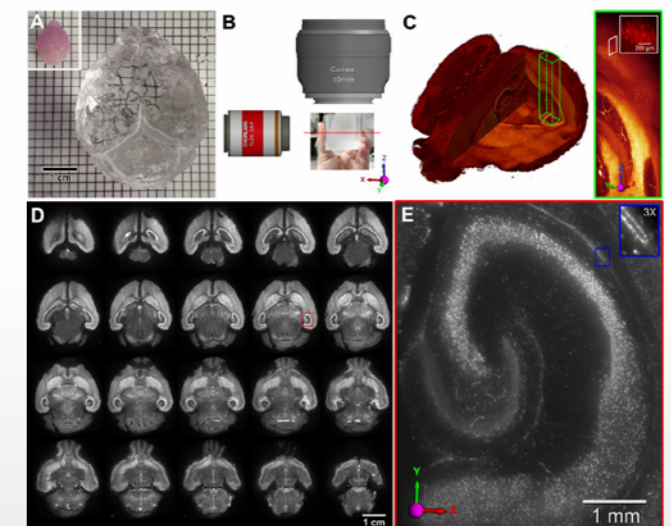


### Macro Photography with Lightsheet Illumination Enables Whole Expanded Brain Imaging with Single-cell Resolution

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.





# Yu-Jung Lin

Assistant Research Fellow

**Education** | Ph.D. Physiology, National Yang-Ming University (2014)

## Positions and Career

- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica, Taiwan (2020-Present)
- Postdoctoral Fellow, Department of Chemical Engineering, National Tsing Hua University, Taiwan (2015-2020)
- Visiting Scholar, Department of Physiology, University of Kentucky, Lexington, Kentucky, USA (2011-2013)

## Honors and Awards

- 2022 Cross-Generation Young Scholars Program (Emerging Young Scholars), National Science and Technology Council, Taiwan
- 2020 Young Investigator Award, Prof. Chau-Jen Lee Biomedical Engineering Development Foundation, Taiwan
- 2019 Best Research Paper Award for Postdoctoral Fellows, Ministry of Science and Technology, Taiwan

## Research Interests

- Development of drug delivery systems
- Development of therapeutic gas-generating systems

## Selected Publications

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 H<sub>2</sub> storage system as an in situ H<sub>2</sub>/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.
5. Miao, Y. B.†, **Lin, Y. J.†**, Chen, K. H.†, Luo, P. K., Chuang, S. H., Yu, Y. T., Tai, H. M., Chen, C. T., Lin, K. J., Sung, H. W. Engineering nano- and microparticles as oral delivery vehicles to promote intestinal lymphatic drug transport. *Advanced Materials* 2021, 33, e2104139. (†Equal Contribution)
6. Korupalli, C., Li, H., Nguyen, N., Mi, F. L., Chang, Y., **Lin, Y. J.\***, Sung, H. W.\* Conductive materials for healing wounds: their incorporation in electroactive wound dressings, characterization, and perspectives. *Advanced Healthcare Materials* 2021, 10, 2001384.
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.

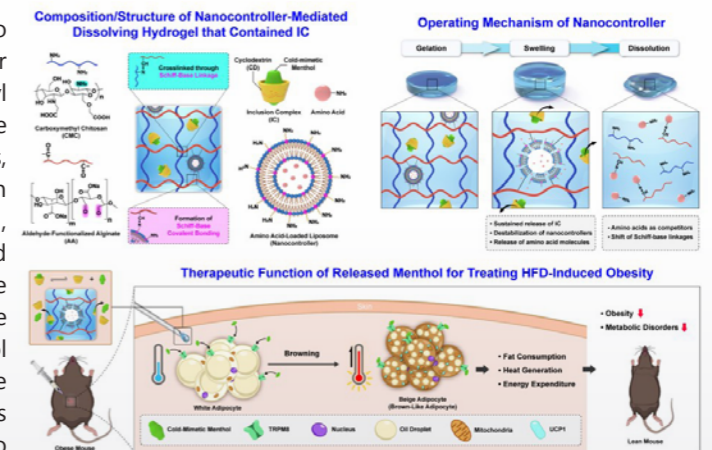
## Research Focus

### 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.

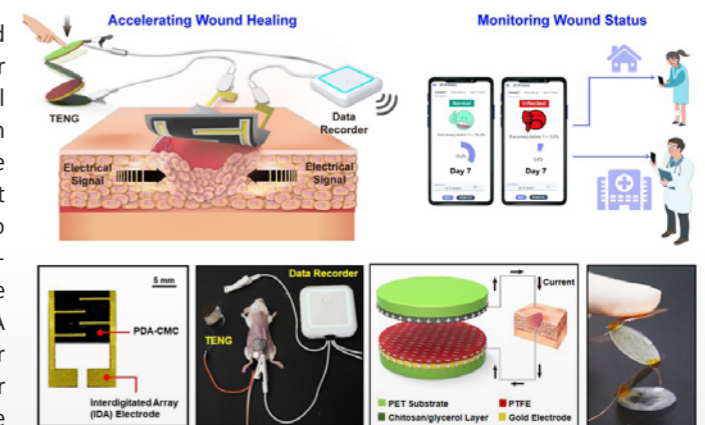


### Engineering an Integrated Electroactive Dressing to Accelerate Wound Healing and Monitor Noninvasively Progress of Healing

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 stimulatory 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.





# Tung-Han Hsieh

Research Specialist

## Education

Ph.D. Physics, National Taiwan University, Taiwan (2002)

## Positions and Career

- Research Specialist, Research Center for Applied Sciences, Academia Sinica (2020 – present)
- Associate Research Specialist, Research Center for Applied Sciences, Academia Sinica (2016 – 2020)
- Assistant Research Specialist, Research Center for Applied Sciences, Academia Sinica (2006 – 2015)
- Assistant Professor, Physics Division, Commission of General Education, National United University (2005 – 2006)
- Postdoctoral fellow, Physics Department, National Taiwan University (2002 – 2005)

## Honors and Awards

- 2023 19th National Innovation Award in the Academic Research Category
- 2005 The Excellent Ph. D. Thesis Award of the Physical Society of the Republic of China.

## Research Interests

- Machine learning.
- Biomedical image processing and signal analysis.
- Computational physics.
- Development and maintenance of high-performance computing facilities.
- Lattice QCD computation.

## Selected Publications

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.

## Research Focus

### 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)

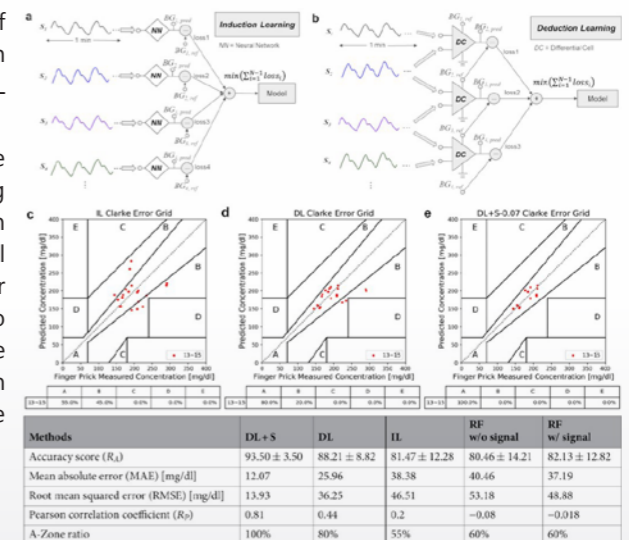
Diabetes mellitus (DM) is a chronic condition of abnormally elevated blood glucose level (BGL), which leads to various complications. Currently, reliable BGL measurement utilize invasive methods.

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.

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

$$BG_k \leftarrow DL(S_k, S_N, BG_N)$$

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.



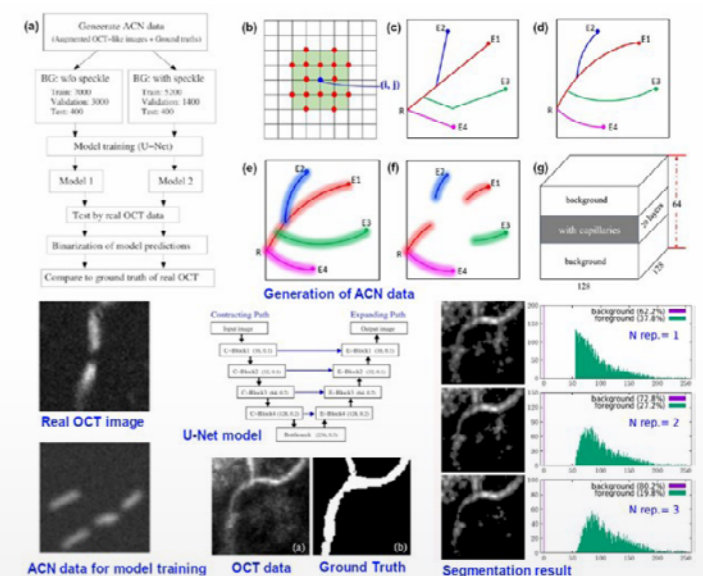
### OCT skin image analysis for capillary network reconstruction

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, microangiography 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 attained accuracy 0.798, and F1 score 0.814.



# Shu-Yi Hsieh

Assistant Research Specialist

**Education** | Ph.D. Department of Chemistry, National Tsing Hua University (2008)

## Selected Publications

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.
5. W. H. Lin, J. T. A. Hsu, S. Y. Hsieh, C. T. Chen, J. S. Song, S. C. Yen, T. Hsu, C. T. Lu, C. H. Chen, L. H. Chou, Y. N. Yang, C. H. Chiu, C. P. Chen, Y. J. Tseng, K. J. Yen, C. F. Yeh, Y. S. Chao, T. K. Yeh, and W. T. Jiaang. "Discovery of 3-phenyl-1H-5-pyrazolylamine derivatives containing a urea pharmacophore as potent and efficacious inhibitors of FMS-like tyrosine kinase-3 (FLT3)." *Jiaang, Bioorganic & medicinal chemistry*, **2013**, *21*(11), 2856-2867.
6. W. H. Lin, S. Y. Hsieh, S. C. Yen, C. T. Chen, T. K. Yeh, T. Hsu, C. T. Lu, C. P. Chen, C. W. Chen, L. H. Chou, Y. L. Huang, A. H. Cheng, Y. I. Chang, Y. J. Tseng, K. R. Yen, Y. S. Chao, J. T. Hsu, W. T. Jiaang. "Discovery and evaluation of 3-phenyl-1H-5-pyrazolylamine-based derivatives as potent, selective and efficacious inhibitors of FMS-like tyrosine kinase-3 (FLT3)." *Bioorganic & medicinal chemistry*, **2011**, *19*(14), 4173-82.
7. S. Y. Hsieh, M. D. Jan, L. N. Patkar, C. T. Chen, C. C. Lin. "Synthesis of a carboxyl linker containing Pk trisaccharide." *Carbohydrate research*, **2005**, *340*(1), 49-57.
8. K. C. Lu, S. Y. Hsieh, L. N. Patkar, C. T. Chen, C. C. Lin. "Simple and Efficient per-O-Acetylation of carbohydrates by lithium perchlorate catalyst." *Tetrahedron*, **2004**, *60*(40), 8967-8973.

## Positions and Career

- Assistant Research Specialist, Research Center for Applied Sciences, Academia Sinica (2020-)
- Postdoctoral Research, Research Center for Applied Sciences, Academia Sinica (2011-2020)
- Postdoctoral Research, Institute of Biotechnology and Pharmaceutical Research, National Health Research Institutes, (2080-2011)

## Research Interests

- Organic Synthesis
- Nanomaterial Synthesis
- Small Molecule Drug Development and Drug Delivery
- Biosensor Development and Applications

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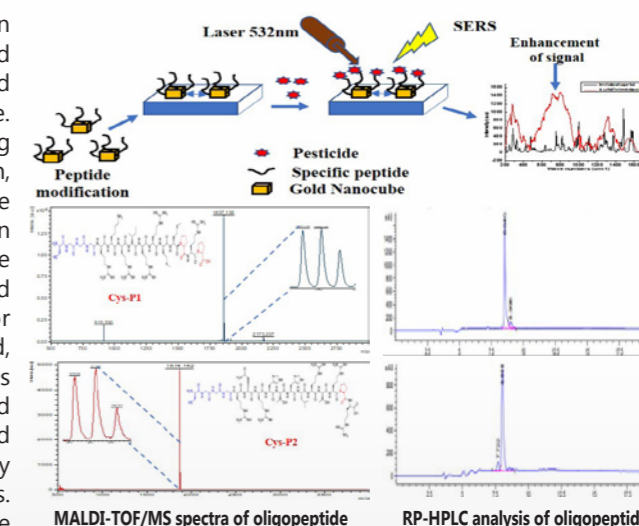
[https://www.rcas.sinica.edu.tw/pi\\_web/shuyihsieh.php](https://www.rcas.sinica.edu.tw/pi_web/shuyihsieh.php)

## Research Focus

### Multiple Pesticides Detection by Integrating Synthetic Peptides and Gold Nanoparticles

Tran Thi Anh Hong,<sup>1</sup> Sheng-Hann Wang,<sup>1</sup> Ting-Wei Chang,<sup>1</sup> Pei-Kuen Wei,<sup>1</sup> Shu-Yi Hsieh<sup>1\*</sup>

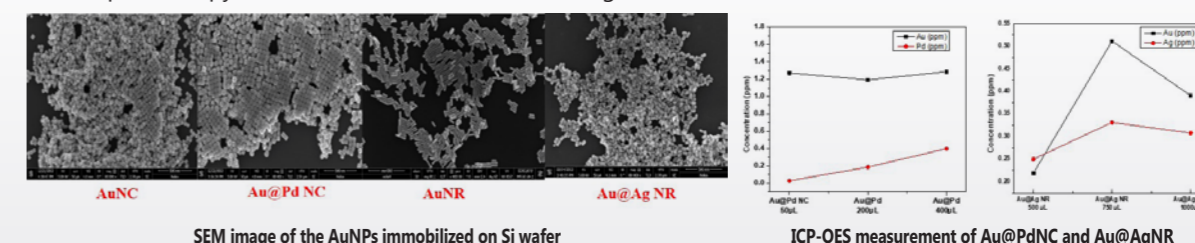
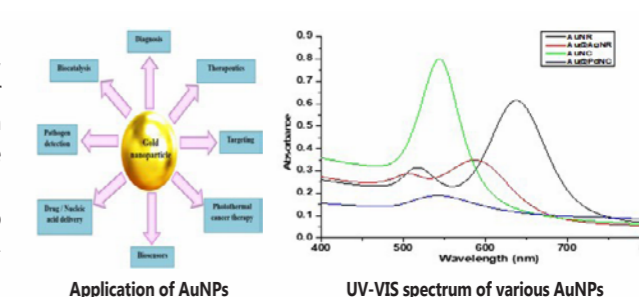
In this study, we attempt to develop a detection system by integrating self-synthesized peptides and gold nanoparticles (AuNPs) that is time-saving and enhances specificity as well as a simple technique. Principally, the surface-enhanced Raman scattering (SERS) technique is applied for pesticide detection, herein, AuNPs can be used as SERS substrate due to its roughened surfaces induces Raman signal enhancement. In addition, oligopeptide sequences CGGGRKRIRMMMPRPS (Cys-P1) and CGGGRNRHHLRTRPR (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.



### Various Gold Nanoparticles Synthesis: Property, Morphology and Applications

Tran Thi Anh Hong,<sup>1</sup> Shu-Yi Hsieh<sup>1\*</sup>

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.



# Chih Wei Chu

Executive Officer of the TCGT and Research Fellow

**Education** | Ph.D. Materials Science and Engineering, University of California, Los Angeles (2006)

## Positions and Career

- Deputy Director, Research Center for Applied Sciences (RCAS), Academia Sinica (2016 – 2022)
- Acting Executive Officer of the thematic center for Mechanics and Engineering Science, Academia Sinica (2023 –)
- Adjunct Professor, Department of Photonics, National Yang-Ming Chiao Tung University (2019 –)
- Adjunct Professor, Department of Materials Science and Engineering, National Tsing Hua University, (2017 – 2020)
- Research Fellow, RCAS, Academia Sinica (20014-)
- Adjunct Professor, College of Engineering, Chang Gung University (2014 –)
- Associate Research Fellow, RCAS, Academia Sinica (2010 – 2014)
- Assistant Research Fellow, RCAS, Academia Sinica (2006 – 2010)

## Honors and Awards

- 2022 World's Top 2% Scientists
- 2022 SPIE Senior Member
- 2019 Young Scientist of Asia Pacific Academy of Materials
- 2019 Associate Academician of Asia Pacific Academy of Materials
- 2014 Career Development Award, Academia Sinica

## Research Interests

Organic electronics and optoelectronics  
Perovskite solar cells  
Flexible electronics and optoelectronics  
Li metal batteries

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## Selected Publications

1. Chintam Hanmandlu, Rohan Paste, Hsinhan Tsai, Shyam Narayan Singh Yadav, Kuan-Wen Lai, Yen-Yu Wang, Chandra Shekar Gantepogu, Chen-Hung Hou, Jing-Jong Shyue, Yu-Jung Lu, Tushar Sanjay Jadhav, Jian-Ming Liao, Hsien-Hsin Chou, Hui Qi Wong, Ta-Jen Yen, Chao-Sung Lai, Dibyajyoti Ghosh, Sergei Tretiak, Hung-Ju Yen\*, Chih Wei Chu\*, "3D Nanographene Precursor Suppress Interfacial Recombination in PEDOT: PSS based Perovskite Solar Cells" *Nano Energy*, 107, 108136 (2023).
2. 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\*, "Intimate interaction of TFSI- anions with MoO<sub>3</sub>- x oxygen vacancies boost ionic conductivity of cathode-supported solid polymer electrolyte" *Chemical Engineering Journal*, 452, 139088 (2023).
3. Syed Ali Abbas, Hsin-An Chen, Anisha Mohapatra, Anupriya Singh, Chun-Wei Pao, Chih Wei Chu\*, "Sweetening Lithium Metal Interface by High Surface and Adhesive Energy Coating of Crystalline  $\alpha$ -D-Glucose Film to Inhibit Dendrite Growth" *Small*, 18, 2201349 (2022).
4. Chintam Hanmandlu, Mamina Sahoo, Chi-Ching Liu, Yun-Chorng Chang, Chih Wei Chu\*, Chao-Sung Lai\*, "Few-layer fluorine-functionalized graphene hole-selective contacts for efficient inverted perovskite solar cells" *Chemical Engineering Journal*, 430, 132831 (2021).
5. Anupriya Singh, Po-Ting Lai, Anisha Mohapatra, Chien-Yu Chen, Hao-Wu Lin, Yu-Jung Lu, Chih Wei Chu\*, "Panchromatic heterojunction solar cells for Pb-free All-Inorganic Antimony Based Perovskite" *Chemical Engineering Journal*, 419, 129424 (2021).
6. Anisha Mohapatra, Anupriya Singh, Syed Ali Abbas, Yu-Jung Lu, Karunakara Moorthy Boopathi, Chintam Hanmandlu, Nahid Kaiser, Chih-Hao Lee, Chih-Wei Chu\*, "Bilayer polymer solar cells prepared with transfer printing of active layers from controlled swelling/deswelling of PDMS" *Nano Energy*, 63, 103826 (2019).
7. Mriganka Singh, Annie Ng, Zhiwei, Ren, Hanlin, Hu, Hong-Cheu Lin\*, Chih Wei Chu\*, Gang Li\*, "Facile synthesis of composite tin oxide nanostructures for highperformance planar perovskite solar cells" *Nano Energy*, 60, 275 (2019).
8. Yen-An Lu, Ting-Hsiang Chang, Shang-Hsuan Wu, Chi-Ching Liu, Kuan-Wen Lai, Yun-Chorng Chang, Yia-Chung Chiang, Hsin-Chun Lu, Chih Wei Chu, Kuo-Chuan Ho, Coral-like perovskite nanostructures for enhanced light-harvesting and accelerated charge extraction in perovskite solar cells", *Nano Energy*, 58, 138 (2019).

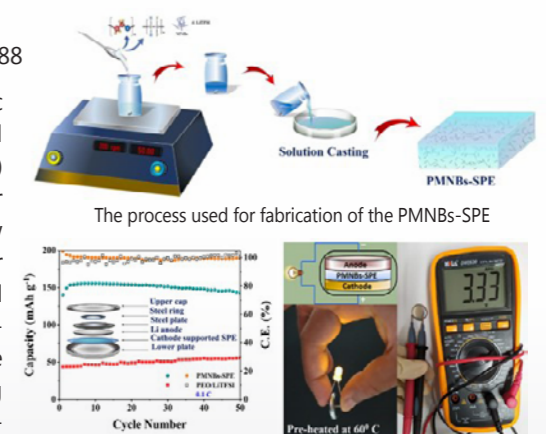
## Research Focus

### Intimate Interaction of TFSI- Anions with MoO<sub>3</sub> 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 MoO<sub>3</sub>-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.



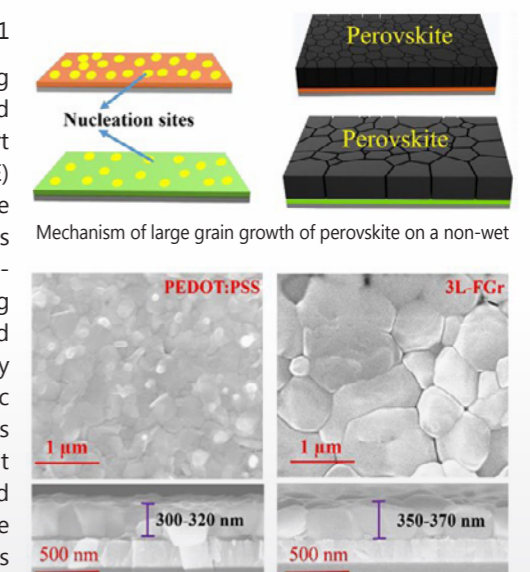
The process used for fabrication of the PMNBs-SPE  
Cycling performance of PEO/LiTFSI and PMNBs-SPE with an LFP cathode and Li anode at 0.1C and at 60°C  
LED test and measured value of Voc of a CR2032 cell containing PMNBs-SPE

### 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

# Chun-Wei Pao

Research Fellow

**Education** | Ph.D. Mechanical and Aerospace Engineering, Princeton University (2007)

## Selected Publications

- Po-Yu Yang, Yu-Hsuan Chiang, Chun-Wei Pao\*, Chien-Cheng Chang\* (2023), "Hybrid Machine Learning-Enabled Potential Energy Model for Atomistic Simulation of Lithium Intercalation into Graphite from Plating to Overlithiation", *Journal of Chemical Theory and Computation* (in press).
- 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\* (2022), "A Highly Distorted Ultra-Elastic Chemically Complex Elinvar Alloy", *Nature* **602**, 251.
- Q.F. He\*, P.H. Tang, H.A. Chen, S. Lan, J.G. Wang, J.H. Luan, M. Du, Y. Liu, C.T. Liu, C.W. Pao\*, Y. Yang\* (2021), "Understanding chemical short-range ordering/demixing coupled with lattice distortion in solid solution high entropy alloys", *Acta Materialia* **216**, 117140.
- Hsin-An Chen, Ping-Han Tang, Guan-Jie Chen, Chien-Cheng Chang\*, Chun-Wei Pao\* (2021), "Microstructure Maps of Complex Perovskite Materials from Extensive Monte Carlo Sampling Using Machine Learning-Enabled Energy Model", *Journal of Physical Chemistry Letters* **12**, 3591.
- Po-Yu Yang, Chun-Wei Pao (2021), "Molecular Simulations of the Microstructure Evolution of Solid Electrolyte Interphase during Cyclic Charging/Discharging", *ACS Applied Materials & Interfaces*, **13**, 5017.
- Chih-Hung Chen, Chun-Wei Pao (2021), "Phase-field study of dendritic morphology in lithium metal batteries", *Journal of Power Sources* **484**, 229203
- Cheng-Lun Wu, Fang-Cheng Li, Chun-Wei Pao\*, David J. Srolovitz\* (2017), "Folding Sheets with Ion Beams", *Nano Letters* **17**, 249-254.
- Cheng-Kuang Lee, Chun-Wei Pao\* (2016), "Multiscale Molecular Simulation of Solution Processing of SMDPPEH:PCBM Small Molecule Organic Solar Cells", *ACS Applied Materials & Interfaces* **8**, 20691-20700
- Cheng-Kuang Lee, Chun-Wei Pao\*, Chun-Wei Chen (2013), "Correlation of nanoscale organizations of polymer and nanocrystals in polymer/inorganic nanocrystal bulk heterojunction hybrid solar cells: insights from multiscale molecular simulations", *Energy & Environmental Science* **6**, 307.
- Te-Huan Liu, Grzegorz Gajewski, Chun-Wei Pao\*, Chien-Cheng Chang\* (2011), "Structure, energy, and structural transformations of graphene grain boundaries from atomistic simulations", *CARBON* **49**, 2306-17.

## Positions and Career

- Adjunct Professor, Department of Photonics, National Yang Ming Chiao Tung University (2020 - )
- Joint Professor, Department of Materials Science and Engineering, National Dong Hwa University, (2018 - )
- Research Fellow, Research Center for Applied Sciences, Academia Sinica (2018- )
- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica (2014 – 2018)
- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica (2009 – 2014)
- Postdoctoral Research Associate, Theoretical Division, Los Alamos National Laboratory, Los Alamos, NM, USA (2007 – 2009)

## Honors and Awards

- 2023 Y. Z. Hsu Scientific Paper Award
- 2022 Investigator Award, Academia Sinica
- 2018 IUPAC Distinguish Award for Novel Materials and their Synthesis
- 2015 Career Development Award, Academia Sinica
- 2014 Youth Award
- 2014 Young Theorist Award, National Center for Theoretical Sciences
- 2013 Project for Excellent Junior Research Investigators, National Science Council of Taiwan

## Research Interests

Multiscale Simulation of Materials

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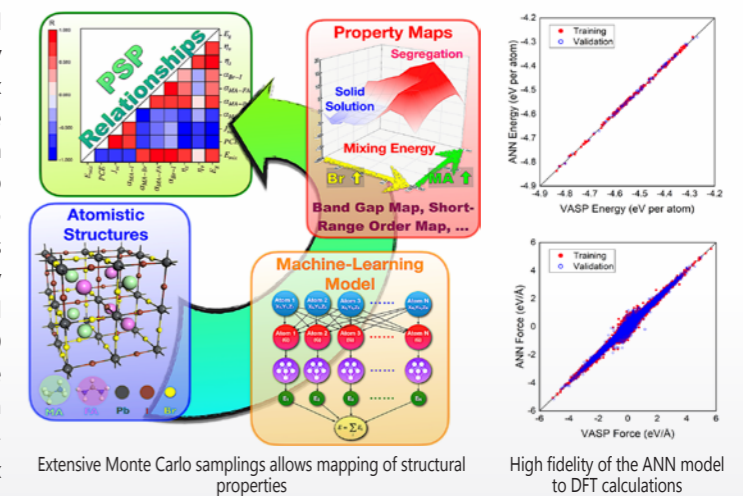
## Research Focus

### 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)

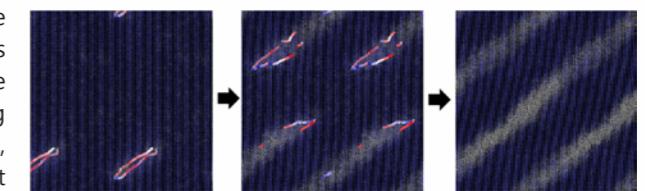
In this work, we trained an artificial neural network (ANN) potential energy model of the  $MA_xFA_{1-y}Pb(Br_xI_{1-x})_3$  complex perovskite material and investigated the microstructure over the composition space using extensive Monte Carlo simulations. We sampled around  $8.1 \times 10^5$  structures 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.



### A Highly Distorted Ultra-Elastic Chemically Complex Elinvar Alloy

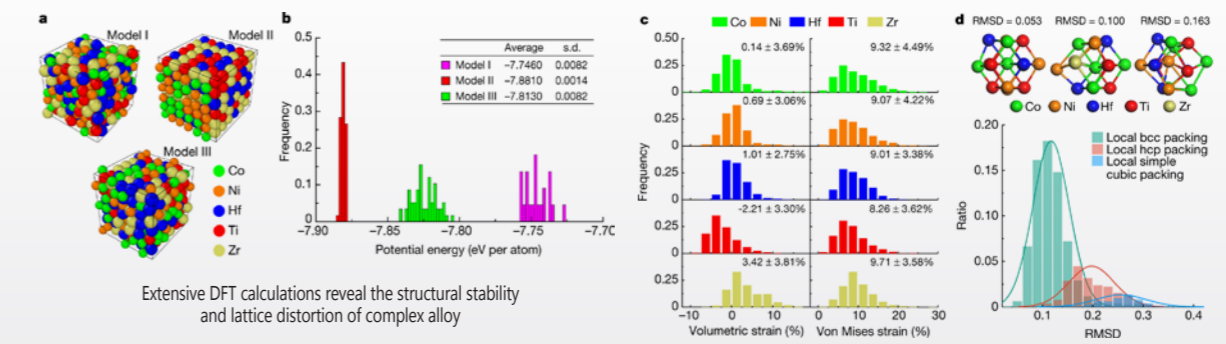
Quanfeng He, J.G. Wang, Hsin-An Chen, Z.Y. Ding, Z.Q. Zhou, L.H. Xiong, Junhua Luan, J.M. Pelletier, J.C. Qiao, Q. Wang, L.L. Fan, Yang Ren, Qiaoshi Zeng, Chain Liu, C.W. Pao\*, David Srolovitz\*, Yong Yang\*

*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



Plastic deformation from MLMD simulations (ongoing)

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.





# Yun-Chorng Chang

Associate Research Fellow

**Education** | Ph.D. Electrical Engineering, North Carolina State University (2001)

## Positions and Career

- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica (2014- Now)
- Adjunct Associate Professor, Dept. of Photonics, National Yang-Ming Chiao Tung Univ, (2018 -Now)
- Adjunct Associate Professor, Dept. of Physics, National Taiwan Univ. (2016 -Now)
- Adjunct Professor, Dept. of Photonics, National Cheng Kung Univ., (2014 - Now)
- Professor, Dept. of Photonics, National Cheng Kung Univ. (2013 – 2014)
- Associate Professor, Dept. of Photonics, National Cheng Kung Univ. (2008 – 2013)
- Assistant Professor, Inst. of Electro-Optical Science and Engineering, National Cheng Kung Univ. (2003 – 2008)
- Postdoctoral Research, Department of Electrical and Computer Engineering, North Carolina State University (2002 – 2003)

## Honors and Awards

- 2022 IEEE Senior Member
- 2014 SPIE Senior Member
- 2012 2012 Innovative Research Award for Young Scholars, 3rd place, Taiwan Comprehensive University System

## Research Interests

Nanofabrication and Nanophotonics  
Semiconductor and Biosensing

## Selected Publications

1. C. C. Liu, H. H. Hsiao, Y. C. Chang\*, "Nonlinear Two-photon Pumped Vortex Lasing Based on Quasi-Bound States in the Continuum from Perovskite Metasurface", *Science Advances*, 2023/05, 9, eadf6649.
2. C. Y. Li, C. C. Liu, W. C. Lai, Y. -C. Lan\*, and Y. C. Chang\*, "Quantifying the Plasmonic Generation Rate of Non-Thermal Hot Carriers with an AlGaIn/GaN High-Electron-Mobility Transistor", *Advanced Science*, 2021/07, 8(13) 2100362.
3. C. Y. Lin, C. C. Liu, Y. Y. Chen, K. Y. Chiu, J. D. Wu, B. L. Lin, C. H. Wang, Y. F. Chen, S. -H. Chang\*, and Y. C. Chang\*, "Molecular chirality detection with periodic arrays of three-dimensional twisted metamaterials", *ACS Applied Materials & Interfaces*, 2021/01, 11(01), 1152–1157.
4. M. C. Chou, C. Y. Lin, B. L. Lin, C. H. Wang, S. H. Chang, W. C. Lai, K. Y. Lai, and Y. C. Chang\*, "Polarization-Selecting III-Nitride Elliptical Nanorod Light-Emitting Diodes Fabricated with Nanospherical-Lens Lithography", *ACS Nano*, 2018/08, 12(08), 8748–8757.
5. Y. H. Chien, C. H. Wang, C. C. Liu, S. H. Chang, K. V. Kong, and Y. C. Chang\*, "Large-scale nanofabrication of designed nanostructures using Angled Nanospherical-Lens Lithography for Surface Enhanced Infrared Absorption Spectroscopy", *ACS Applied Materials & Interfaces*, 2017/07, 9(29), 24917–24925.
6. Y. C. Chang\*, H. C. Chung, S. C. Lu, T. F. Guo, "Large-scale sub-100nm Au nanodisk array fabricated using Nanospherical-Lens Lithography: a low-cost localized surface plasmon resonance sensor", *Nanotechnology*, 2013/03, 24(09), 095302.
7. I. T. Chen, P. H. Chang, Y. C. Chang\*, T. F. Guo\*, "Lighting Up Ultraviolet Fluorescence From Chicken Albumen Through Plasmon Resonance Energy Transfer of Gold Nanoparticles", *Scientific Reports*, 2013/03, 3, 1505.
8. Y. C. Chang\*, S. C. Lu, H. C. Chung, S. M. Wang, T. D. Tsai, T. F. Guo, "High-Throughput Nanofabrication of Infra-red and Chiral Metamaterials using Nanospherical-Lens Lithography", *Scientific Reports*, 2013/11, 3, 3339.
9. Y. H. Liao, Y. J. Chang, Y. Yoshiike, Y. C. Chang\*, Y. R. Chen\*, "Negatively charged gold nanoparticles inhibit Alzheimer's amyloid-beta fibrillization, induce fibril dissociation, and mitigate neurotoxicity", *Small*, 2012/12, 8(23), 3631–3639.

10. Y. C. Chang\*, S. M. Wang, H. C. Chung, C. B. Tseng, S. H. Chang, "Observation of Absorption-Dominated Bonding Dark Plasmon Mode from Metal-Insulator-Metal Nanodisk Arrays fabricated by Nanospherical-Lens Lithography", *ACS Nano*, 2012/04, 6(4), 3390–3396.

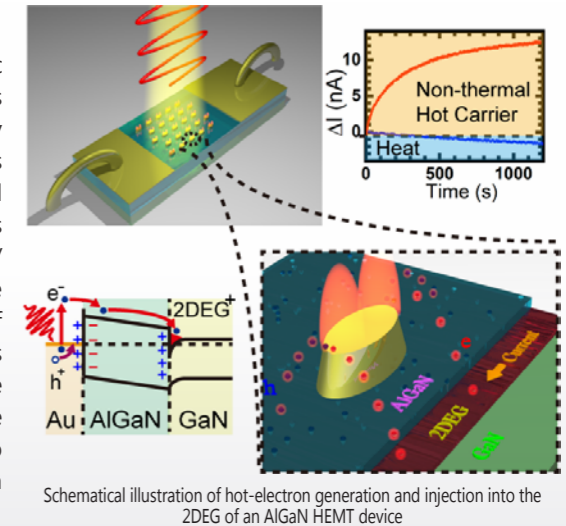
## Research Focus

### Quantifying the Plasmonic Generation Rate of Non-Thermal Hot Carriers with an AlGaIn/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/adv.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 AlGaIn/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.

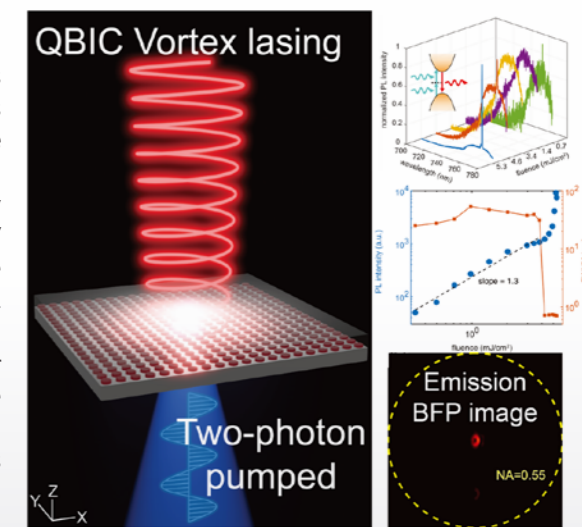


### Nonlinear Two-photon Pumped Vortex Lasing Based on Quasi-Bound States in the Continuum from Perovskite Metasurface

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<sup>2</sup>, 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.



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

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# Yuh-Jen Cheng

Associate Research Fellow

Education | Ph.D. Applied Physics, Stanford University (1997)

## Positions and Career

- Associate Research Fellow, Academia Sinica, 2012-present.
- Assistant Research Fellow, Academia Sinica, 2008-2012.
- Associate Research Technical Staff, Academia Sinica, 2006-2007.
- Staff Optical Engineer/project lead, Bookham Technologies, 2000-2005.
- Senior Engineer, Seagate Technology, 1997-2000.

## Research Interests

- Photoelectrochemical water splitting and electrocatalysis.
- 2D material epitaxy and optoelectronic devices.
- Sustainable green energy and carbon capture.
- Quantum photonic devices.

## Selected Publications

1. Chi-Huang Chuang, Pei-Hao Kang, Yung-Yu Lai, Cheng-Hung Hou, Wei-Che Tseng, Yan-Jia Huang, Mu-Huai Fang, Jing-Jong Shyue, Chao-Cheng Kaun, and Yuh-Jen Cheng\*, "Highly Active NiO-Ni(OH)<sub>2</sub>-Cr<sub>2</sub>O<sub>3</sub>/Ni Hydrogen Evolution Electrocatalyst through Synergistic Reaction Kinetics", *ChemSusChem* 2023, e202300820.
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).
3. Yung-Yu Lai, Chi-Huang Chuang, Yen-Wei Yeh, Cheng-Hung Hou, Shih-Chieh Hsu, Yi Chou, Yi-Chia Chou, Hao-Chung Kuo, Yew-Chung Sermon Wu, and Yuh-Jen Cheng\*, "Substrate Lattice Guided MoS<sub>2</sub> Crystal Growth: Implications for van der Waals epitaxy", *ACS Appl. Nano Mater.* 4, 4930–4938 (2021).
4. Yung-Yu Lai, Yen-Wei Yeh, An-Jye Tzou, Yi-Yuan Chen, Yew-Chung Sermon Wu, Yuh-Jen Cheng\*, and Hao-Chung Kuo\*, "Dependence of Photoresponsivity and On/Off Ratio on Quantum Dot Density in Quantum Dot Sensitized MoS<sub>2</sub> Photodetector", *Nanomaterials* 2020, 10, 1828.
5. Chi-Huang Chuang, Yung-Yu Lai, Cheng-Hung Hou, and Yuh-Jen Cheng\*, "Annealed Polycrystalline TiO<sub>2</sub> Interlayer of the n-Si/TiO<sub>2</sub>/Ni Photoanode for Efficient Photoelectrochemical Water Splitting," *ACS Appl. Energy Mater.* 3, 4, 3902-3908 (2020).
6. Yen-Hsien Yeh, Chi-Huang Chuang, Tzu-Yi Yu, Mei-Chun Liu, and Yuh-Jen Cheng\*, "Junction energetics engineering using Ni/NiOx core-shell nanoparticle coating for efficient photoelectrochemical water splitting," *Int J Hydrogen Energy* 44, 16594-16602 (2019).
7. Kun-Ching Shen, Chen-Ta Ku, Chieh Hsieh, Hao-Chung Kuo, Yuh-Jen Cheng, and Din Ping Tsai\*, "Deep-Ultraviolet Hyperbolic Metacavity Laser," *Adv. Mater.* 30, 1706918 (2018).
8. Kun-Ching Shen, Chieh Hsieh, Yuh-Jen Cheng, and Din Ping Tsai\*, "Giant enhancement of emission efficiency and light directivity by using hyperbolic metacavity on deep-ultraviolet AlGaIn emitter," *Nano Energy* 45, 353–358 (2018).
9. Yen-Hsien Yeh, Tzu-Yi Yu, Mei-Chun Liu, and Yuh-Jen Cheng\*, "Enhanced water splitting performance of GaN photoanode using self-assembled nickel/nickeloxide nanoparticle catalyst," *Int J Hydrogen Energy* 42, 27066-27072 (2017).
10. Chien-Ting Kuo, Lung-Hsing Hsu, Yung-Yu Lai, Shan-Yun Cheng, Hao-Chung Kuo, Chien-Chung Lin, and Yuh-Jen Cheng\*, "Site-controlled crystalline InN growth from the V-pits of a GaN substrate," *Appl. Surf. Sci.* 405, 449–454 (2017).

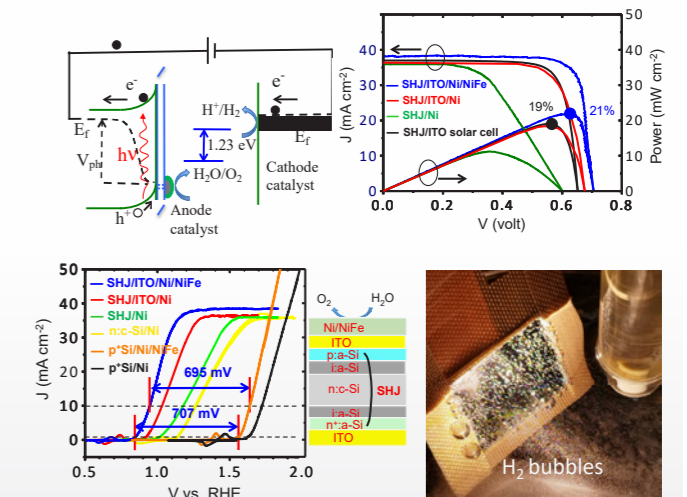
## Research Focus

### 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 CO<sub>2</sub> 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-splitting 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.

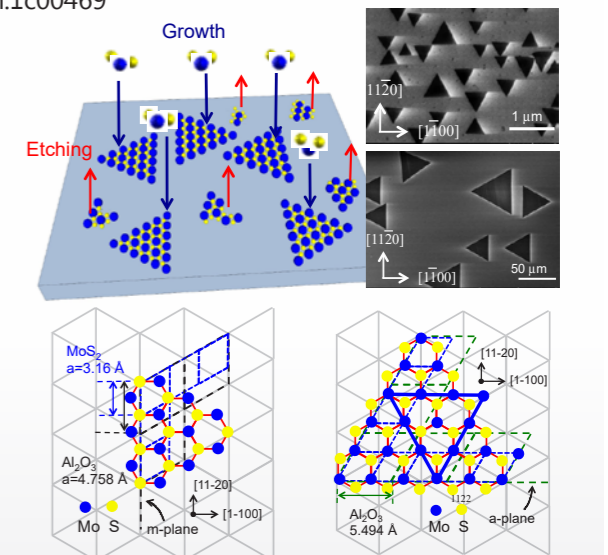


### Substrate Lattice Guided MoS<sub>2</sub> Crystal Growth

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

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

Two-dimensional (2D) monolayer molybdenum disulfide (MoS<sub>2</sub>) 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<sub>2</sub>, 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<sub>2</sub> on (2x2) sapphire and (5x5) MoS<sub>2</sub> on (3x3) sapphire. The commensurate of MoS<sub>2</sub> crystal with sapphire lattice in superlattice lowers the surface energy of MoS<sub>2</sub> 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.







# Yu-Jung Lu

Associate Research Fellow

**Education** | Ph.D. in Physics, National Tsing Hua University (2013)

## Selected Publications

1. Mriganka Singh#, I-Hung Ho#, Anupriya Singh, Ching-Wen Chan, Jing-Wei Yang, Tzung-Fang Guo, Hyeyoung Ahn, Vincent Tung, Chih Wei Chu, and Yu-Jung Lu\*. Unveiling Ultrafast Carrier Extraction in Highly Efficient 2D/3D Bilayer Perovskite Solar Cells. *ACS Photonics* 9, 3584–3591 (2022)
2. Sheng-Zong Chen, Jing-Wei Yang, Tzu-Yu Peng, Yu-Cheng Chu, Ching-Chen Yeh, I-Fan Hu, Swapnil Mhatre, Yu-Jung Lu\*, and Chi-Te Liang\*. Disorder-Induced 2D Superconductivity in a NbTiN Film Grown on Si by Ultrahigh-Vacuum Magnetron Sputtering. *Superconductor Science and Technology* 35, 064003 (2022)
3. Zong-Yi Chiao, Yu-Chia Chen, Jia-Wern Chen, Yu-Cheng Chu, Jing-Wei Yang, Tzu-Yu Peng, Wei-Ren Syong, Ho Wai Howard Lee, Shi-Wei Chu, and Yu-Jung Lu\*. Full-Color Generation Enabled by Refractory Plasmonic Crystals. *Nanophotonics* 11, 2891–2899 (2022)
4. Meng-Ju Yu, Chih-Li Chang, Hao-Yu Lan, Zong-Yi Chiao, Yu-Chia Chen, Ho Wai Howard Lee, Yia-Chung Chang, Shu-Wei Chang, Takuo Tanaka, Vincent Tung, Ho-Hsiu Chou\*, and Yu-Jung Lu\*. Plasmon-Enhanced Solar-Driven Hydrogen Evolution Using Titanium Nitride Metasurface Broadband Absorbers. *ACS Photonics* 8, 3125–3132 (2021).
5. Hao-Yu Lan, Yu-Hung Hsieh, Zong-Yi Chiao, Deep Jariwala, Min-Hsiung Shih, Ta-Jen Yen, Ortwin Hess, and Yu-Jung Lu\*. Gate-Tunable Plasmon-Enhanced Photodetection in a Monolayer MoS<sub>2</sub> Phototransistor with Ultrahigh Photoresponsivity. *Nano Letters* 21, 3083–3091 (2021).
6. Yu-Jung Lu\*, Teng Lam Shen, Kang-Ning Peng, Pi-Ju Cheng, Shu-Wei Chang, Ming-Yen Lu, Chih Wei Chu, Tzung-Fang Guo, and Harry Atwater\*. Upconversion Plasmonic Lasing from an Organolead Trihalide Perovskite Nanocrystal with Low Threshold. *ACS Photonics* 8, 335–342 (2021).
7. 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\*. Perovskite Quantum Dot Lasing in a Gap-Plasmon Nanocavity with Ultralow Threshold, *ACS Nano* 14, 11670–11676 (2020).
8. Hsu-Sheng Tsai, Yung-Hung Huang, Po-Cheng Tsai, Yi-Jia Chen, Hyeyoung Ahn, Shih-Yen Lin, and Yu-Jung Lu\*. Ultrafast Exciton Dynamics in Scalable Monolayer MoS<sub>2</sub> Synthesized by Metal Sulfurization, *ACS Omega* 5, 10725–10730 (2020).
9. Yu-Jung Lu, Ruzan Sokhoyan, Wen-Hui Cheng, Ghazaleh Kafaie Shirmanesh, Artur Davoyan, Ragip A. Pala, Krishnan Thyagarajan, and Harry A. Atwater\*. Dynamically Controlled Purcell Enhancement of Visible Spontaneous Emission in a Gated Plasmonic Heterostructure, *Nature Communications* 8, 1631 (2017).

## Positions and Career

- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica (2022 –)
- Joint Appointment Professor, Department of Physics, National Taiwan University (2018 –)
- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica (2017 – 2022)
- Visiting Scholar, Applied Physics and Materials Science, California Institute of Technology (Caltech), USA (2017 –)
- Postdoctoral Scholar, Applied Physics and Materials Science, California Institute of Technology (Caltech), USA (2015 – 2017)
- Postdoctoral Scholar, Department of Physics, National Tsing Hua University (2013– 2015)

## Honors and Awards

- 2021 SPIE Women in Optics Planner, USA
- 2020 Youth Photonics Award, Taiwan Photonics Society, Taiwan
- 2018 Career Development Award, Academia Sinica, Taiwan
- 2018 56th Ten Outstanding Young Persons, Taiwan
- 2014 Postdoctoral Research Abroad Fellowship, Taiwan
- 2013 Taiwan Outstanding Women in Science—Chui-Chu Mon Fellowship, Taiwan
- 2013 Chien-Shiung Wu Fellowship, Taiwan Physical Society, Taiwan
- 2010 The President's Scholarship of NTHU, Taiwan
- 2010 The Honorary Member of the Phi Tau Phi Scholastic Honor Society, Taiwan
- Associate Editor of Optics Continuum (Optica; 2021-present)
- Associate Editor of Advanced Photonics (SPIE; 2021-present)
- Associate Editor of Journal of Lightwave Technology (IEEE; 2022-present)

## Research Interests

- 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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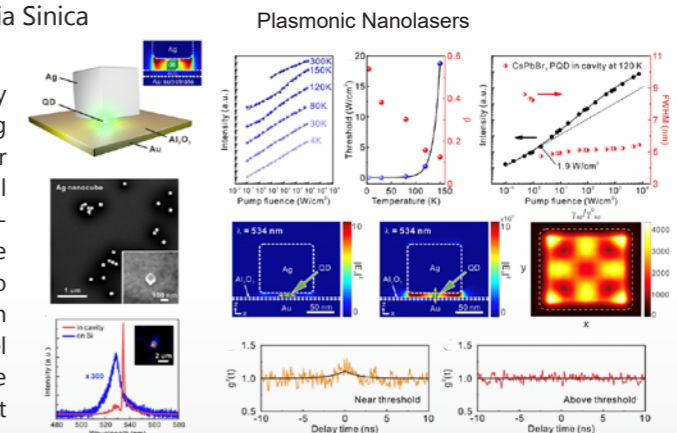
## Research Focus

### 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).

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<sub>3</sub>) quantum dot (PQD) in a plasmonic gap-mode nanocavity with an ultralow threshold of 1.9 Wcm<sup>-2</sup> under 120 K. The calculated ultrasmall mode volume (~0.002 λ<sup>3</sup>) 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.



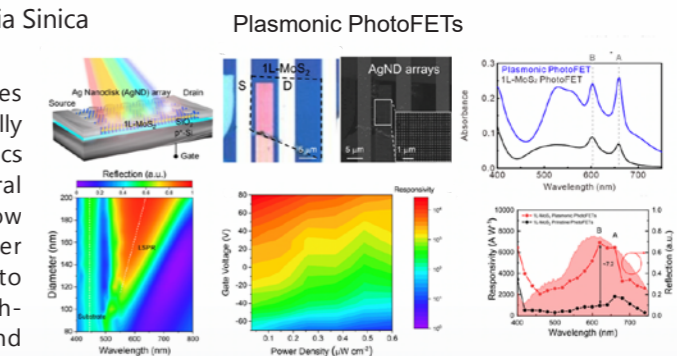
Lasing signatures and the lasing mechanism of a single perovskite quantum dot (PQD) in a localized gap plasmon cavity at 120 K. The temporal coherence signature of the PQD nanolasing under 120 K was determined.

### Gate-Tunable Plasmon-Enhanced Photodetection in a Monolayer MoS<sub>2</sub> Phototransistor with Ultrahigh Photoresponsivity

Hao-Yu Lan, Yu-Hung Hsieh, Zong-Yi Chiao, Deep Jariwala, Min-Hsiung Shih, Ta-Jen Yen, Ortwin Hess, and Yu-Jung Lu\*

Research Center for Applied Sciences, Academia Sinica  
*Nano Letters* 21, 3083–3091 (2021)

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<sub>2</sub>) photoFETs integrated with the two-dimensional plasmonic crystals. The plasmonic photoFET has an ultrahigh photoresponsivity of 2.7x10<sup>4</sup> AW<sup>-1</sup>, 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<sub>2</sub>. 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.



Monolayer MoS<sub>2</sub> plasmonic phototransistors (photoFETs) that consist of a monolayer MoS<sub>2</sub> 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<sub>2</sub> plasmonic photoFETs.

# Mu-Huai Fang

Assistant Research Fellow

Education | Ph.D. Department of Chemistry, National Taiwan University (2018)

## Selected Publications

- 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.
- Zhang, Y.-Y.; Liu, K.-T.; **Fang, M. H.\***; Leung, M.-k.\* Quantum Dot-vitrimer Composites: An Approach for Reprocessable, Self-healable, and Sustainable Luminescent Materials. *ChemSusChem* **2023**, 16, 202300227e.
- 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.
- Fang, M. H.**; Bao, Z.; Huang, W. T.; Liu, R. S.\* Evolutionary Generation of Phosphor Materials and Their Progress in Future Applications for Light-Emitting Diodes. *Chem. Rev.* **2022**, 122, 11474–11513.
- Fang, M. H.**; Chen, K. C.; Majewska, N.; Leśniewski, T.; Mahlik, S.; Leniec, G.; Kaczmarek, S. M.; Yang, C. W.; Lu, K. M.; Sheu, H.-S.; Liu, R. S.\* Hidden Structural Evolution and Bond Valence Control in Near-Infrared Phosphors for Light-Emitting Diodes. *ACS Energy Lett.* **2021**, 6, 109–144.
- Fang, M. H.**; Li, T. Y.; Huang, W. T.; Cheng, C. L.; Bao, Z.; Majewska, N.; Mahlik, S.; Yang, C. W.; Lu, K. M.; Leniec, G.; Kaczmarek, S. M.; Sheu, H.-S.; Liu, R. S.\* Surface-Protected High-Efficiency Nanophosphors via Space-Limited Ship-in-Bottle Synthesis for Broadband Near-Infrared Mini-Light-Emitting Diodes. *ACS Energy Lett.* **2021**, 6, 659–664.
- Fang, M. H.**; Mahlik, S.; Lazarowska, A.; Grinberg, M.; Molochev, M. S.; Sheu, H. S.; Lee, J. F.; Liu, R. S.\* Structural Evolution and Neighbor-Cation Control of Photoluminescence in  $\text{Sr}(\text{LiAl}_{3-1-x}(\text{SiMg}_3)_x\text{N}_4:\text{Eu}^{2+})$  Phosphor. *Angew. Chem. Int. Ed.* **2019**, 58, 7767–7772.
- 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  $\text{Na}_3\text{HTi}_{1-x}\text{Mn}_x\text{F}_8$  Narrow-Band Phosphor for Light-Emitting Diodes. *ACS Energy Lett.* **2019**, 4, 527–533.
- Fang, M. H.**; Leño, J. L.; Liu, R. S.\* Control of Narrow-Band Emission in the Phosphor Materials for the Application in Light-Emitting Diodes. *ACS Energy Lett.* **2018**, 3, 2573–2586.
- Fang, M. H.**; Wu, W. L.; Jin, Y.; Lesniewski, T.; Mahlik, S.; Grinberg, M.; Brik, M. G.; Srivastava, A. M.; Chiang, C. Y.; Zhou, W.; Jeong, D.; Kim, S. H.; Leniec, G.; Kaczmarek, S. M.; Sheu, H.-S.; Liu, R. S.\* Control of Luminescence via Tuning of Crystal Symmetry and Local Structure in  $\text{Mn}^{4+}$ -Activated Narrow Band Fluoride Phosphors. *Angew. Chem. Int. Ed.* **2018**, 57, 1797–1801.

## Positions and Career

- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica (2021–now)
- Postdoctoral Research, Department of Chemistry, National Taiwan University (2019–2021)

## Honors and Awards

- 2023 Career Development Award, Academia Sinica
- 2019 Scholarship for Postdoctoral Fellow, National Science and Technology Council
- 2018 Outstanding Award, Chinese Chemical Society
- 2018 Yan's Award of Thesis, National Taiwan University
- 2018 Dean's Prize, College of Science, National Taiwan University
- 2017 Excellent Conference Report Award, Rare-Earth Luminescent Materials Symposium

## Research Interests

- Phosphors
- Quantum Dots
- Optoelectronic Materials
- Energy Materials
- Solid-state Materials

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## Research Focus

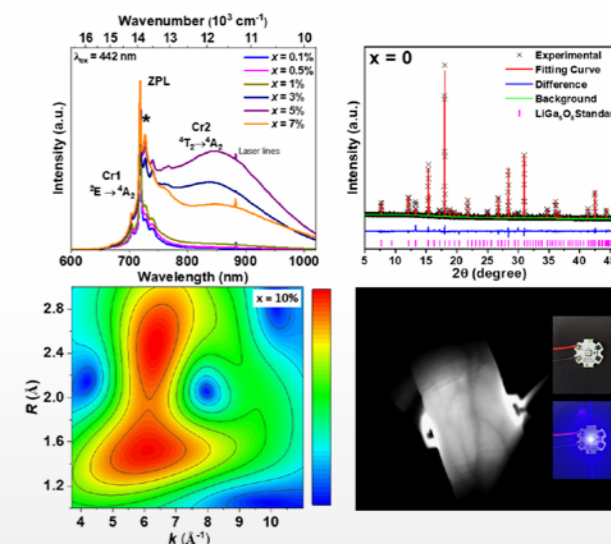
### Sharp Emission Infrared Phosphors for the Application in Light-Emitting Diodes

Jia-Yu Hsu, Ren-Jei Chung, Natalia Majewska, Dominik Kreft, Sebastian Mahlik, and Mu-Huai Fang\*

*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  $\text{Cr}^{3+}$ -doped phosphors, and the control mechanism of  $\text{Cr}^{3+}$ -doped phosphors with sharp line emission remains ambiguous. Here, we report systematic research on  $\text{LiGa}_5\text{O}_8:\text{Cr}^{3+}$  phosphors by tuning the local structure via the incorporation of  $\text{Al}^{3+}$  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  $\text{Cr}^{3+}$ -doped sharp emission phosphor and reveals their potential for LED applications.

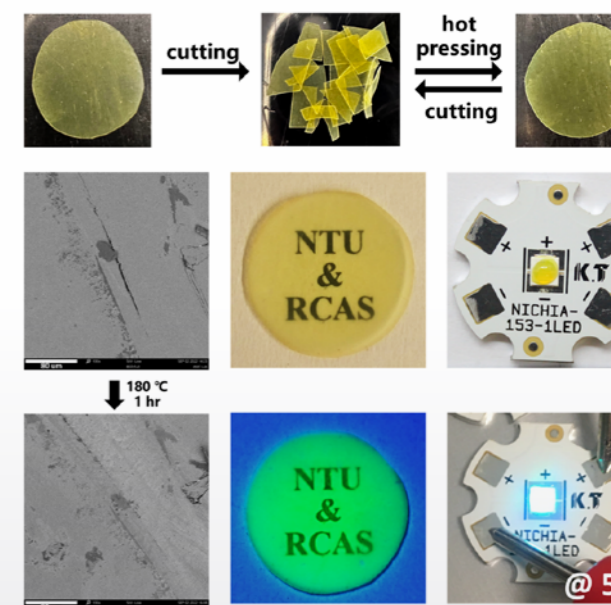


### Quantum Dot-vitrimer Composites: An Approach for Reprocessable, Self-healable, and Sustainable Luminescent Materials

Yong-Yun Zhang, Kaun-Ting Liu, Mu-Huai Fang\*, Man-kit Leung\*

*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.





# Wen-Hao Chang

Executive Officer of the TCQP and  
Distinguished Research Fellow

Education | Ph.D. in Physics, National Central University (2001)

## Positions and Career

- Distinguished Research Fellow, Research Center for Applied Sciences, Academia Sinica (2020.11 -)
- Acting Executive Officer, Thematic Center for Quantum Photonics, Academia Sinica (2020.11 -)
- Distinguished Professor, Department of Electrophysics, National Yang Ming Chiao Tung University (NYCU) (2018.05 -)
- Professor, Department of Electrophysics, NYCU (2012 -)
- Associate Professor, Department of Electrophysics, NYCU (2009 - 2012)
- Assistant Professor, Department of Electrophysics, NYCU (2005 - 2009)
- Postdoctoral Researcher, Department of Physics, National Central University (2001 - 2005)

## Honors and Awards

- 2021 Fellow, The Physical Society of Taiwan
- 2020 Achievement in Asia Award (Robert T. Poe Prize), International Organization of Chinese Physicists and Astronomers (OCPA)
- 2018 Distinguished Research Award, National Science and Technology Council (NSTC), Taiwan
- 2018 Sun Yet-Sen Academic Award, Sun Yet-Sen Academic and Cultural Foundation
- 2018 Distinguished Professorship, NYCU
- 2010 Wu Ta-Yu Memorial Award, NSTC, Taiwan

## Research Interests

Semiconductor quantum light sources, microcavity, cavity quantum electrodynamics  
Quantum optics of nanophotonics  
Spin dynamics in semiconductors  
2D layered materials: synthesis, material properties and device applications

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## Selected Publications

1. 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\*, Wen-Hao Chang\*, Remarkably Deep Moiré Potential for Intralayer Excitons in MoSe<sub>2</sub>/MoS<sub>2</sub> Twisted Heterobilayers, *Nano Letters* **23**, 1306–1312 (2023).
2. Cheng-Chu Chung, Han Yeh, Po-Hsien Wu, Cheng-Chieh Lin, Chia-Shuo Li, Tien-Tien Yeh, Yi Chou, Chuan-Yu Wei, Cheng-Yen Wen, Yi-Chia Chou, Chih-Wei Luo, Chih-I Wu, Ming-Yang Li, Lain-Jong Li, Wen-Hao Chang\*, Chun-Wei Chen\*, Atomic-Layer Controlled Interfacial Band Engineering at Two-Dimensional Layered PtSe<sub>2</sub>/Si Heterojunctions for Efficient Photoelectrochemical Hydrogen Production, *ACS Nano* **15**, 4627–4635 (2021)
3. 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\*, and Wen-Hao Chang\*, Moiré potential impedes interlayer exciton diffusion in van der Waals heterostructures, *Science Advances* **6**, eaba8866 (2020)
4. Li-Syuan Lu, Guan-Hao Chen, Hui-Yu Cheng, Chih-Piao Chuu, Kuan-Cheng Lu, Chia-Hao Chen, Ming-Yen Lu, Tzu-Hung Chuang, Der-Hsin Wei, Wei-Chen Chueh, Wen-Bin Jian, Ming-Yang Li, Yu-Ming Chang, Lain-Jong Li\*, Wen-Hao Chang\*, Layer-Dependent and In-Plane Anisotropic Properties of Low-Temperature Synthesized Few-Layer PdSe<sub>2</sub> Single Crystals, *ACS Nano* **14**, 4963–4972 (2020)
5. Tse-An Chen, Chih-Piao Chuu, Chien-Chih Tseng, Chao-Kai Wen, H-S Philip Wong, Shuangyuan Pan, Rongtan Li, Tzu-Ang Chao, Wei-Chen Chueh, Yanfeng Zhang, Qiang Fu, Boris I Yakobson\*, Wen-Hao Chang\*, Lain-Jong Li\*, Wafer-scale single-crystal hexagonal boron nitride monolayers on Cu (111), *Nature* **579**, 219–223 (2020)
6. Wei-Ting Hsu, Li-Syuan Lu, Po-Hsun Wu, Ming-Hao Lee, Peng-Jen Chen, Pei-Ying Wu, Yi-Chia Chou, Horng-Tay Jeng, Lain-Jong Li, Ming-Wen Chu & Wen-Hao Chang\*, Negative circular polarization emissions from WSe<sub>2</sub>/MoSe<sub>2</sub> commensurate heterobilayers, *Nature Comm.* **9**, 1356 (2018)
7. Wei-Ting Hsu, Li-Syuan Lu, Dean Wang, Jing-Kai Huang, Ming-Yang Li, Tay-Rong Chang, Yi-Chia Chou, Zhen-Yu Juang, Horng-Tay Jeng, Lain-Jong Li & Wen-Hao Chang\*, Evidence of indirect gap in monolayer WSe<sub>2</sub>, *Nature Comm.* **8**, 929 (2017)

## Research Focus

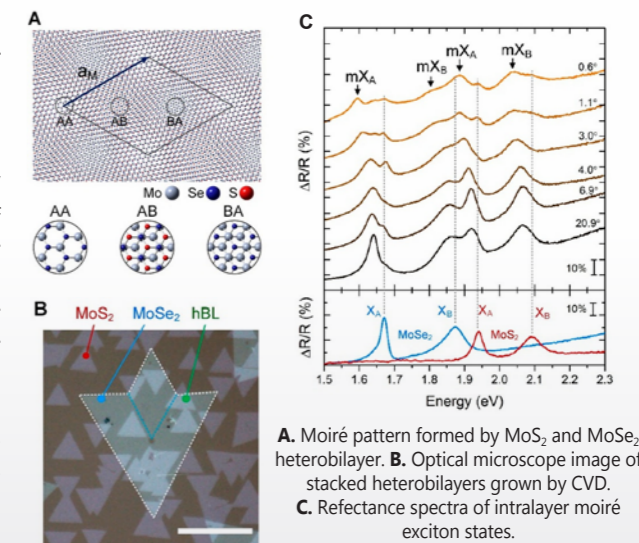
### Remarkably Deep Moiré Potential for Intralayer Excitons in MoSe<sub>2</sub>/MoS<sub>2</sub> Twisted Heterobilayers

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

Academic Sinica, Research Center for Applied Sciences  
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<sub>2</sub>/MoS<sub>2</sub> 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.



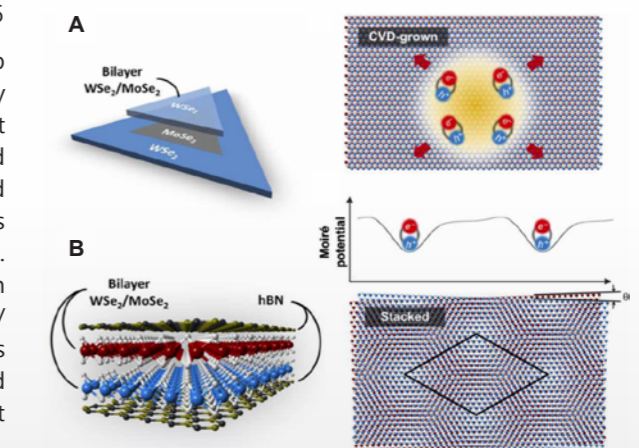
### Moiré Potential Impedes Interlayer Exciton Diffusion in Van der Waals Heterostructures

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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Department of Electrophysics, National Yang Ming Chiao Tung University

*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<sub>2</sub>/MoSe<sub>2</sub> heterostructures by comparing several samples prepared with chemical vapor deposition (CVD) and mechanical stacking with accurately controlled twist angles.



**A.** Commensurate WSe<sub>2</sub>/MoSe<sub>2</sub> heterobilayer without moiré potential formed by direct CVD growth. **B.** Mechanically stacked twisted WSe<sub>2</sub>/MoSe<sub>2</sub> heterobilayer with moiré potential formed by direct CVD growth.

# Min-Hsiung Shih

Deputy Director and Research Fellow

## Education

Ph.D. Electrical Engineering, University of Southern California (USC), CA, U.S.A.(2006)

## Selected Publications

1. Y-H Chang, Y-S Lin, J. S. Konthoujam, H-T Lin, C-Y Chang, Z-Z Chen, Y-W Zhang, S-Y Lin, H-C Kuo, M-H Shih\*, "AC-driven multicolor electroluminescence from a hybrid WSe<sub>2</sub> monolayer/AlGaInP quantum well light-emitting device", *Nanoscale*, 15(3), 1347 (2023).
2. H-T Lin, C-Y Chang, C-L Yu, A. B. Lee, S-Y Gu, L-S Lu, Y-W Zhang, S-Y Lin, W-H Chang, S-W Chang, M-H Shih\*, "Boost Lasing Performances of 2D Semiconductor in a Hybrid Tungsten Diselenide Monolayer/ Cadmium Selenide Quantum Dots Microcavity Laser", *Advanced Optical Materials*, 10, 2200799 (2022).
3. C-Y Chang, C-L Yu, C-A Lin, H-T Lin, A B Lee, Z-Z Chen, L-S Lu, W-H Chang, H-C Kuo, M-H Shih\*, "Hybrid Composites of Quantum Dots, Monolayer WSe<sub>2</sub>, and Ag Nanodisks for White Light-Emitting Diodes", *ACS Applied Nano Materials*, 3(7) 6855 (2020).
4. C-Y Chang, H-T Lin, M-S Lai, C-L Yu, C-R Wu, H-C Chou, S-Y Lin, C. Chen and M-H Shih\*, "Large-Area and Strain-Reduced Two-Dimensional Molybdenum Disulfide Monolayer Emitters on a Three-Dimensional Substrates", *ACS Applied Materials & Interfaces*, 11, 26243 (2019)
5. H-T Lin, C-Y Chang, P-J Cheng, M-Y Li, C-C Cheng, S-W Chang, L. L. J. Li, C-W Chu, P-K Wei, M-H Shih\*, "Circular Dichroism Control of Tungsten Diselenide (WSe<sub>2</sub>) Atomic Layers with Plasmonic Metamolecules", *ACS Applied Materials & Interfaces*, 10, 15996 (2018)
6. M.-H. Shih\*, K.-S. Hsu, K. Lee, K.-T. Lai, C.-T. Lin, and P.-T. Lee, "Compact Tunable Laser With InGaAsP Photonic Crystal Nanorods for C-Band Communication," *IEEE Journal of Selected Topics in Quantum Electronics*, 21, 1, (2015)
7. Kevin C. J. Lee, Y.-H. Chen, H.-Y. Lin, C.-C. Cheng, P.-Y. Chen, T.-Y. Wu, M.-H. Shih\*, K.-H. Wei, L.-J. Li & C.-W. Chang, "Plasmonic Gold Nanorods Coverage Influence on Enhancement of the Photoluminescence of Two-Dimensional MoS<sub>2</sub> Monolayer", *Scientific Reports*, 5, 16374 (2015)
8. M.-H. Shih\*, L.-J. Li, Y.-C. Yang, H.-Y. Chou, C.-T. Lin, C.-Y. Su, "Efficient Heat Dissipation of Photonic Crystal Microcavity by Monolayer Graphene", *ACS Nano*, 7(12), 10818 (2013)
9. C-W Cheng, M. N. Abbas, C-W Chiu, K-T Lai, M.-H. Shih\*, and Y.-C. Chang, "Wide-angle polarization independent infrared broadband absorbers based on metallic multi-sized disk arrays," *Optics Express* 20(9), 10376 (2012)
10. M.-H. Shih\*, K. Hsu, W. Kuang, Y. Yang, Y. Wang, S. Tsai, Y. Liu, Z. Chang, and M. Wu, "Compact optical curvature sensor with a flexible microdisk laser on a polymer substrate", *Optics Letters* 34, 2733 (2009)

## Positions and Career

- Deputy Director, Research Center for Applied Sciences (RCAS), Academia Sinica (2023 – )
- Acting Executive Officer of the thematic center for Green Technology, RCAS, Academia Sinica (2020 – 2022)
- Research Fellow, RCAS, Academia Sinica, Taiwan (2016 – )
- Associate Research Fellow, RCAS, Academia Sinica, Taiwan (2011 – 2016)
- Assistant Research Fellow, RCAS, Academia Sinica, Taiwan (2007 – 2011)
- Adjunct Professor, Department of Photonics, National Yang Ming Chiao Tung University, Taiwan (2017 – )
- Adjunct Professor, Department of Photonics, National Sun Yat-sen University, Taiwan (2017 – )
- Postdoctoral Associate, University of Southern California (USC), USA (2006 – 2007)

## Honors and Awards

- 2021 International Electron Devices & Materials Symposium (IEDMS), Excellent paper award.
- 2021 Optics & Photonics Taiwan International Conference (OPTIC), Paper award.
- The Optical Society (OSA) Senior member (2016 – )
- 2010 Lam Research PhD Thesis Award, National Chiao Tung University (Advisor)
- 2011 Taiwan Photonics Society PhD Thesis Award (Advisor)
- 2016 Lam Research PhD Thesis Award, National Chiao Tung University (Advisor)

## Research Interests

- Nanophotonics
- Two-dimensional materials and devices
- Plasmonic devices
- Photonic crystal devices
- High-Q cavities for quantum communication

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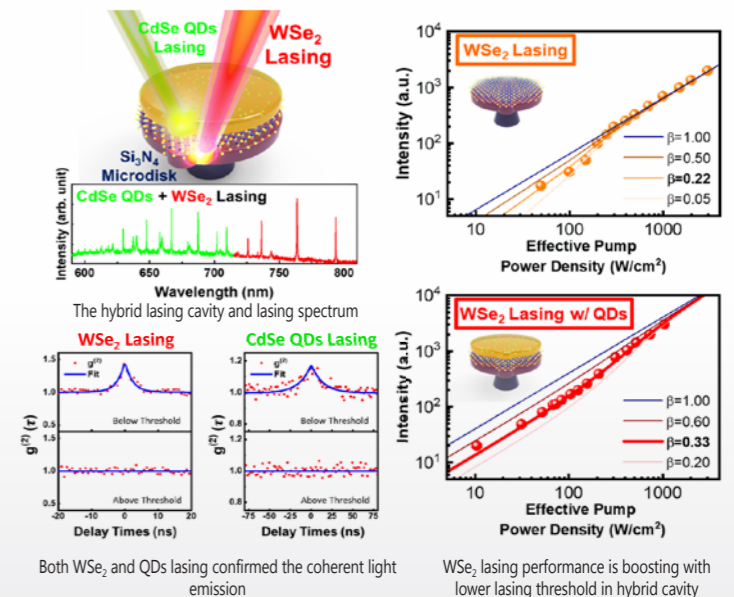
## Research Focus

### 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\*

Academic Sinica, Research Center for Applied Sciences  
Advanced Optical Materials, 2022, DOI: 10.1002/adom.202200799

We investigated dual-color continuous-wave microcavity lasers by integrating a tungsten diselenide (WSe<sub>2</sub>) monolayer and cadmium selenide (CdSe) quantum dots (QDs) into a single microdisk cavity. The hybrid WSe<sub>2</sub>/QDs microcavity device not only provides the lasing action in two distinct wavelength regions, but also boost the lasing performances of WSe<sub>2</sub> monolayer because of the energy conversion between two gain materials. The results indicate the lasing threshold of the 2-D WSe<sub>2</sub> monolayer cavity with the CdSe QDs reduces more than 2.5 times, compared to the WSe<sub>2</sub> 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.

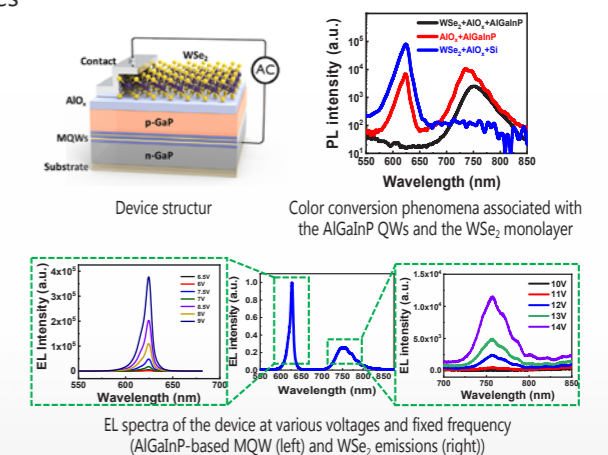


### AC-driven multicolor electroluminescence from a hybrid WSe<sub>2</sub> monolayer/AlGaInP quantum well light-emitting device

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<sub>2</sub> monolayer and AlGaInP–GaInP multiple quantum well (MQW) structures. The CVD-grown WSe<sub>2</sub> 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<sub>2</sub> monolayer was observed to boost the WSe<sub>2</sub> 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<sub>2</sub> 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.



# Chao-Cheng Kaun

Research Fellow

Education | Ph.D. in Physics, McGill University (2004)

## Positions and Career

- Research Fellow, Research Center for Applied Sciences, Academia Sinica (2017 - )
- Adjunct Professor, Department of Physics, National Tsing Hua University (2018 - 2021)
- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica (2013 - 2017)
- Adjunct Associate Professor, Department of Physics, National Tsing Hua University (2014 - 2018)
- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica (2006 - 2013)
- Adjunct Assistant Professor, Department of Physics, National Tsing Hua University (2006 - 2014)
- Postdoctoral Fellow, Department of Chemistry, Northwestern University (2004 - 2006)

## Honors and Awards

- 2022 Future Tech Award, National Science and Technology Council
- 2021 Future Tech Award, Ministry of Science and Technology

## Research Interests

Computational nanoelectronics and spintronics  
Quantum transport in mesoscopic systems  
Emerging materials for sustainable energy

## Selected Publications

1. W.-C. Tseng, C.-W. Chang, C.-C. Kaun\*, and Y.-H. Su\*, "Catalytic hydrogen evolution reaction on surfaces of metal-nanoparticle-coated zinc-based oxides by first-principles calculations", *International Journal of Hydrogen Energy* 47, 40768 (2022).
2. M. R. Aziza, C.-W. Chang, C.-C. Kaun\*, and Y.-H. Su\*, "Hydrogen Evolution Driven by Photoexcited Entangled Skyrmion on Perovskite  $\text{Ca}_2\text{Nan-3NbnO}_{3n+1}$  Nanosheet", *J. Phys. Chem. Lett.* 12, 6244 (2021).
3. M. R. Aziza, C.-W. Chang, A. Mohapatra, C.-W. Chu, C.-C. Kaun\*, and Y.-H. Su\*, "Dion-Jacobson Phase Perovskite  $\text{Ca}_2\text{Nan-3NbnO}_{3n+1}$  ( $n = 4, 5, 6$ ) Nanosheets as High- $\kappa$  Photovoltaic Electrode Materials in a Solar Water-Splitting Cell", *ACS Appl. Nano Mater.* 3, 6367 (2020)
4. I.-H. Hong\*, C.-J. Gao, K.-B. Lin, and C.-C. Kaun\*, "Self-organized C70/C60 heterojunction nanowire arrays on Si(110) for Si-based molecular negative differential resistance nanodevices", *Applied Surface Science* 531, 147338 (2020).
5. K.-B. Lin, Y.-H. Su\*, and C.-C. Kaun\*, "Interfacial effects on leakage currents in Cu/ $\alpha$ -cristobalite/Cu junctions", *Scientific Reports* 10, 5303 (2020).
6. H.-W. Tsao, C.-C. Kaun\*, and Y.-H. Su\*, "Decorating a WSe2 monolayer with Au nanoparticles: A study combined first-principles calculation with material genome approach", *Surf. Coat. Technol.* 388, 125563 (2020).
7. K. P. Dou, C.-H. Chang, and C.-C. Kaun\*, "Gate-Tunable Fano Resonances in Parallel-Polyacene-Bridged Carbon Nanotubes", *J. Phys. Chem. C* 123, 4605 (2019).
8. L.-W. Huang, Y.-H. Su\*, and C.-C. Kaun\*, "Conductance Switching in Single-Peptide Molecules through Interferer Binding", *ACS Omega* 3, 9191 (2018).
9. C.-C. Kaun and Y.-C. Chen\*, "Thermoelectric Charge and Spin Current Generation in Magnetic Single-Molecule Junctions: First-Principles Calculations", *J. Phys. Chem. C* 122, 12185 (2018).
10. C.-H. Chang\*, K.-P. Dou, G.-Y. Guo, and C.-C. Kaun\*, "Quantum-well-induced engineering of magnetocrystalline anisotropy in ferromagnetic films", *NPG Asia Mater.* 9, e424 (2017).

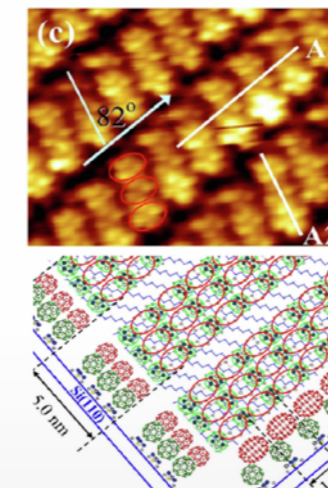
## Research Focus

### Self-organized C<sub>70</sub>/C<sub>60</sub> heterojunction nanowire arrays on Si(110) for Si-based molecular negative differential resistance nanodevices

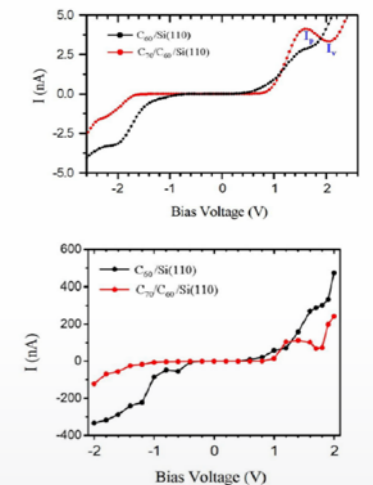
Ie-Hong Hong, Chai-Jung Gao, Kuan-Bo Lin, and Chao-Cheng Kaun

Academic Sinica, Research Center for Applied Sciences  
Applied Surface Science, 2020, DOI:10.1016/j.apsusc.2020.147338

The parallel-aligned C<sub>70</sub>-triplet/C<sub>60</sub>-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<sub>70</sub>/C<sub>60</sub> 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<sub>70</sub>/C<sub>60</sub> heterojunction nanowires on Si(1 1 0) is due to the relatively weak interaction between C<sub>70</sub> molecules and Si(1 1 0) via the spacers of C<sub>60</sub> 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.



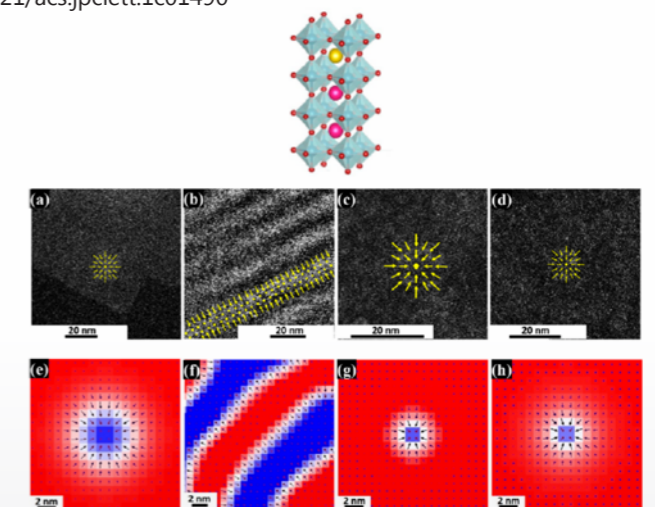
The measured and calculated I-V curves of the systems.

### Hydrogen Evolution Driven by Photoexcited Entangled Skyrmion on Perovskite $\text{Ca}_2\text{Nan}_3\text{Nb}_n\text{O}_{3n+1}$ Nanosheet

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

Academic Sinica, Research Center for Applied Sciences  
*Journal of Physical Chemistry Letters*, 2021, DOI:10.1021/acs.jpcllett.1c01490

We demonstrate the real-space observation of skyrmions in Dion-Jacobson phase perovskite,  $\text{Ca}_2\text{Nan-3NbnO}_{3n+1}$  (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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# Shih-Yen Lin

Research Fellow

Education | Ph.D. in Electrical Engineering, NTU (2001)

## Positions and Career

1. Research Fellow, RCAS, Academia Sinica (2016.5~now)
2. Adjunct Professor, GIEE, National Taiwan University (2016.8~now)
3. Adjunct Professor, DoEE, National Cheng Kung University (2017.2~now)
4. Adjunct Professor, DMSE, National Dong Hwa University (2016.8~now)
5. Associate Research Fellow, RCAS, Academia Sinica (2011.9~2016.5)
6. Assistant Research Fellow, RCAS, Academia Sinica (2006.10~2011.8)
7. Engineer and PI, Industrial Technology Research Institute (2003.2~2006.10)
8. RD deputy manager, LandMark Optoelectronics Corp. (2001.6~2003.1)

## Honors and Awards

1. Research Scholarship award from Wen-Yuan Pan Foundation (2005)
2. Outstanding young engineer (2011, Chinese Institute of Engineers, Taiwan)
3. IEEE senior Member, 2012.8
4. Outstanding Young Scholar Research Project, NSC (2013.8-2016.7)

## Research Interests

2D Materials, Semiconductor nano-structures, Optical and electrical devices

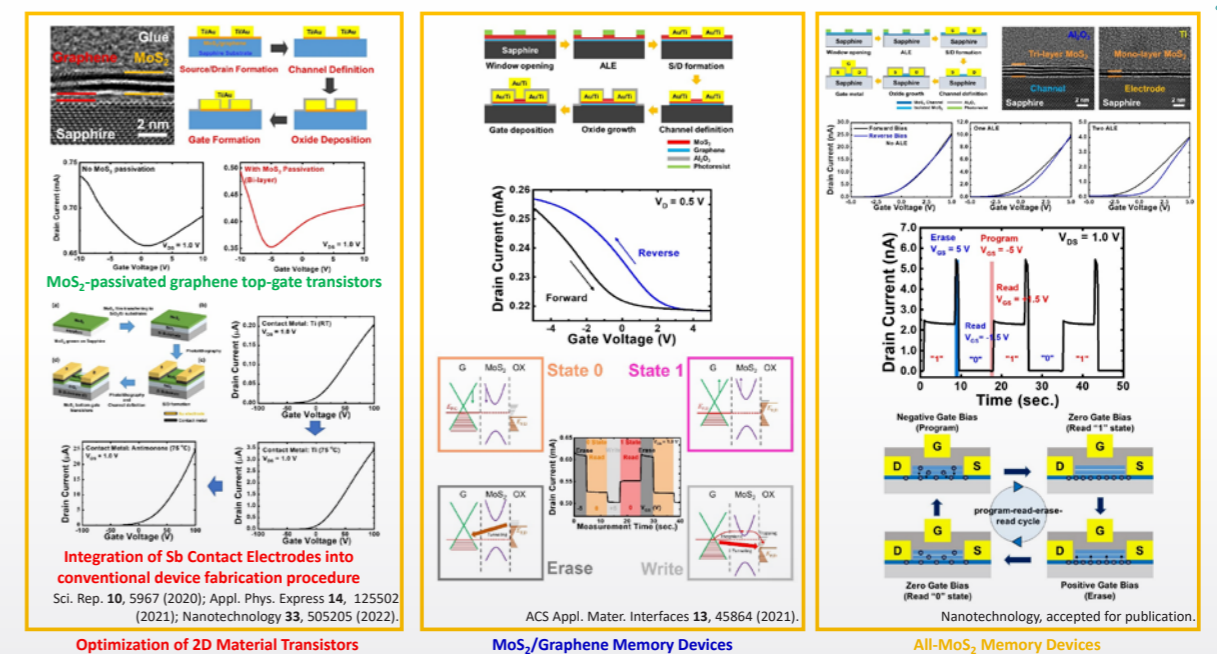
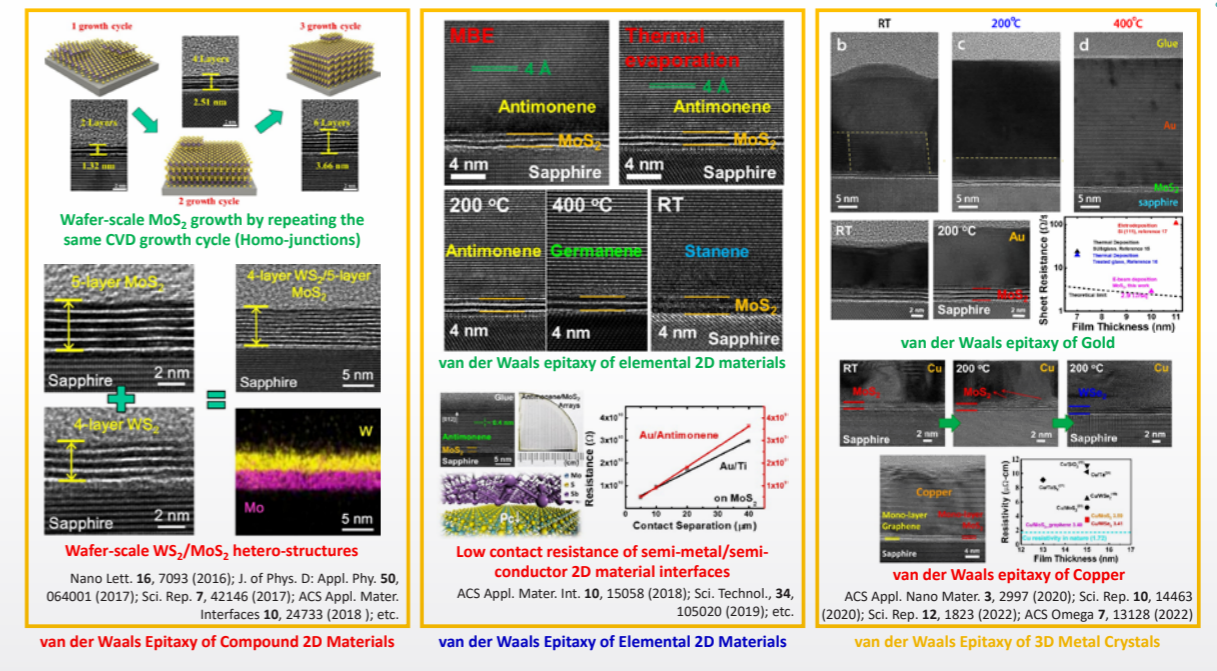
## Selected Publications

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.
2. **Shih-Yen Lin\***, Chi-Che Tseng, Wei-Hsun Lin, Shu-Cheng Mai, Shung-Yi Wu, Shu-Han Chen and Jen-Inn Chyi, "Room-Temperature Operation Type-II GaSb/GaAs Quantum-Dot Infrared Light-Emitting Diode", *Appl. Phys. Lett.*, vol. 96, pp. 123503, March 2010.
3. Wei-Hsun Lin, Kai-Wei Wang, Shu-Wei Chang, Min-Hsiung Shih and **Shih-Yen Lin\***, "Type-II GaSb/GaAs Coupled Quantum Rings: Room-Temperature Luminescence Enhancement and Recombination Lifetime Elongation for Device Applications", *Appl. Phys. Lett.* vol. 101, no. 3, pp. 031906, July 2012.
4. Meng-Yu Lin, Wei-Ching Guo, Meng-Hsun Wu, Pro-Yao Wang, Te-Huan Liu, Chun-Wei Pao, Chien-Cheng Chang, Si-Chen Lee and **Shih-Yen Lin\***, "Low-temperature grown graphene films by using molecular beam epitaxy", *Appl. Phys. Lett.* vol. 101, no. 22, pp. 221911, November 2012.
5. Meng-Yu Lin, Chung-En Chang, Cheng-Hung Wang, Chen-Fung Su, Chi Chen, Si-Chen Lee, and **Shih-Yen Lin\***, "Toward Epitaxially Grown Two-Dimensional Crystal Hetero-Structures: Single and Double MoS<sub>2</sub>/Graphene Hetero-Structures by Chemical Vapor Depositions", *Appl. Phys. Lett.* vol. 105, no. 7, pp. 073501, August 2014.
6. Chong-Rong Wu, Xiang-Rui Chang, Tung-Wei Chu, Hsuan-An Chen, Chao-Hsin Wu, and **Shih-Yen Lin\***, "Establishment of 2D Crystal Heterostructures by Sulfurization of Sequential Transition Metal Depositions: Preparation, Characterization, and Selective Growth", *Nano Lett.*, vol. 16, no. 11, pp. 7093-7097, November 2016.
7. Kuan-Chao Chen, Tung-Wei Chu, Chong-Rong Wu, Si-Chen Lee and **Shih-Yen Lin\***, "Atomic Layer Etchings of Transition Metal Dichalcogenides with Post Healing Procedures: Equivalent Selective Etching of 2D Crystal Hetero-structures", *2D Materials*, vol. 4, no. 3, pp. 034001, June 2017.
8. Hsuan-An Chen, Hsu Sun, Chong-Rong Wu, Yu-Xuan Wang, Po-Hsiang Lee, Chun-Wei Pao, and **Shih-Yen Lin\***, "Single-Crystal

Antimonene Films Prepared by Molecular Beam Epitaxy: Selective Growth and Contact Resistance Reduction of the 2D Material Heterostructure", *ACS Appl. Mater. Interfaces*, vol. 10, no. 17, pp. 15058-15064, May 2018.

9. Po-Cheng Tsai, Chun-Wei Huang, Shou-Jinn Chang, Shu-Wei Chang\*, and **Shih-Yen Lin\***, "Charge Storage of Isolated Monolayer Molybdenum Disulfide in Epitaxially Grown MoS<sub>2</sub>/Graphene Heterostructures for Memory Device Applications", *ACS Appl. Mater. Interfaces*, vol. 13, no. 38, pp. 45864-45869, September 2021.

## Research Focus



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# Shu-Wei Chang

Associate Research Fellow

Education | Ph.D., University of Illinois at Urbana-Champaign (2006)

## Positions and Career

- Adjunct Associate Professor, National Chiao-Tung University (2015 – )
- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica (2015 – )
- Adjunct Assistant Professor, National Chiao-Tung University (2011 – 2015)
- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica (2010 – 2015)
- Postdoctoral Research, University of Illinois at Urbana-Champaign, (2008 – 2010)

## Honors and Awards

- 2015 OSA Senior Member
- 2015 IEEE, Senior Member
- 2006 John Bardeen Graduate Memorial Award, ECE, Dept. University of Illinois at Urbana-Champaign

## Research Interests

- Non-Hermitian Photonics
- Chiral Photonics
- Semiconductor Photonics
- Device Physics

## Selected Publications

1. C. Y. Peng, H. T. Cheng, Y. H. Hong, W. C. Hsu, F. H. Hsiao, T. C. Lu, S. W. Chang, S. C. Chen\*, C. H. Wu\*, and H. C. Kuo\*, "Performance analyses of photonic-crystal surface-emitting laser: toward high-speed optical communication," *Nanoscale Res. Lett.* 17, 90 (2022). [DOI: 10.1186/s11671-022-03728-x]
2. W. C. Tang, Y. T. Liu, C. H. Yeh, C. H. Lu, C. H. Tu, Y. L. Lin, Y. C. Lin, T. L. Hsu, L. Gao, S. W. Chang, P. Chen, and B. C. Chen\*, "Optogenetic manipulation of cell migration with high spatiotemporal resolution using lattice lightsheet microscopy," *Commun. Biol.*, 5 879 (2022) [DOI: 10.1038/s42003-022-03835-6]
3. H. T. Lin, C. Y. Chang, C. L. Yu, A. B. Lee, S. Y. Gu, L. S. Lu, Y. W. Zhang, S. Y. Lin, W. H. Chang, S. W. Chang, and M. H. Shih\*, "Boost lasing performances of 2D semiconductor in a hybrid tungsten diselenide monolayer/cadmium selenide quantum dots microcavity laser," *Adv. Optical Mater.* 2200799 (2022) [DOI: 10.1002/adom.202200799]
4. H. T. Lin, Y. Y. Hsu, P. J. Cheng, W. T. Wang, S. W. Chang, and M. H. Shih\*, "In situ tunable circular dichroism of flexible chiral metasurfaces composed of plasmonic nanorod trimers," *Nanoscale Adv.* 4, 2428 (2022) [DOI: 10.1039/d2na00144f]
5. C. T. Tung, S. W. Chang, and C. H. Wu\*, "Analytical modeling of tunnel junction transistor lasers," *IEEE J. Sel. Top. Quantum Electron.* 28 1501008 (2022). [DOI: 10.1109/JSTQE.2021.3090527]
6. M. J. Yu, C. L. Chang, H. Y. Lan, Z. Y. Chiao, Y. C. Chen, H. W. H. Lee, Y. C. Chang, S. W. Chang, T. Tanaka, V. Tung, H. H. Chou\*, and Y. J. Lu\*, "Plasmon-enhanced solar-driven hydrogen evolution using titanium nitride metasurface broadband absorbers," *ACS Photon* 8, 3125 (2021). [DOI: 10.1021/acsp Photonics.1c00927]
7. P. C. Tsai, C. W. Huang, S. J. Chang, S. W. Chang\*, and S. Y. Lin\*, "Charge storage of isolated monolayer molybdenum disulfide in epitaxially grown MoS2/graphene hetero-structures for memory device applications," *ACS Appl. Mater. & Inter.* 13, 45864 (2021). [DOI: 10.1021/acsaami.1c12064]
8. C. T. Tai, P. Y. Chiu, C. Y. Liu, H. S. Kao, C. T. Harris, T. M. Lu, C. T. Hsieh, S. W. Chang, and J. Y. Li\*, "Strain effects on Rashba spin-orbit coupling of two-dimensional hole gases in GeSn/Ge heterostructures," *Adv. Mater.* 33, 2007862 (2021). [DOI: 10.1002/adma.202007862]
9. L. A. Chu\*, S. W. Chang, W. C. Tang, Y. T. Tseng, P. Chen, B. C. Chen\*, "5D superresolution imaging for a live cell nucleus," *Current Opinion in Genetics & Development* 67, 77 (2021). [DOI: 10.1016/j.gde.2020.11.005]

j.gde.2020.11.005]

10. C. H. Lin, D. W. Huang, T. T. Shih, H. C. Kuo, and S. W. Chang\*, "Increasing responsivity-bandwidth margin of germanium waveguide photodetector with simple corner reflector," *Opt. Express* 29, 10364 (2021). [DOI: 10.1364/OE.414691]

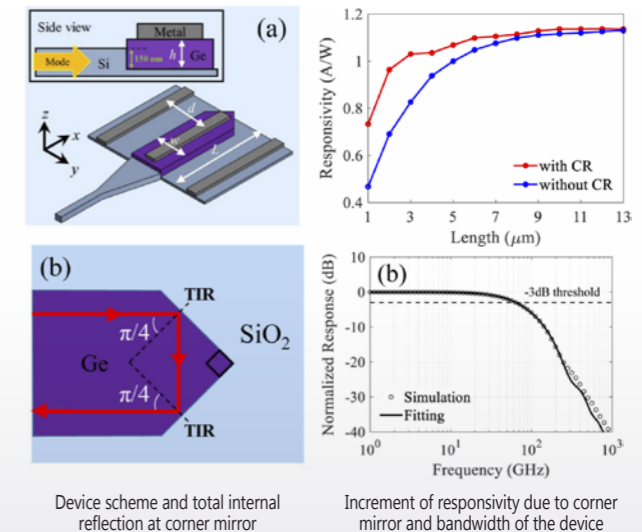
## Research Focus

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

Chih-Hsien Lin, Ding-Wei Huang, Tien-Tsornng 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.

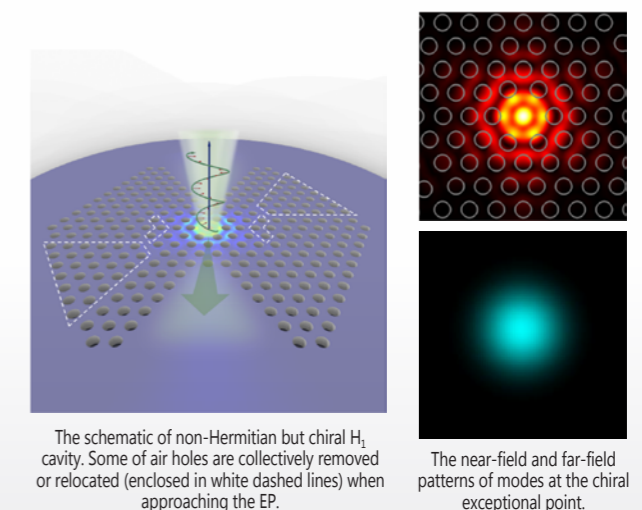


### Spinning Mode with Maximum Chirality in Photonic Crystal Defect Cavity at Exceptional Point

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

Academic Sinica, Research Center for Applied Sciences  
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.



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# Chi Chen

Associate Research Fellow

Education | Ph.D. Chemistry, University of California-Irvine (2009)

## Positions and Career

2022- Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica.  
2013-22 Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica.  
2009-13 Postdoctoral researcher, Nanophotonics laboratory, RIKEN, Japan

## Honors and Awards

2022 Academia Sinica career development award.  
2014 "96 Achievements at RIKEN in 100 years", RIKEN, Japan.  
2008-09 University of California Regent's dissertation fellowship award.  
2002 Dr. Yan's thesis award in National Taiwan University.  
2002 Chinese chemical society outstanding thesis award.

## Research Interests

- Scanning near-field optical microscopy
- Tip-enhanced optical spectroscopy
- AFM, STM, and SNOM instrumentation
- Low-dimensional materials
- Mesoscopic molecular assemblies

## Selected Publications

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  $W_xMo_{1-x}S_2$  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)
6. W.-P. Chan, J.-H. Chen, W.-L. Chou, W.-Y. Chen, H.-Y. Liu, H.-C. Hu, C.-C. Jeng, J.-R. Li, C. Chen, S.-Y. Chen\*, "Efficient DNA-driven nanocavities for approaching quasi-deterministic strong coupling to a few fluorophores", *ACS Nano*, 15, 13085 (2021)
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  $MoS_2$  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, S10801 (2019)

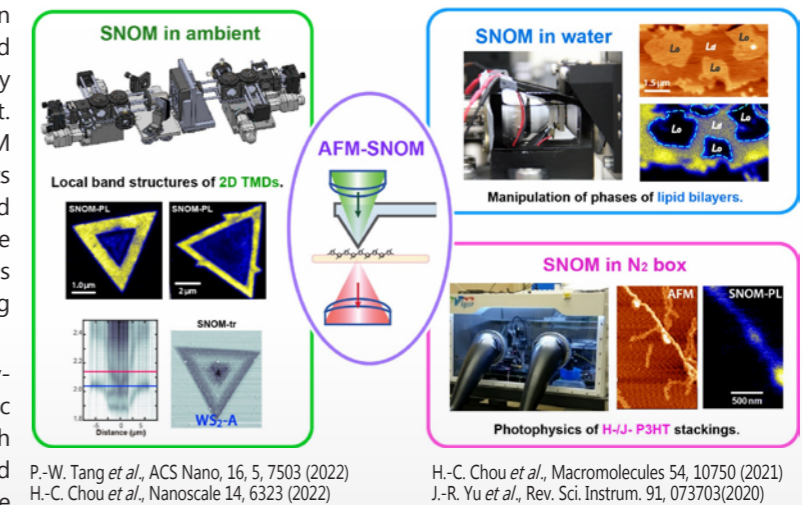
## Research Focus

### 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.

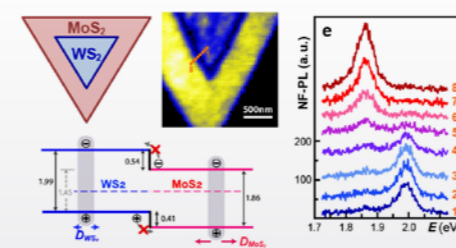


### Revealing the Local Band Structures of $WS_2/MoS_2$ Heterojunction $W_xMo_{1-x}S_2$ Alloy by Near-Field Optical Imaging

P.-W. Tang, H.-C. Chou, S.-Y. Shiau, J.-R. Yu, X.-Q. Zhang, Y.-H. Lee\*, and Chi Chen\* (RCAS & NTU)

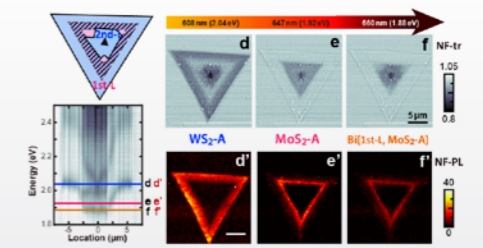
#### Lateral Heterojunction

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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# Yu-Chen Chen

Assistant Research Fellow

**Education** | Ph.D. Department of Materials, University of Oxford (2017)

## Positions and Career

- Assistant Research Fellow, Research Center for Applied Sciences, Academia Sinica (2022-)
- Postdoctoral Researcher, Research Center for Applied Sciences, Academia Sinica (2021-2022)
- Postdoctoral Researcher, 3rd Institute of Physics, University of Stuttgart (2018-2020)

## Honors and Awards

- 2013-2016 DPhil programme scholarship sponsored by De Beers

## Research Interests

Fabrication and femtosecond laser writing of spin defects in wide band gap materials  
Manipulation of spin states

## Selected Publications

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).
2. M. Niethammer\*, M. Widmann, T. Rendler, N. Morioka, **Y. C. Chen**, R. Stöhr, J. Ul Hassan, S. Onoda, T. Ohshima, S. Y. Lee, A. Mukherjee, J. Isoya, N. T. Son, and J. Wrachtrup. Coherent electrical readout of defect spins in silicon carbide by photo-ionization at ambient conditions. *Nature Communications* 10, 5569 (2019).
3. C. J. Stephen, B. L. Green, Y. N. D. Lekhai, L. Weng, P. Hill, S. Johnson, A. C. Frangeskou, P. L. Diggle, Y.-C. Chen, J. Strain, E. Gu, M. E. Newton, J. M. Smith, P. S. Slater, and G. W. Morley\*. Deep three-dimensional solid-state qubit arrays with long-live spin coherence. *Physical Review Applied* 12, 064005 (2019).
4. M. Widmann\*, M. Niethammer, D. Y. Fedyanin, I. A. Khramtsov, T. Rendler, I. D. Booker, J. Ul Hassan, N. Morioka, **Y. C. Chen**, I. G. Ivanov, N. T. Son, T. Ohshima, M. Bockstedte, A. Gali, C. Bonato, S. Y. Lee\*, and J. Wrachtrup. Electrical charge state manipulation of single silicon vacancies in a silicon carbide quantum optoelectronic device. *Nano Letters* 19, 10, 7173-7180 (2019).
5. **Y. C. Chen**, B. Griffiths, L. Weng, S. S. Nicley, S. N. Ishmael, Y. Lekhai, S. Johnson, C. J. Stephen, B. L. Green, G. W. Morley, M. E. Newton, M. J. Booth, P. S. Salter, and J. M. Smith\*. Laser writing of individual nitrogen-vacancy defects in diamond with near-unity yield. *Optica* 6, 5, 662-667 (2019).
6. R. Nagy, M. Niethammer, M. Widmann, **Y. C. Chen**, P. Udyarhelyi, C. Bonato, J. Ul Hassan, R. Karhu, I. G. Ivanov, N. T. Son, J. R. Maze, T. Ohshima, O. O. Soykal, A. Gali, S. Y. Lee\*, F. Kaiser\*, and J. Wrachtrup. High-fidelity spin and optical control of single silicon-vacancy centres in silicon carbide. *Nature Communications* 10, 1954 (2019).
7. **Y. C. Chen**\*, P. S. Salter, M. Niethammer, M. Widmann, F. Kaiser, R. Nagy, N. Morioka, C. Babin, J. Erlekampf, P. Berwian, M. J. Booth, and J. Wrachtrup. Laser writing of scalable single color centers in silicon carbide. *Nano Letters* 19, 4, 2377-2383 (2019).
8. P. R. Dolan, S. Adekanye, A. A. P. Trichet, S. Johnson, L. C. Flatten, **Y. C. Chen**, L. Weng, D. Hunger, H.-C. Chang, S. Castelletto, and J. M. Smith\*. Robust, tunable, and high purity triggered single photon source at room temperature using a nitrogen-vacancy defect in diamond in an open microcavity. *Optics Express* 26, 6, 7056-7065 (2018).

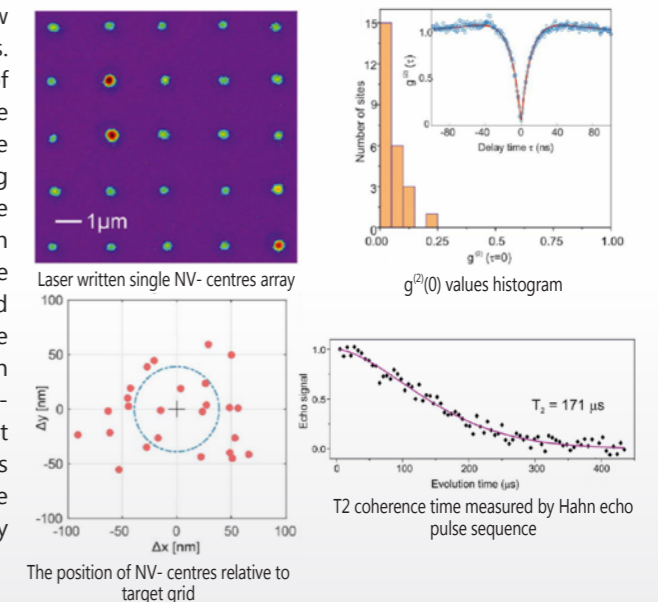
## Research Focus

### 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  $\mu$ s by standard Hahn echo measurements.

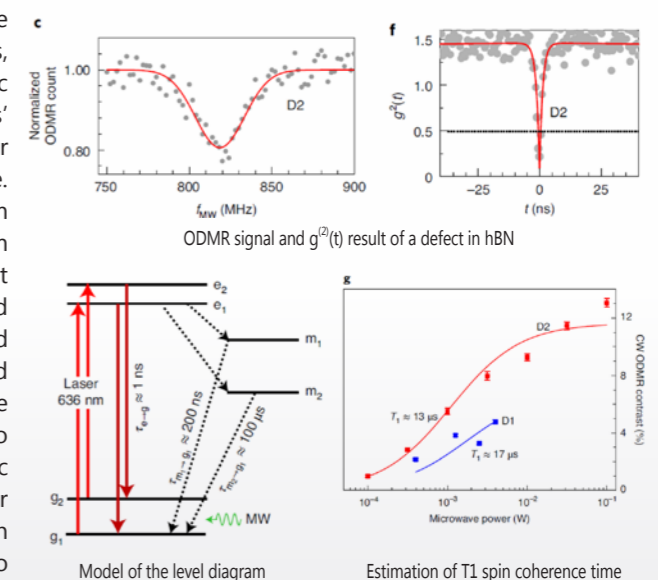


### Spin readout and manipulation of single defect in hBN 2D material

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  $T_1$  spin coherence time of the spin defects were estimated to be around 13~17  $\mu$ s.





# Chii-Dong Chen

Executive Officer of the TCQC and  
Distinguished Research Fellow

**Education** | Ph.D. Applied Physics, Chalmers University of  
Technology (1994)

## Positions and Career

- Distinguished Research Fellow, Institute of Physics, Academia Sinica (2023 - )
- Executive Officer of the thematic center of Quantum Computer (2021 - )
- Adjunct Professor, Department of Physics, National Dong-Hwa University (2014 - )
- Adjunct Professor, Department of Physics, National Cheng-Kung University (2008 - )
- Research Fellow, Institute of Physics, Academia Sinica (2007 - )
- Associate Research Fellow, Institute of Physics, Academia Sinica (2002 - 2007)
- Assistant Research Fellow, Institute of Physics, Academia Sinica (1997 - 2002)

## Honors and Awards

- 2022, Academia Sinica Presidential Scholar Program
- 2003, Academia Sinica Research Award for Junior Research

## Research Interests

- Fabrication, Physics, and Applications of Nanoelectronic Devices
- Electronic Transport Properties of Nanomaterials
- Fundamental Research and Applications of Superconducting and Magnetic Single-Electron Transistors
- Superconducting Quantum Chips and Control Systems

## Selected Publications

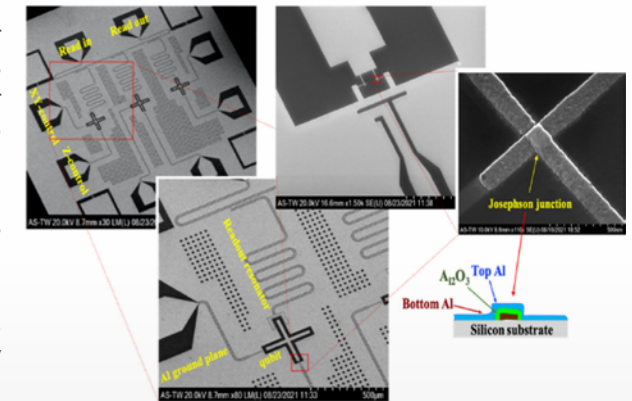
1. Joshua Condcion Esmenda, Myrron Albert Callera Aguila, Jyh-Yang Wang, Chi Yuan Yang, Kung Hsuan Lin, Kuei-Shu Chang-Liao, Nadav Katz, Sergey Kafanov, Yuri A. Pashkin, and ChiiDong Chen, "Observing off resonance motion of nanomechanical resonators as modal superposition", *Advanced Science*, 2005041 (2021)
2. Alberto Ronzani, Bayan Karimi, Jordan Senior, Yu-Cheng Chang, Joonas T. Peltonen, ChiiDong Chen and Jukka P. Pekola, "Tunable photonic heat transport in a quantum heat valve", *Nature Physics* 14, 991-995 (2018)
3. Carlos M. Torres, Jr., Yann-Wen Lan, Caifu Zeng, Jyun-Hong Chen, Xufeng Kou, Aryan Navabi, Jianshi Tang, Mohammad Montazeri, James R. Adleman, Mitchell B. Lerner, Yuan-Liang Zhong, Lain-Jong Li, Chii-Dong Chen, and Kang L. Wang, "High-Current Gain Two-Dimensional MoS<sub>2</sub>-Base Hot-Electron Transistors", *Nano Lett.*, 15, 12, 7905 (2015)
4. Linh-Nam Nguyen, Yann-Wen Lan, Jyun-Hong Chen, Tay-Rong Chang, Yuan-Liang Zhong, Horng-Tay Jeng, Lain-Jong Li, and Chii-Dong Chen, "Resonant tunneling through discrete quantum states in stacked atomic-layered MoS<sub>2</sub>", *Nano Letters*, 14, 2381-2386 (2014)
5. Chia-Jung Chu, Chia-Sen Yeh, Chun-Kai Liao, Li-Chu Tsai, Chun-Ming Huang, Hung-Yi Lin, Jing-Jong Shyue, Yit-Tsong Chen, and Chii-Dong Chen, "Improving Nanowire Sensing Capability by Electrical Field Alignment of Surface Probing Molecules", *Nano Letters*, 13, 2564-2569 (2013)
6. Yuan-Liang Zhong, Andrei Sergeev, Chii-Dong Chen, and Juhn-Jong Lin, "Direct Observation of Electron Dephasing due to Inelastic Scattering from Defects in Weakly Disordered AuPd Wires", *Physical Review Letters*, 104, 206803 (2010).
7. M. C. Lin, C. J. Chu, L. C. Tsai, H. Y. Lin, C. S. Wu, Y. P. Wu, Y. N. Wu, D. B. Shieh, Y. W. Su, and C. D. Chen, "Control and detection of organosilane polarization on nanowire field-effect-transistors", *Nano Letters*, 7, 3656 (2007).
8. Yu-Lun Chueh, Mong-Tzong Ko, Li-Jen Chou, Lih-Juann Chen, Cen-Shawn Wu, and Chii-Dong Chen, "TaSi<sub>2</sub> Nanowires: A Potential Field Emitter and Interconnect", *Nano Letters*, 6, 1637-1644 (2006).
9. C. D. Chen, Watson Kuo, D. S. Chung, J. H. Shyu, C. S. Wu, "Evidence for suppression of superconductivity by spin imbalance in Co-Al-Co single electron transistors", *Physical Review Letters*, 88, 047004, (2002).
10. W. Kuo and C.D. Chen, "Scaling Analysis of Magnetic Field Tuned Phase Transitions in One-Dimensional Josephson Junction Arrays", *Physical Review Letters*, 87, 186804, (2001).

## Research Focus

### 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.

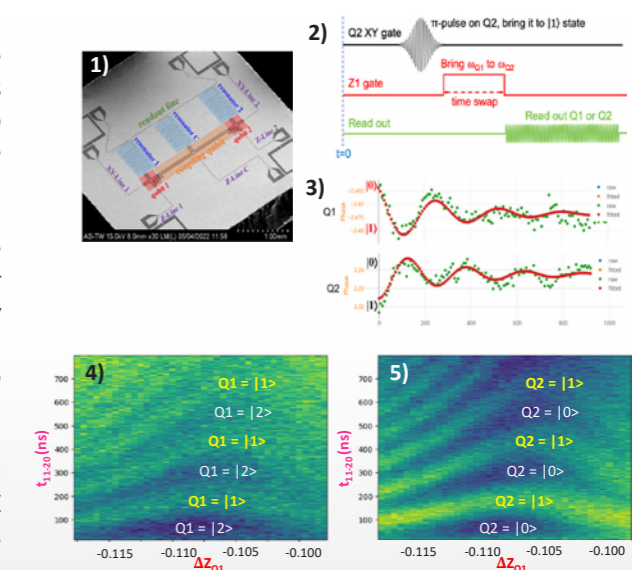


SEM images of a 3-qubit device crafted through a single-step, all-electron-beam lithography lift-off procedure are displayed. Josephson junctions are fashioned using the widely employed tilt-angle evaporation technique, and the lower-right panel exhibits a cross-sectional view of the setup.

### 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  $\pi$ -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  $|01\rangle$  and  $|10\rangle$  at a frequency corresponding to the Q1-Q2 coupling strength. Similarly, we fine-tuned the CZ gate by bringing Q1<sub>1-2</sub> and Q2<sub>0-1</sub> into resonance. This resulted in the coherent exchange of energy between  $|20\rangle$  and  $|11\rangle$ , 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.



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2023

<b>Mu-Huai Fang</b>	Career Development Award, Academia Sinica
<b>Chun-Wei Pao</b>	Y. Z. Hsu Scientific Paper Award

2022

<b>Chun-Wei Pao</b>	Investigator Award, Academia Sinica
<b>Chih Wei Chu</b>	World's Top 2% Scientists
<b>Chih Wei Chu</b>	SPIE Senior Member
<b>Yu-Jung Lin</b>	Cross-Generation Young Scholars Program (Emerging Young Scholars), National Science and Technology Council, Taiwan
<b>Chi Chen</b>	Academia Sinica Career Development Award
<b>Fu-Liang Yang</b>	19th National Innovation Award
<b>Tung-Han Hsieh</b>	19th National Innovation Award in the Academic Research Category
<b>Chao-Cheng Kaun</b>	Future Tech Award, National Science and Technology Council

2021

<b>Yu-Jung Lu</b>	SPIE Women in Optics Planner, USA
<b>Min-Hsiung Shih</b>	International Electron Devices & Materials Symposium (IEDMS), Excellent Paper Award
<b>Min-Hsiung Shih</b>	Optics & Photonics Taiwan International Conference (OPTIC), Paper Award
<b>Peilin Chen</b>	Investigator Award, Academia Sinica, Taiwan
<b>Bi-Chang Chen</b>	Academia Sinica Early-Career Investigator Research Achievement Award
<b>Pei-Kuen Wei</b>	Presidential scholars, Academia Sinica
<b>Chao-Cheng Kaun</b>	Future Tech Award, Ministry of Science and Technology

2020

<b>Yu-Jung Lu</b>	Youth Photonics Award, Taiwan Photonics Society, Taiwan
<b>Yu-Jung Lin</b>	Young Investigator Award, Prof. Chau-Jen Lee Biomedical Engineering Development Foundation, Taiwan
<b>Bi-Chang Chen</b>	18th Y. Z. Hsu Science Paper Award, Optoelectronics Science & Technology Category
<b>Chih-Yu Kuo</b>	Research Paper Award, Journal of Chinese Soil Water Conservation
<b>Fu-Liang Yang</b>	17th National Innovation Award

2019

<b>Chih Wei Chu</b>	Associate Academician of Asia Pacific Academy of Materials
<b>Chih Wei Chu</b>	Young Scientist of Asia Pacific Academy of Materials
<b>Jung Hsin Lin</b>	Academia Sinica Investigator Award
<b>Peilin Chen</b>	Fellow, the Royal Society of Chemistry

2018

<b>Yu-Jung Lu</b>	56th Ten Outstanding Young Persons (JCI TOYP Taiwan)
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2015

<b>Bi-Chang Chen</b>	The 2015 AAAS Newcomb Cleveland Prize
<b>Shu Wei Chang</b>	Senior Member, Institute of Electrical and Electronics Engineers (IEEE)

2014

<b>Yun-Chorng Chang</b>	Senior Member, SPIE
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2012

<b>Fu-Liang Yang</b>	9th National Innovation Award in the Academic Research Category
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The core facilities in Research Center of Applied Sciences (RCAS) provide service to the researchers of RCAS and Academia Sinica. All instruments are located on 6<sup>th</sup>, 4<sup>th</sup> and B2 floors in Interdisciplinary Research Building for Science and Technology (IRBST). The RCAS core facilities can be divided into three categories by features : Microscope, Materials Analysis and Micro Fabrication.

**Table 1. The information of core facilities**

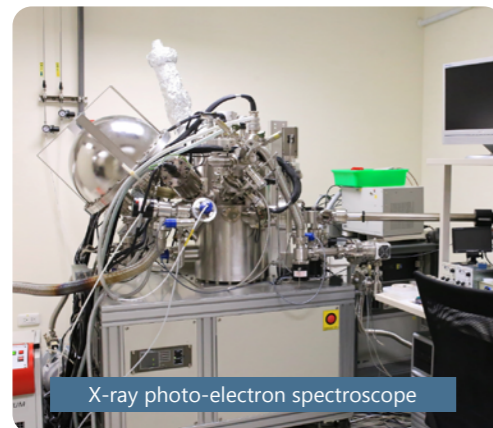
	Instruments	Features	Brand Model	Location
Microscope	Atomic force microscope	Material surface analysis	Bruker DM-CAFM	NCTU TKP506
	Laser scanning Confocal Spectral Microscope	Bio and fluorescent sample detection	Leica TCS-SP5	IRBST 4B20
	Atomic force microscope	Bio materials and nano components detection	JPK Nano Wizard II & III	IRBST B2 public lab
	High resolution Raman microscope	Fluorescence and crystallization analysis	Jobin Yvon HR800	IRBST 6B08
	Field emission scanning electron microscope	Analysis of surface morphology and elemental analysis	Nova 200 NPE 44/ D8187	IRBST 4C05
Materials Analysis	X-ray photo-electron spectroscopy	Surface and Depth Analysis of Elementals	ULVAC-PHI PHI-5000 Versaprobe	IRBST 4C05
	Scanning Ion Microscope	Surface and Depth Analysis of Molecules and Atoms	ULVAC-PAI TRIFTV	IRBST 4C05
	Time-resolved confocal microscope for single molecule spectrometer	Multi-Channel time resolve spectroscopy	PicoQuant Micro Time 2000	IRBST 6B10
	Variable angle spectroscopic ellipsometer	Material film thickness and refractive index analysis	VUV-VASE, Gen-II	IRBST 6A02
	Color 3D Laser Scanning Microscope	Surface profile and roughness detection	Keyence VK9710K S/N 2190011	IRBST 4C01
Micro Fabrication	Benchtop maskless lithography system	Structure production of photoresist on components	Heidelberg uPG501	IRBST B2 Micro Fabrication lab
	Specimen Preparation Equipment	Thin-film growth and etching	Gated Sted SKE104005	IRBST 6A02
	Focus Ion Beam	Structure production of nano components	FEI NanoLab660	IRBST 4B19
	Inductively coupled plasma etching system	Dry and wet etching of nano components	OXFORD ICP65	IRBST B2 Micro Fabrication lab

# Administration Staffs

The core facilities provide assistances for the researchers to conduct various experiments in bio-image detection, material surface analysis, components structure production and micro sample fabrication. Furthermore, several public laboratories on 6<sup>th</sup>, 4<sup>th</sup> and B2 floors in IRBST are established for our members to do researches in fabrication, imaging, cell and protein.

Every user should pass the safety course of Academia Sinica. After finishing the training of instruments, users could get the license. However, toxic chemicals (as defined by EPA and regardless if it is under controlled by EPA), volatile, radio-active and explosive substances are prohibited. Biological-active materials should be remarked on usage record. Based the requirement of each instrument, administrators can disallow additional types of samples such as (include, but not limited by) magnetic, powder, etc. For all facilities, users should make reservations on the web site (<http://scheduler.rcas.sinica.edu.tw/>) in advance and fill in usage records indeed.

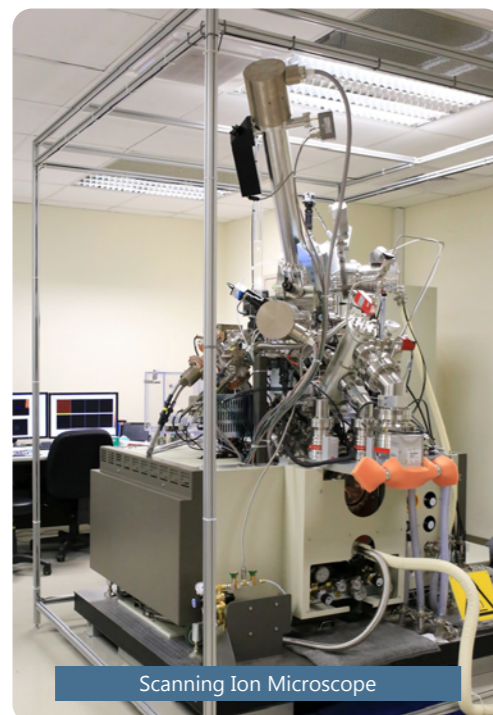
In addition to routine maintenance every year, we would upgrade the facilities and improve the laboratory configuration. Moreover, we have suitable plan and management for every lab and instrument in safety considerations of research.



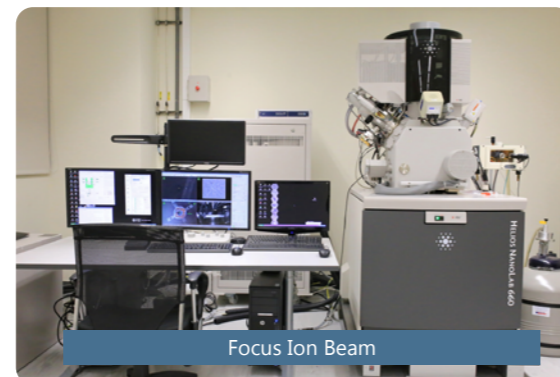
X-ray photo-electron spectroscopy



Laser scanning Confocal Spectral Microscope



Scanning Ion Microscope



Focus Ion Beam



Specimen Preparation Equipment

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