



# 118 , 119

## 2018/2019 NATIONAL TSING HUA UNIVERSITY R&D REPORT

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Engineering

Biomedical Technology

Material Science

Humanities and Social Science



National Tsing Hua University

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## About NTHU

National Tsing Hua University (NTHU) has a long and proud history. First established as the Tsing Hua Academy at Tsing Hua Garden in Beijing in 1911, the Academy was renamed as National Tsing Hua University in 1928 when its curricula were expanded to that of comprehensive university.

In 1956, NTHU was reinstalled on its current campus in Hsinchu, Taiwan. Since its reinstallation, NTHU has developed from an institute focusing on nuclear science and technology to that of a comprehensive research university offering degree programs ranging from baccalaureate to doctorate in science, technology, engineering, humanities and social sciences as well as management.

NTHU has been consistently ranked as one of the premier universities in Taiwan and is widely recognized as the best incubator for future leaders in industries as well as academics. Such stellar records are particularly exemplified by the outstanding achievements of our alumni, including two Nobel laureates in physics Drs. Cheng-Ning Yang and Tsung-Dao Lee, one Nobel laureate in chemistry Dr. Yuan-Tseh Lee and one Wolf Prize winner in mathematics Dr. Shiing-Shen Chern.

On the first of November 2016, NTHU formally incorporated the National Hsinchu University of Education. This merger further diversifies and expands our curricula and creates a more comprehensive learning environment including arts and education to better prepare students to take on the challenge of a changing world.

## Message from the President



*Dr. Hong Hocheng*  
President

*National Tsing Hua University  
Hsinchu, Taiwan  
November 2019*

National Tsing Hua University (NTHU) is a research university with a long and proud tradition. Since the reestablishment in Hsinchu in 1956, NTHU has been known for excellent academic programs, stellar research output as well as outstanding alumni.

NTHU provides a stimulating and nurturing environment within which our faculty can offer quality teaching and conduct innovative research. Regarded as one of the top-tier research universities, our research activities emphasize fundamental discoveries at the forefronts of basic sciences and exploration of breakthrough technologies with a high potential for applications. These are reflected in our publications in the world's preeminent journals, international patents received, and technology transferred. In the 2018-2019 R&D annual report, we highlight several important breakthroughs in five fields and also provide the facts and figures related to other important R&D activities. This volume is undoubtedly too limited to give the full scope of R&D at NTHU but a glimpse into our recent achievements. Hopefully, this can serve as a catalyst for further interactions, exchange of ideas, and establishment of collaborations.

Built on our proud heritage, NTHU will continue to promote excellent teaching and innovative research with the goal of achieving important scientific discoveries and innovative technologies. I hope that you will find this R&D annual report informative and will give us your precious opinions and suggestions.



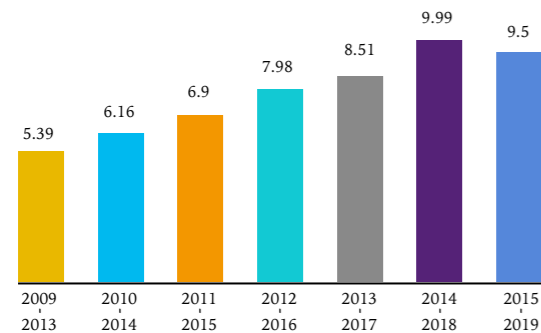
## R&D Facts and Figures

### 2019 QS World University Rankings by Subject

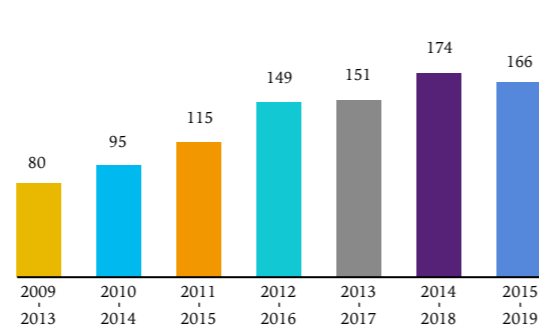
#### Top 50-100

Engineering and Technology - 53	Chemical Engineering - 75
Electrical & Electronic Engineering - 63	Chemistry - 92
Mechanical - 64	Physics & Astronomy - 93
Materials Science - 71	Statistics & Operational Research - 95
Linguistics - 72	Computer Science - 97

#### Citations Per Paper



#### Highly Cited Paper



### 2018 Ranking of Top Universities in Greater China (ARWU)

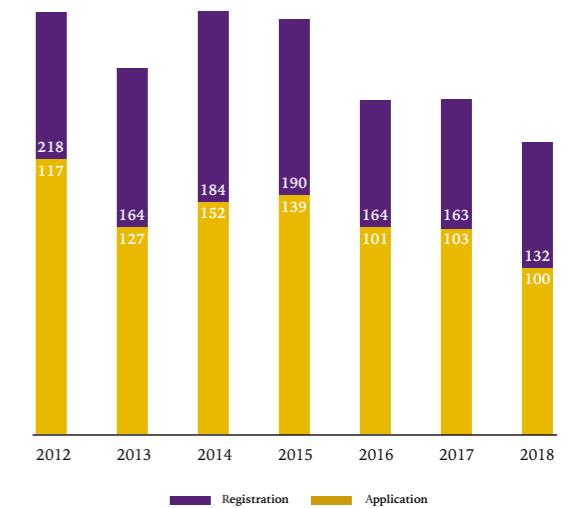
Rank	Institution
1	Tsinghua University
2	Peking University
<b>3</b>	<b>National Tsing Hua University</b>
4	The Chinese University of Hong Kong
5	Zhejiang University
6	University of Science and Technology of China
7	Shanghai Jiao Tong University
8	The University of Hong Kong
9	National Taiwan University
10	Fudan University

### Number of Awarded US Patents

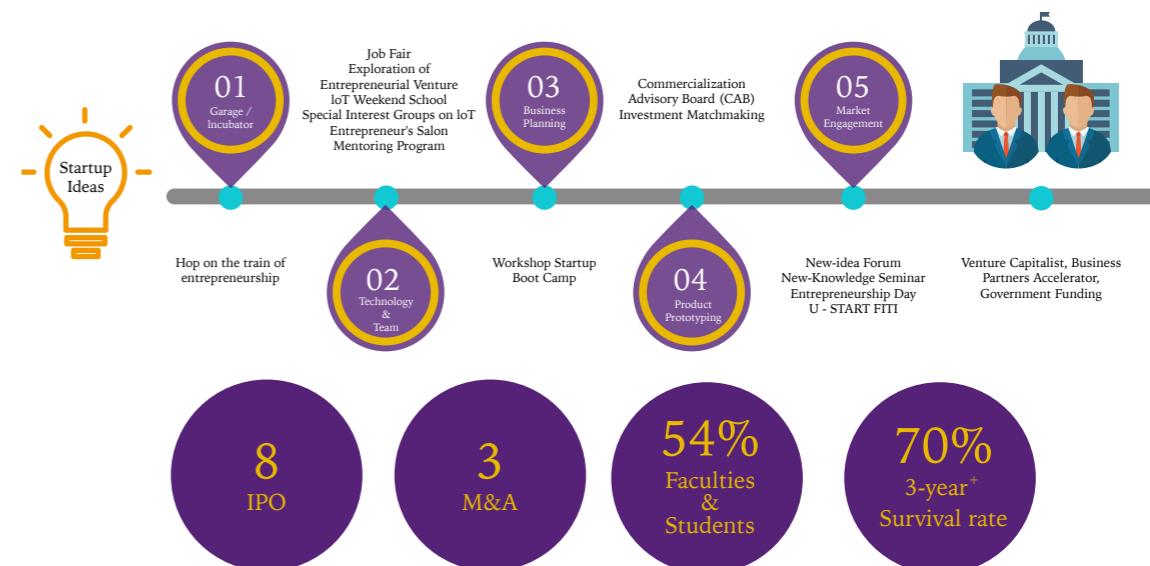
#### Taiwan Ranking NO.1 2012-2018

Year	2012	2013	2014	2015	2016	2017	2018
World Ranking							
	15	15	11	15	25	23	24
Taiwan Ranking							
	2	2	<b>NO.1</b>				

### International Patent Application and Registration (2012-2018)



### National Tsing Hua University - Entrepreneurship Avenue

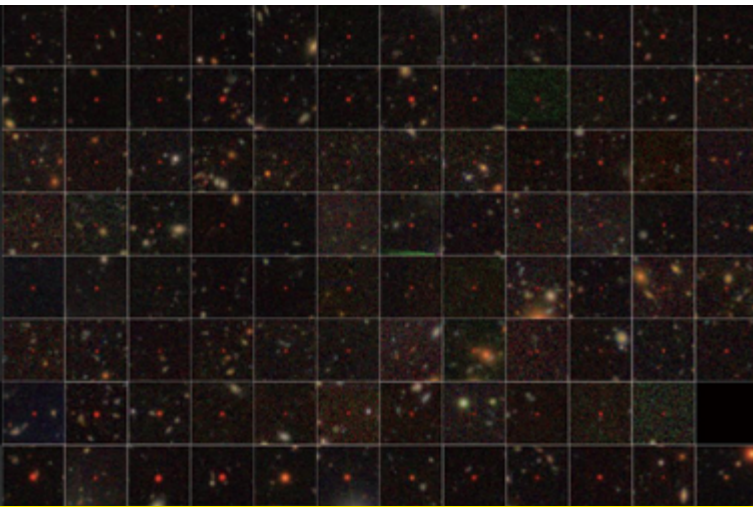




## ***Natural Science***

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- *Revealing Cosmic Re-ionization Using Black Holes as Background Lights*
- *Highly Efficient Gene Release in Spatiotemporal Precision Approached By Light and pH Dual Responsive Copolymers*
- *NIR Light Activatable Nanomaterials-mediated Phototheranostic Nanomedicines : An Emerging Paradigm for Cancer Treatment*
- *Copper Photoredox Catalyzed A3' Coupling of Arylamines, Terminal Alkynes, and Alcohols via a HAT Process*
- *Aggregation and Sedimentation of Shattered Graphene Oxide Nanoparticles in Dynamic Environments : A Solid-body Rotational Approach*



Super massive black holes we have newly discovered (image credit: National Astronomy Observatory of Japan).

Professor. Tomo Goto  
tomo@phys.nthu.edu.tw

## Revealing Cosmic Re-ionization Using Black Holes as Background Lights

The Universe experienced a big phase change in its early stage, from neutral to ionized. This process is called the cosmic re-ionization, which however, has been one of the remaining mysteries in cosmology. It has been difficult to map out this cosmic re-ionization observationally, because as we approach the earlier, the more neutral Universe; >99% of the UV light is absorbed by the neutral hydrogen, escaping the pursuit of even the largest telescopes. This is why the epoch is called the dark age of the Universe.

How do we observe the dark age when little light is coming out? One of the innovative approaches to reveal the cosmic re-ionization is to use the bright light of distant super massive black holes (SMBHs) as a background torch to shine through the dark age of the Universe. The bright light of distant SMBHs allows us to measure the intervening neutral hydrogen absorption, which imprints the reionization history of the Universe, i.e., The more neutral, the more absorption. However, distant SMBHs are extremely rare. It has been a challenge for astronomers to find them in quantity.

Our research team has advanced the field in the following two aspects:

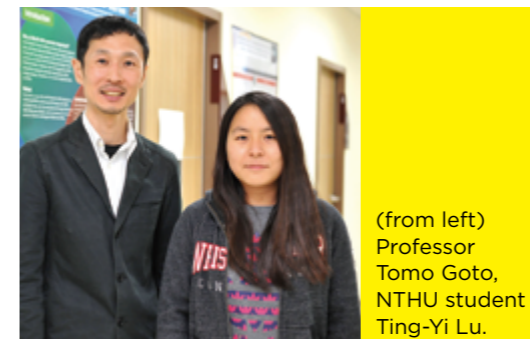
(i) Discovery of one of the most distant SMBHs at  $z=6.6$  (12.9 billion years ago). Distant SMBHs are extremely rare. How rare? They are only one in billion objects, much smaller probability than any lotteries. A student and myself have carefully selected SMBH candidates out of billions of objects in our unprecedentedly large survey. We used the Subaru 8m telescope at the Maunakea observatory in Hawaii for spectroscopic confirmation. On the first observing night, immediately after we started observation, we successfully discovered a distant SMBH. It was an exciting moment for us, to see a widely broadened hydrogen line, which is a sign of  $\sim$ billion solar mass black hole. It was the moment that years of our preparation payed off. This SMBH was so bright that we mapped out the cosmic re-ionization up to  $z=6.4$ , using a single SMBH.

(ii) In collaboration with a larger international team including US and Japan, we are also hunting for fainter SMBHs than previous ones in the

distant Universe. Our large program has obtained 300 nights of Subaru telescope's time to survey unprecedentedly large area of  $1400 \text{ deg}^2$  with the depth of an 8m telescope ( $\sim$ worth 100 million NTD). Such deep and wide survey data never existed in the past. After two years from the start of the survey, we have already found 100 SMBHs at  $z=6$ , where only  $\sim$ 10 were known previously. Since finding 100 SMBHs is a milestone for our project, the result was released to the press in US, Japan, Germany, and in Taiwan. In Taiwan, more than 30 newspapers/website have reported the result.

Using these 100 SMBHs, we have, for the first time, statistically ruled out that radiation from SMBHs is not the source of the cosmic re-ionization. Our result is an important step in understanding what astronomical objects have ionized the Universe.

“However, distant SMBHs are extremely rare. It has been a challenge for astronomers to find them in quantity.”



(from left)  
Professor  
Tomo Goto,  
NTHU student  
Ting-Yi Lu.

### Research Highlights

- The student involved won the PSROC best oral presentation award (2019), and the NTHU physics department best poster award.
- The discovery was covered by at least 17 TVs and newspapers around the world. In Taiwan, more than 30 newspapers/website have reported the result.

### Research Output

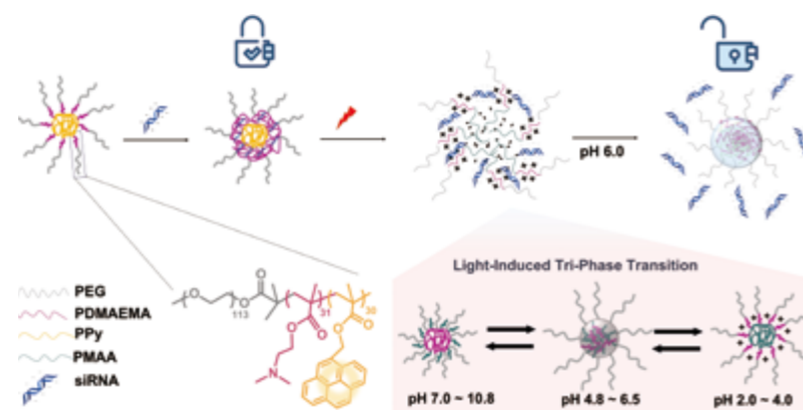
- “A quasar discovered at redshift 6.6 from Pan-STARRS1”, Tang et al., Monthly Notices of Royal Astronomy Society, 466 (2017), 4568 “Discovery of the First Low-luminosity Quasar at  $z > 7$ ”, Matsuoka et al., The Astrophysical Journal Letters, 872 (2019), 2
- “Discovery of the First Low-luminosity Quasar at  $z > 7$ ”, Matsuoka et al., The Astrophysical Journal Letters, 872 (2019), 2
- “Subaru High- $z$  Exploration of Low-luminosity Quasars (SHELLQs). V. Quasar Luminosity Function and Contribution to Cosmic Reionization at  $z = 6$ ”, Matsuoka et al. 2018, The Astrophysical Journal, 869 (2018), 150
- Subaru High- $z$  Exploration of Low-Luminosity Quasars (SHELLQs). II. Discovery of 32 quasars and luminous galaxies at  $5.7 < z \leq 6.8$ ”, Matsuoka et al., Publications of the Astronomical Society of Japan, 70 (2018), S35
- “Subaru High- $z$  Exploration of Low-luminosity Quasars (SHELLQs). I. Discovery of 15 Quasars and Bright Galaxies at  $5.7 < z < 6.9$ ”, Matsuoka et al., The Astrophysical Journal, 828 (2016), 26



Professor Chi-How Peng  
chpeng@mx.nthu.edu.tw

## Highly Efficient Gene Release in Spatiotemporal Precision Approached by Light and pH Dual Responsive Copolymers

Illustration of encapsulating and releasing siRNA by micelles formed from triblock copolymers via the structural transitions in response to light and pH stimuli.



Gene therapy using small interference RNA (siRNA) is one of the strategies developed in the past few decades for cancer treatment at gene level. The function of siRNA is to activate the RNA induced silencing complex (RISC) that can degrade the targeted messenger RNA (mRNA) and thus block the formation of targeted cancer protein. Gene fragments are easily degraded by enzymes. Therefore, siRNA needs a carrier protecting it to reach the cancer cells in circulation system. An ideal carrier should have the properties of both high stability and efficient siRNA releasing.

In present work, triblock copolymer of poly(ethylene glycol)-b-poly(2-dimethylaminoethyl methacrylate)-b-poly(pyrenylmethyl methacrylate) (PEG-b-PDMAEMA-b-PPy) was synthesized for a gene delivery system. The PEG segment acts as the hydrophilic segment. The PDMAEMA segment could be protonated to carry the positive charges that bind siRNA through the ionic interaction.

PPy performs as the hydrophobic core to stabilize the polymeric micelle. The micelle of tri-block copolymers was prepared by typical nanoprecipitation under sonication. Dynamic laser scattering (DLS) analysis revealed that the hydrodynamic diameter of micelle was 83 nm with uniform dispersity of 0.11 and retained homogeneous particle dispersity (PDI < 0.14) with a size around 85 nm in 5 days at 25°C.



*The siRNA releasing efficiency could therefore reach up to 91% with the irradiation of UV light.*



The tri-block copolymer micelle showed a siRNA condensation efficiency approaching 90% at N/P ratio (the ratio between the nitrogen on PDMAEMA and phosphine on siRNA) as low as 5 at pH 6.0. Moreover, the siRNA-encapsulated micelle is stable under physiological condition, illustrated by a low leakage rate (26%) in 24 h. The release of siRNA could be triggered by the irradiation of UV light that converts PPy to poly(methyl methacrylic acid) (PMAA). This conversion results in not only the destruction of the hydrophobic core of the micelle, but also the repulsion between the negative charged siRNA and PMAA at pH 4.3 to 6.5. The siRNA releasing efficiency could therefore reach up to 91% with the irradiation of UV light.

The material-cytotoxicity tests indicated that the tri-block copolymer self-assembled micelles

### Research Highlights

- 2018 Shui-Mu Foundation of Chemistry, Award for Outstanding Young Scholar

### Research Output

- Hung-Hsun Lu, Cheng-Hung Huang, Ting-Yun Shiue, Fu-Sheng Wang, Ko-Kai Chang, Yunching Chen and Chi-How Peng\* Chem. Sci., 2019, 10, 284



High-performance polymers from controlled/living polymerization group

have negligible cytotoxicity before and after UV irradiation. Further in vitro tests suggested that the siRNA condensed micelle showed a better siRNA uptake efficiency associated with high protein knockdown efficiency compared to free siRNA, revealing the potential of this gene delivery system for further in vivo transfection.

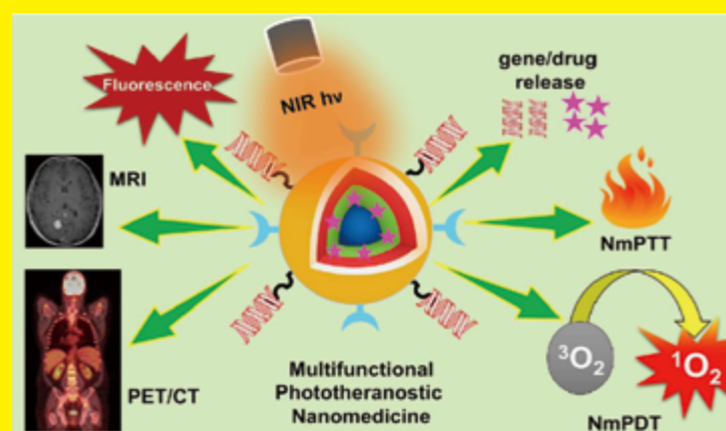
Conclusively, the photo- and pH-responsive triblock copolymer of PEG-b-PDMAEMA-b-PPy has therefore been demonstrated as an ideal siRNA carrier that has shown the properties of not only remarkable siRNA condensation, high stability, and efficient siRNA release but also great performance in in vitro tests of cytotoxicity, siRNA uptake efficiency, and protein knockdown efficiency.



Professor Kuo Chu Hwang  
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## NIR Light Activatable Nanomaterials-mediated Phototheranostic Nanomedicines: An Emerging Paradigm for Cancer Treatment

Cancer is one of the most deadly diseases threatening the lives of humans. Although many treatment methods have been developed to tackle cancer, each modality of cancer treatment has its own limitations and drawbacks. The development of minimally invasive treatment modalities for cancers remains a great challenge. Near-infrared (NIR) light-activated nanomaterial-mediated phototherapies, including photothermal and photodynamic therapies, provide an alternative means for spatially and temporally controlled minimally invasive treatments of cancers. Nanomaterials can serve as nanocargoes for the delivery of chemo-drugs, diagnostic contrast reagents, and organic photosensitizers, and can be used to directly generate heat or reactive oxygen species for the treatment of tumors without the need for organic photosensitizers with NIR-light irradiation. Here, current progress in NIR-light-activated nanomaterial-mediated photothermal therapy and photodynamic therapy is summarized. Furthermore, the effects of size, shape, and surface functionalities of nanomaterials on intracellular uptake, macrophage clearance, biodistribution, cytotoxicities, and biomedical efficacies are discussed. The use of various types of nanomaterials, such as gold nanoparticles,



Cancer is one of the deadliest diseases threatening the lives of human beings. NIR light activatable nanomedicines is an emerging paradigm for treating tumors, including those deeply seated inside tissues. In this article, topics including NIR light mediated photothermal therapy, NIR-mediated photodynamic therapy, NIR light triggered drug release from nanocarriers, and the use of nanomaterials as carriers for delivery of organic photosensitizers and chemodrugs, were reviewed.

carbon nanotubes, graphene, and many other inorganic nanostructures, in combination with diagnostic and therapeutic modalities for solid tumors, is briefly reviewed.

### Research Output

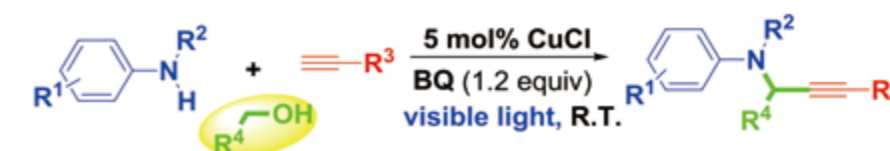
- Raviraj Vankayala and Kuo Chu Hwang\*, "NIR Light Activatable Nanomaterials-mediated Phototheranostic Nanomedicines: An Emerging Paradigm for Cancer Treatment", *Adv. Mater.* 2018, 30, 1706320.

“The development of minimally invasive treatment modalities for cancers remains a great challenge.”

Professor Kuo Chu Hwang  
kchwang@mx.nthu.edu.tw



## Copper Photoredox Catalyzed A3' Coupling of Arylamines, Terminal Alkynes, and Alcohols via a HAT Process



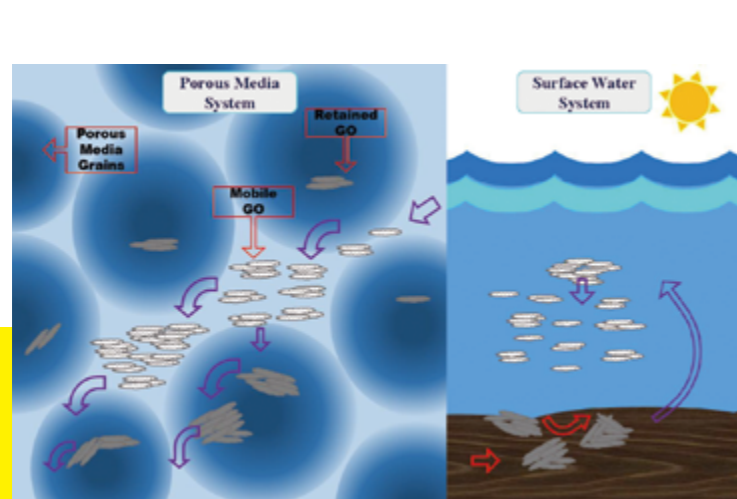
- alcohols act as solvents and substrates
- featuring a HAT with alcohol
- formation of C-C/C-N bonds
- selective  $\alpha$ -C-H bond activation of alcohol

The first successful example of the three-component coupling of N-alkylanilines, terminal alkynes, and alcohols was achieved at room temperature by a visible-light-mediated copper-catalyzed photoredox hydrogen-atom transfer process. This method allows preparation of propargylamines through uniquely selective  $\alpha$ -C@H bond activation of unactivated alkyalcohols. Preliminary studies indicate that formation of  $\alpha$ -oxy radical is operative. This approach facilitates rapid access to biologically important propargylamines from methanol as an abundant feedstock.

Methanol C-H bond Activation by HAT-process: A visible-light copper photoredox-catalyzed process can enable the HAT process with alcohols (formation of  $\alpha$ -oxy radical) to accomplish the propargylamines via three-component coupling reactions at room temperature. This transformation represents a sustainable and atom economical approach to the preparation of biologically important propargylamines from abundant methanol feedstock.

### Research Output

- Arunachalam Sagadevan, V. Kishore Kumar Pampana, and Kuo Chu Hwang\*, Copper Photoredox Catalyzed A3' Coupling of Arylamines, Terminal Alkynes, and Alcohols via a HAT Process, *Angew Chem.* 2019, 58, 3838–3842



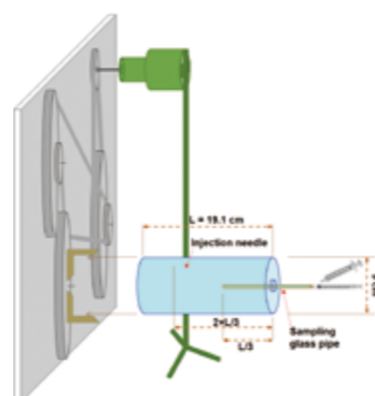
Professor. Ruey-an Doong  
radoong@mx.nthu.edu.tw

Illustration of nanoparticle aggregation in surface water and porous media systems.

## Aggregation and Sedimentation of Shattered Graphene Oxide Nanoparticles in Dynamic Environments : A Solid-body Rotational Approach

With the increasing global proliferation of commercial applications for nanomaterials, they are becoming increasingly released into the natural environment either accidentally in waste streams or deliberately within environmental clean-up, agronomy, and petroleum reservoir recovery applications. Once nanoparticulate enter aquatic environments, aggregation of such particles can significantly affect their functionality and transport behaviour, particularly in aqueous and porous media. Despite the existence of many studies on homo- and hetero-aggregation of various nanoparticles (NP), and abundant reports on the impacts of various factors on the aggregation behaviour of these NP, it remains a question how system dynamics modify aggregation rates. It is particularly of paramount importance in groundwater (GW) and surface water (SW) systems to understand how such complex multi-cascade processes such as advective and diffusive transport, tortuosity, and arrival of aggregates from up-gradient pores in GW systems, or resuspension phenomenon in SW system can impact the aggregation behaviour of NP.

To investigate such systems, we developed a newly experimental device in which these impacts are simulated by slowly continuous rotation in a cylinder. This simple apparatus allows monitoring the particle size dynamics during aggregation which is cumbersome in other experimental approaches commonly used for studying the NP fate, e.g., packed column experiments or mesocosm tests. This system consists of a cylinder which is filled with water and is placed horizontally to rotate around its axis slowly so that no significant shear is induced in the fluid inside. The main objective of using such a system is to investigate how NP aggregation behaviour changes over time when the local mass



Schematic of the experimental setup for SGO aggregation.



Left : Professor R. A. Doong,  
Right : Dr. Peyman Babakhani

concentration is kept constant, a phenomenon that can occur in pores of subsurface porous media and in resuspending surface waters. Using such a rotating cylinder, the angle between NP displacement directions and the gravity or removal direction is continuously changing without significant mechanical shear, thus preventing particle removal via settling within the axial area of the cylinder. This allows aggregates to develop to very large dimensions until the gravity force impacting on large grown aggregates overcome rotational displacements. In addition to conducting the tracer dye experiments, static and dynamic experiments with shattered graphene oxide NP (with hydrodynamic diameter <math><100\text{ nm}</math>), trajectory analysis on the movement of aggregates inside the cylinder, and population balance modelling on the aggregation of NP are also carried out to obtain a better insight into experimental results.

Results show that at the early stage of experiments, whilst most particles remain suspended, maintenance of mass concentration in the axial area of the rotating cylinder increases the number of collisions induced by Brownian motion and arising from differential sedimentation collisions with resuspending larger aggregates. This enhances the aggregation and sedimentation rates, with subsequent increase in differential-sedimentation aggregation, further enhancing the aggregation rate, and eventually leading to an immediate formation of large and compact aggregates on the cylinder wall. Thus, we propose that higher aggregation rates typically observed in groundwater, surface-water and other natural environmental systems compared to quiescent batch experiments may relate to environmental dynamics which need to be considered in future models.

### Research Highlights

- 2019 Ho Chin Tui Outstanding Award in the Environmental Protection Category
- 2018 Y.Z. Hsu Science Paper Award in the Green Science and Technology Category
- 2016 International Honorable Member Award of "American Academy of Environmental Engineers and Scientists"
- 2015 Outstanding Research Award, Ministry of Science and Technology, Taiwan

“ arising from differential sedimentation collisions with resuspending larger aggregates.”

### Research Output

- Ganganboina, A. B.; Doong, R. A.\* (2019). Impedimetric label-free N, S-graphene quantum dots decorated gold-polyaniline nanowire immunosensor for the ultrasensitive detection of carcinoembryonic antigen. *Sci. Rep.*, 9, 7214.
- Nguyen, T. B.; Huang, C. P.; Doong, R. A.\* (2019). Enhanced catalytic reduction of nitrophenols by sodium borohydride over highly recyclable Au@graphitic carbon nitride nanocomposites. *Appl. Catal. B Environ.* 240, 337-347.
- Babakhani, P.; Bridge, J.\*; Doong, R. A. (2018). The significance of early and late stages of coupled aggregation and sedimentation in the fate of nanoparticles: measurement and modelling. *Environ. Sci. Technol.* 52, 8419-8428.
- Ganganboina, A. B.; Dutta Chowdhury, A.; Doong, R. A.\* (2018). N-doped graphene quantum dots decorated V2O5 nanosheet for fluorescence turn off-on detection of cysteine. *ACS Appl. Mater. Interfaces.* 10, 614-624.





# Engineering

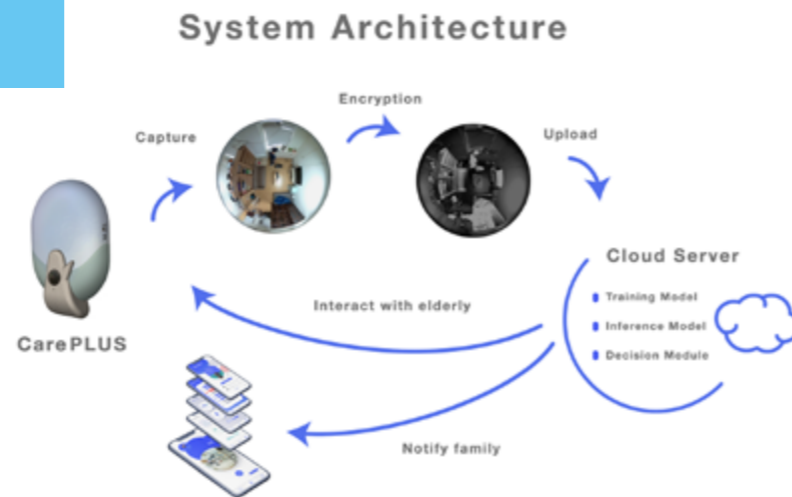
- *Smart 360 Home Assistant - Understanding Indoor Environment with AI.*
- *Ultrathin Metalenses Based on Van Der Waals Materials*
- *Multiobjective  $H_2/H_\infty$  Control Design of Nonlinear Mean-field Stochastic Jump-diffusion Systems Via Fuzzy Approach.*
- *SPWM-based Direct Digital Control with Average-voltage Model and  $D-\Sigma$  Process for Paralleled  $3\Phi 3W$  Grid-connected Converters to Reduce Circulating Currents*
- *Eye-in-hand Adaptive Gripper for Object Recognition and Tracking*



## Smart 360 Home Assistant - Understanding Indoor Environment with AI.

Professor. Min Sun  
sunmin@ee.nthu.edu.tw

Our CarePLUS first captures a fisheye image with large FoV information. Then we use de-identification technology to encrypt it into privacy-free representation and upload it to our AI cloud system. Our system will detect several information and feedback to CarePLUS to handle different kinds of dangerous situations.



Vision Science Lab (VSLab) started in NTHU in Fall 2014, focusing on computer vision and practical applications. Currently, we devote to intelligent home applications with in-depth research toward three areas: edge computing, image analysis with voice interaction, indoor layout prediction.

In an aging society, it is common to see people and their parents not living together. However, if their parents had an urgent need at home, they often cannot take actions immediately if knowing the accident. Moreover, people might miss the golden period if they are not aware of the need. Therefore, we develop an image analysis with voice interaction device, called as "CarePLUS." CarePLUS encrypts and "de-identify" the personal information and uploads image to the

cloud through the network. After analyzed by our dedicated AI model from the cloud, prediction results send to our edge device and interact with the user.

This solution has three aspects, "Privacy-Preserving," "Adaptive Deep Learning," and "Human-Centered AI." First, Privacy-Preserving would be our top priority. To protect user's privacy, we utilize AI-driven de-identification technology on the edge device shielding any leak of personal information. Second, Adaptive Deep Learning can quickly adjust to different environments. We tailor the model for our users by leveraging indoor 3D layout prediction and reconstruction

combining with human poses, object detection, and other technologies. In terms of indoor layout prediction and depth estimation, our proposed general layout post-processing outperforms the previous state of the arts with a clear margin on a worldwide benchmark. We also reduce post-processing time from dozens of seconds to less than a second. Last, Human-Centered AI is to establish a personalized service, such as fall-down notification, abnormal behavior notification, medication reminder, outbound reminder, and so on, remind our users through a mobile phone and keep users' parents accompany with a smart speaker.

We now have completed a product prototype and field studies. From the demo, we see CarePLUS creates an excellent opportunity for users to minimize the undesired consequence. With the success of our first step, we are looking for more places to explore the generalizability of our model. Soon, our CarePLUS will enlighten the life of elders around the world with a caring assistant.



Professor Min Sun (the third one from the left) and the team members of his laboratory.

“

*With the success of our first step, we are looking for more places to explore the generalizability of our model.*

”

### Research Highlights

- 2018 Ta-You Wu Memorial Award, Ministry of Science and Technology (MOST) (2018)
- Outstanding Scholar Awards, Foundation for the Advancement of Outstanding Scholarship (FAOS) (06/2018)
- Junior Research Award (新進人員研究獎), College of Electrical Engineering and Computer Science, National Tsing Hua University (NTHU) (05/2018)
- Conference on Visualization, Graphics and Image Processing (CVGIP) Best Paper Awards. (2015, 2016, 2017)

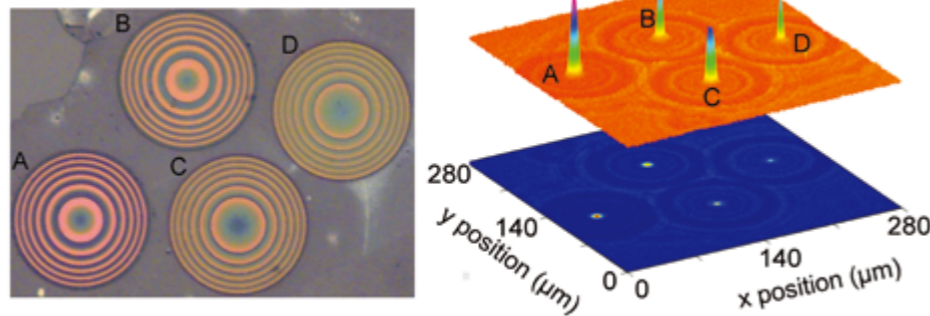
### Research Output

- S. Yang, F. Wang, C. Peng, P. Wonka, M. Sun, and H. Chu. Dula-net: A dual-projection network for estimating room layouts from a single RGB panorama. (CVPR 2019)
- C. Sun, C. Hsiao, M. Sun, and H. Chen. HorizonNet: Learning room layout with 1D representation and pano stretch data augmentation. (CVPR 2019)
- W. Chang, W. Chiang, S. Lu, T. Wu, and M. Sun, "Heapified Active Learning With Overconfidence Awareness Through Eigenvalue Analysis", Computer Vision, Graphic and Image Processing (CVGIP 2019)



# Ultrathin Metalenses Based on Van Der Waals Materials

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Lenses are ubiquitous elements in today's optical systems, but the continual downscaling of these systems poses significant limitations on conventional refractive or diffractive lenses. In this regard, recently developed metasurfaces are considered promising candidates, as they consist of arrays of planar scatters and can tailor the phase, amplitude, and polarization of lightwaves at subwavelength resolution in a compact form factor. The initial works in this field successfully used metallic nanoantennas to demonstrate metalenses as well as other optical components, such as polarization optics, reflectors, and holograms. Although utilizing these metallic structures can enable compact optical devices with deep-subwavelength thickness, they usually suffer from the challenges of high absorption loss and strong polarization sensitivity.

An alternative approach to overcome these challenges is to exploit arrays of dielectric resonators. Thus far, diverse set of high-efficiency dielectric lenses exist, extending from infrared to the visible range, and they provide a powerful

platform for developing a new generation of flat optical devices. Despite their promising progress, there are still multiple limitations that could hinder the applicability of dielectric metalenses. One critical challenge is that the design of dielectric metalenses generally require full 0 to  $2\pi$  phase control, and it is therefore necessary to create arrays of planar resonators with spatially varying radii. To reach this  $2\pi$  coverage condition, the dielectric resonators are usually near-wavelength-thick for phase accumulation, considerably thicker than metallic structures. Although thinner and efficient dielectric devices can be ideally realized using high index materials with low absorption loss, such as III-V AlGaAs, GaP, or other chalcogenide compounds, it is quite difficult to directly grow these optical materials on diverse substrates. Furthermore, to impart a small phase shift, smaller radii resonators must be fabricated. Fabricating these delicate high-aspect-ratio structures while simultaneously keeping low sidewall roughness is a challenging nanofabrication task and may limit the adoption of metalenses for different applications.

In this work, we approach the challenges from both the materials and photonic structures perspective to circumvent the problems. Specifically, in our designs, the dielectrics are composed of emerging van der Waals (vdW), including hexagonal boron nitride and molybdenum disulfide. Due to the nature of vdWs interactions, the vdW metalenses can be readily transferred onto diverse platforms, distinct from typical dielectric metasurfaces, limited by bottom-up material growths. Additionally, as vdW materials exhibit a rich variety of optical properties, they can be applied to different wavelength regimes and enable new conceptual devices. Building on this foundation, we further adapt the concept of incomplete phase modulation into the design of scattering elements, which can effectively reduce the required thickness of dielectric resonators to one-tenth to one-half of the wavelengths of

substrates, for stretching and tunable focusing applications. These demonstrations show the potential to realize deep-subwavelength-thick and functional dielectric metasurfaces, paving the way toward miniaturized optoelectronic systems.



Tian-Yun Chang, De-In Luo, Jia-Xin Li, Ya-Yun Zhang, Wei-Qing Li, Po-Liang Chen, Professor Chang-Hua Liu

“ Making an array of nanostructures with the low sidewall roughness is a challenging task and this would limit the applications of dielectric metalenses. ”

light that they focus. By exploiting such features, we demonstrate these ultrathin vdW metalenses not only can be applied at the infrared or visible wavelength regimes, showing near diffraction-limited focusing, but also exhibit their capabilities for imaging applications. More strikingly, the fabricated dielectric metalenses can be transferred onto different substrates, including flexible

## Research Highlights

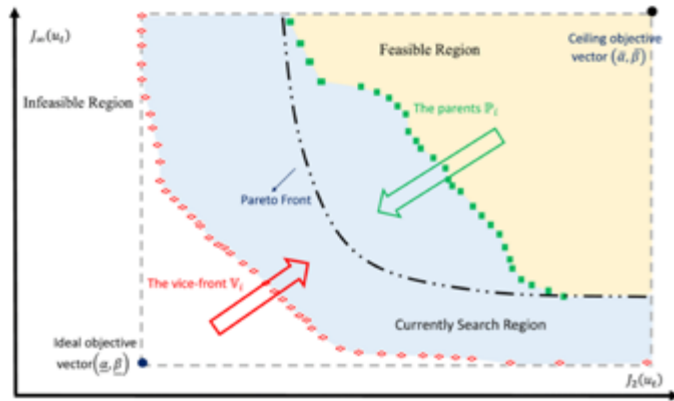
- Media coverage by Ceramics.org, Futurity.org, knowridge.com, Optics.org, Asianscientist.com, Techexplorist.com, Phys.org, ScienceDaily, PhotonicsViews.com, Newsbeezzer.
- TV and news coverage in Taiwan

## Research Output

- Chang-Hua Liu, J. Zheng, S. Colburn, T. Fryett, Y. Chen, X. Xu and A. Majumdar, "Van der Waals materials integrated nanophotonic devices." *Optical Materials Express* 9, 384 (2019). (Invited review article)
- Chang-Hua Liu, J. Zheng, S. Colburn, T. Fryett, Y. Chen, X. Xu and A. Majumdar, "Ultrathin van der Waals metalenses." *Nano Letters* 18, 6961 (2018).



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Multiobjective  $H_2/H_\infty$  Control Design of Nonlinear Mean-field stochastic jump-diffusion systems via fuzzy approach.

# Multiobjective $H_2/H_\infty$ Control Design of Nonlinear Mean-field Stochastic Jump-diffusion Systems via Fuzzy Approach.

For issue (III), an indirect method is proposed to solve the multiobjective  $H_2/H_\infty$  control design for MFSJD systems by simultaneously minimizing the upper bound vectors  $(\alpha, \beta)$  of the  $H_2$  and  $H_\infty$  performance in (3) and (4) in the Pareto optimal sense. By concurrently decreasing the upper bound vectors  $(\alpha, \beta)$  in the nondominating sense, the Pareto optimal solution set of the multiobjective  $H_2/H_\infty$  control in (2) for the nonlinear MFSJD system in (1) can be approached indirectly. As long as the Pareto front is obtained, the multiobjective  $H_2/H_\infty$  control problem in (2) for the MFSJD system in (1) can be also solved. To decrease the computational load and improve the computational efficiency, we proposed the fronts-squeezing LMI-constrained MOEA to narrow the search region down from two sides of feasible and infeasible region.

In this study, our two main contributions are as follows: First, we accomplish the multiobjective  $H_2/H_\infty$  fuzzy control design for nonlinear MFSJD systems in (1). It can completely describe the tradeoff between the  $H_2$  and  $H_\infty$  performance. Thus, the optimal  $H_2$  control design and optimal  $H_\infty$  robust control design for nonlinear MFSJD system could be accomplished, simultaneously; and second, a novel LMI-constrained MOEA named fronts-squeezing LMI-constrained MOEA is proposed to efficiently solve the MOP. Once the Pareto front is obtained, the designers can select a fuzzy controller from the Pareto optimal solution set according to their preference.

Consider the following nonlinear MFSJD system driven by Wiener processes and the marked Poisson processes  $\{N_p(t, \theta_i)\}_{i=1}^m$ :

$$(1) \begin{aligned} dx_t &= [f(x_t, Ex_t) + \eta(x_t, Ex_t)u_t + g(x_t)v_t]dt \\ &+ \sum_{i=1}^n \sigma_i(x_t, Ex_t)dW_t^{(i)} + \sum_{i=1}^m T_i(x_t, Ex_t, \theta_i)dN_p(t, \theta_i) \\ x_0 &= x(w, 0) \text{ and } Ex_0 = E\{x(w, 0)\} \end{aligned}$$

Multiobjective  $H_2/H_\infty$  Control problem

$$(2) \min_u (H_2(u), H_\infty(u))$$

$$(3) H_2(u) = E \int_0^\infty x_t^T Q_1 x_t + u_t^T R_1 u_t dt$$

$$(4) H_\infty(u) = \max_v \frac{E \int_0^\infty x_t^T Q_2 x_t + u_t^T R_2 u_t dt}{E \int_0^\infty v_t^T v_t dt}$$

There are three main difficulties about solving the multiobjective  $H_2/H_\infty$  control problem in (2)-(4) for nonlinear MFSJD systems in (1) as follows.

(I) In general, for a multiobjective nonlinear  $H_2/H_\infty$  control design in (2)-(4), we always need to solve Hamilton-Jacobi inequalities (HJIs). However, for the nonlinear MFSJD system, its HJIs are difficult to derive.

(II) Owing to the fact that both the mean term and Poisson jump processes appear in the system dynamical equation, the stability criterion of the nonlinear MFSJD system in (1) needs to be derived.

(III) Multiobjective  $H_2/H_\infty$  control design problems in (2)-(4) are difficult to solve directly and always need to achieve it via multiobjective evolutionary algorithm (MOEA) searching methods. However, the existing linear matrix inequality (LMI) constrained MOEAs always have higher computational load for nonlinear MFSJD system.

For issue (I), we employ Takagi-Sugeno (T-S) fuzzy model to overcome it.

For issue (II), we will propose sufficient conditions for the stability of the nonlinear fuzzy MFSJD systems in the mean square sense by decoupling the MFSJD system into two orthogonal subsystems: the mean subsystem of  $\bar{x}_t = x_t - Ex_t$  and the variation subsystem of  $\bar{v}_t$ . Then, we have the augmented system with system state  $\bar{x}_t = [\bar{x}_t^T, Ex_t^T]^T$ .

“We proposed the fronts-squeezing LMI-constrained MOEA to narrow the search region down from two sides of feasible and infeasible region.”



Prof. Bor-Sen Chen and his student Dr. Cheng-Wei Li.

### Research Highlights

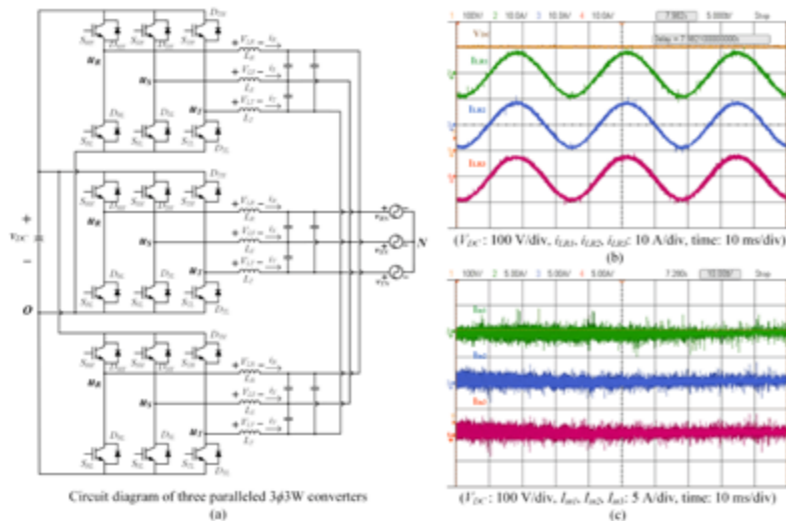
- IEEE Life Fellow
- Ministry of Education's Regulations Governing the Establishment of the National Professorship
- IEEE Taipei Section "Best Impact Award"

### Research Output

- C. Lin, and B. S. Chen, "Achieving Pareto Optimal Power Tracking Control for Interference Limited Wireless Systems via Multi-Objective  $H_2/H_\infty$  Optimization". IEEE Transactions on Wireless Communications 12(12): 6154-6165, 2013.
- B. S. Chen, H. C. Lee, and C. F. Wu "Pareto Optimal Filter Design for Nonlinear Stochastic Fuzzy Systems via Multiobjective  $H_2/H_\infty$  Optimization", IEEE Trans Fuzzy system, Vol. 23, No. 2, pp. 387-399, 2015.
- C. F. Wu, B. S. Chen and W. Zhang, "Multiobjective  $H_2/H_\infty$  Control Design of Nonlinear Mean-field stochastic jump-diffusion systems via fuzzy approach." IEEE Trans. Fuzzy Systems, Vol.27(4), pp.686-700, APR 2019

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## SPWM-Based Direct Digital Control With Average-Voltage Model and D-Σ Process for Paralleled 3Φ3W Grid-Connected Converters to Reduce Circulating Currents



(a) Circuit diagram of three paralleled 3Φ3W converters  
(b) Uniform current distribution  
(c) No circulating current

In this paper, using the D-Σ process to derive control laws directly is extended to parallel operation of multi-converters. Based on sinusoidal PWM (SPWM) and with the direct digital control, each phase of a converter module can track its sinusoidal reference current individually, eliminating circulating currents significantly. Moreover, a third harmonic injection is introduced to the duty-ratio control law to increase dc-bus voltage utilization around 16%.

For a PWM converter, one switching cycle is divided into several time intervals and each time interval is corresponding to a switching-state

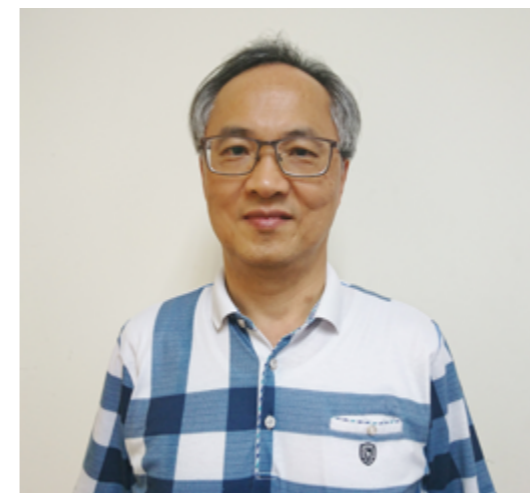
voltage. The average switching-state voltage over one switching cycle is equal to the sum of all products of duty ratios and switching-state voltages, which can help derive state equations and obtain a converter plant.

A direct digital controller with the D-Σ process is then developed to cover the variation effects of system parameters in the plant, which is equivalent to schedule loop gain cycle by cycle.

With switching-state voltage average and common-mode voltage average over one switching cycle, a 3Φ3W converter can be

modeled as a single-phase one. Since all of the switching-state meshes are connected to the average voltage, each 3Φ3W converter can be decomposed into three individual single-phase converters, simplifying the current tracking of a 3Φ3W converter. Additionally, since we can control the converter to track phase-current commands precisely, there will be no circulating current among multiple converters connected in parallel. This is the major merit of the proposed control approach.

Unlike conventional approaches, this paper presents a simple but accurate current tracking method to deal with multiple 3Φ3W converters operated in parallel. It has the following features: (1) without abc-αβ and αβ-dq frame transformations, (2) no need of complicated multiple-loop control, (3) achieving wide bandwidth, (4) covering wide filter inductance variation to allow using smaller cores, (5) accommodating grid-voltage distortion and imbalance, and (6) easy to achieve high-frequency operation, increasing converter power density.



Professor Tsai-Fu Wu

“*a third harmonic injection is introduced to the duty-ratio control law to increase dc-bus voltage utilization around 16%.*”

### Research Output

- Tsai-Fu Wu, Po-Hung Li, Li-Chiun Lin, Chih-Hao Chang, and Yu-Kai Chen, “Circulating Current Reduction for Three-Phase Back-to-Back Transformerless Inverter with SPWM Based D-Σ Digital Control,” IEEE Trans. on Power Electronics, vol. 32, No. 2, pp. 1591-1601, Feb. 2017.
- Tsai-Fu Wu, Mitradatta Misra, Li-Chiun Lin and Yen-Hsiang Huang, “Direct Digital Control of Single-Phase Grid-Connected Inverter with LCL Filter Based on Inductance Estimation Model,” IEEE Trans. on Power Electronics, vol. 34, no. 2, pp. 1851-1862, Feb. 2019
- THREE-PHASE INVERTING APPARATUS AND CONTROL METHOD AND PARALLELED POWER CONVERSION SYSTEM THEREOF, 美國專利號 US 9,680,397,B2。
- 三相換流裝置及其控制方法與並聯式電源轉換系統, 中華民國專利號 I578687。



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## Eye-in-hand Adaptive Gripper for Object Recognition and Tracking



In future industrial applications, being able to hand and grasp objects of any shape precisely and reliably are essential in smart manufacturing operations. Nowadays, a method that grasp objects with a customized fixture installed on a gripper has been widely used in general applications. This method can provide a stable and accurate grasping, but it would sacrifice the compliance of various objects. In this research, we provide a new solution to grasp objects of almost any shape with a single gripper. Comparing with traditional one, the gripper in this research could be dexterous enough to imitate the characteristics of a human hand. There are three major technologies in this research, which includes the structure of intelligent adaptive gripper, the embedded visual recognition module and the integrated visual guiding system.

The mechanism of gripper is featured with its adaptive structure. It is capable of extremely high adaptation by using series of four-bar linkages.

Each linkage can be assumed to be rigid and be able to transmit a strong gripping force when grasps an object. With the well design of the four-bar linkage in series, adaptation and compliance can be achieved. Through analytical modelling and mechatronics integration, the fingers of this NTHU adaptive gripper not only offer compliance and adaptation performance similar to human finger, they also provide satisfactory engineering performance in terms of receptivity and reliability.

In addition to the adaptive actuation, the visual system of this research is also a key technology for industrial upgrades. In Industry 4.0 applications, being adaptive to various products in the same product line is an important ability for a company. Most companies have encountered a barrier when upgrade their factories because the lack of a suitable visual system. A computer vision system could be classified into three techniques, which are Eye-to-Hand, Eye-on-Hand, and Eye-

in-Hand separately. In general, Eye-to-Hand and Eye-on-Hand visual system are more frequently used in a smart factory. However, this image source would be blocked by obstacles sometimes, and the coordinate conversion between the visual coordinates and the end effector is often accompanied by many uncontrollable errors. In this research, the gripper has been integrated with Eye-in-Hand visual system, which provides proper information with the profile and the attitude of the target object. It can not only increase the accuracy of sensors but also strengthen the performance of the gripper.

Finally, the integrated visual guiding system in this research can provide an easier way to process the image or the 3D-model data. The embedded system can make a pre-process for the object' s profile information collected by the gripper, and provide the object' s precise position or orientation data to the controller of a manipulator. With this data, the manipulator could track the target automatically without any other computer. Moreover, it would significantly reduce the cost of a smart factory.

“ It can not only increase the accuracy of sensors but also strengthen the performance of the gripper. ”

### Research Highlights

- 2018 IEEE ICSSE Best Student Paper Award
- 2019 ASME ISPS Conference Scholarships
- 2019 MOST Futuretech Breakthrough Award.
- 2019 Patent Pending

### Research Output

- Cheng, Li-Wei Alex, and Jen-Yuan James Chang. "Design of a Multiple Degrees of Freedom Robotic Gripper for Adaptive Compliant Actuation." 2018 International Conference on System Science and Engineering (ICSSE). IEEE, 2018.
- Shih-Wei Liu, and Jen-Yuan James Chang. "EYE-IN-HAND ROBOTIC GRIPPER VISION FUSION FOR OBJECT RECOGNITION AND TRACKING" ASME 2019 Conference on Information Storage and Processing Systems (ISPS). ASME, 2019.



(from right) Professor J.-Y. Chang, S.-W. Liu and L.-W. Cheng.



## ***Biomedical Technology***

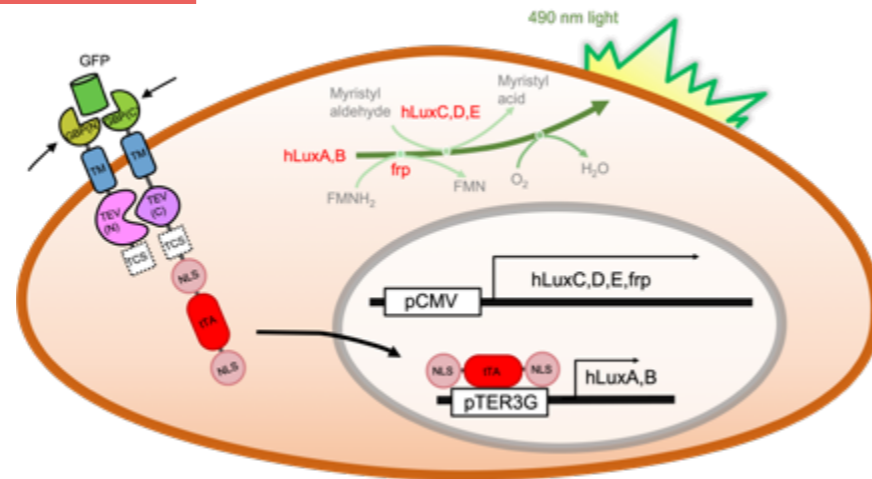
- *BioWatcher : Establishing A Customized Reporter Cell System for Biomarker Diagnosis*
- *Fluorescence-based Nano-oxygen Particles for Spatiometric Monitoring of Cell Physiological Conditions*
- *Enhancing Boron Uptake in Brain Glioma by Boron-Polymer / Microbubble Complex with Focused Ultrasound*



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ycl@life.nthu.edu.tw

## BioWatcher : Establishing A Customized Reporter Cell System for Biomarker Diagnosis

2018 NTHU iGEM team  
in Giant Jamboree



People around the world are growing awareness of their health condition. To monitor the health condition, a wide range of biomarkers-- special substances in the bloodstream representing the physiological and pathological states-- has been used in clinical diagnoses. Blood test is one of the most common way used to detect biomarkers but it suffers from several inevitable drawbacks such as invasiveness, time-consuming procedure, demand for medical staff service, non-real-time tracking and so on. These disadvantages may discourage people from periodic medical checkup. To address this long-standing worldwide issue, we proposed Biowatcher, engineered reporter cells that enable detection and autonomous report of soluble biomarkers in bloodstream. The sensing parts of the reporter cells are powered by nanobodies, single-domain antibodies that can be engineered to detect different biomarkers. Binding of biomarkers on nanobodies triggers the release of transcriptional activator, which activates

the expression of lux gene, as a result, induces bioluminescent emission as a readout for devices to detect. To prove the concept of Biowatcher, a well-studied nanobody, GFP binding protein (GBP), and its antigen, GFP (Green fluorescence protein), were used in our experiments. Simulating the binding of biomarkers to nanobodies, GFP was incubated with reporter cells expressing split GBP nanobodies. GFP acts as a dimerizer to bridge the association of split GBP nanobodies. Dimerization of split GBP conformationally activates TEV protease complex which cleavages the TCS (TEV cutting site) and subsequently releases a transcriptional activator, tTA. Owing to the fusion with NLS (Nuclear localization sequence), soluble tTA translocates into nucleus and triggers the expression of luciferase A/B complex in an inducible manner. Together with the luciferase substrates producing by hLuxC, D, E, and frp, reporter cells will send bioluminescent output signal to Biowatch.

Cells expressing the components of this programmable signaling pathway were incubated with different concentration of GFP. The results showed that the number of cells responding to the stimuli increases as the stimuli, GFP, increases, suggesting that stimuli trigger this programmable signaling pathway in a dose-dependent manner. Moreover, GFP treatment can significantly activate our programmable signaling within 6 hours post-incubation indicating the rapid response of our system to extracellular soluble stimuli. With this developed system, we also successfully used GFP to induce engineered cells to emit bioluminescence signal which can serve as an output for non-invasive diagnosis.

To our knowledge, this is the first programmable system capable of receiving the input, stimulation from extracellular space (soluble biomarkers), and triggering autonomous bioluminescent output for non-invasive real-time detection. Such autonomous reporting system can have great varieties of application collaborating with wearable devices, watch, for example. With required software, the wearable devices can noninvasively track the level of biomarkers as real-time diagnosis.

### Research Highlights

- 2018 International Genetically Engineered Machine Competition (iGEM) Gold Medal
- Nominated for the Best Presentation (iGEM)
- Nominated for the Best Diagnostic Project (iGEM)

“ Engineering cells to realtime track specific biomarkers. ”

### Research Output

- Hsuan Cheng, Yi-Chien Chuang, Hong-Rui Lin, Chin-Lin Kao, Yu-Hsun Chen, Shi-Rong Hong, Ya-Chu Chang, Hui-Chun Cheng, Chieh-Cheng Huang, Lee-Wei Yang, Yu-Chun Lin. Programmable Input-N-Output Signaling (PINOS) triggering by extracellular soluble molecules (Manuscript in preparation)
- U.S. Patent. User-oriented programmable cell signaling pathways triggering by extracellular soluble molecules (Pending)



(from left, 1st row)  
Liang-Yu Ko , Professor Yu-Chun Lin,  
Chin-Lin Kao.

(from left, 2nd row)  
Yu-Chi Chang, Chia-Jo Chen, Hsuan Cheng,  
Yi-Chien Chuang, Shu-Mei Chi, Chi-Hsuan Hsu.

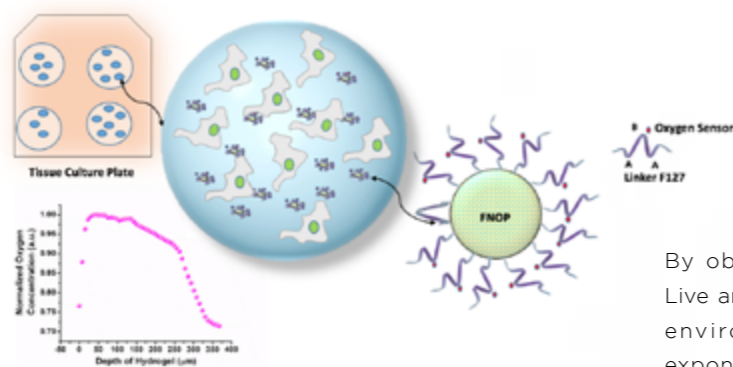
(from left, 3rd row)  
Guan-Xian Chen, Hsin-Ying Wen, Li-Chi Chen,  
Bo-Ruei Huang.





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## Fluorescence-based Nano-oxygen Particles for Spatiometric Monitoring of Cell Physiological Conditions



Culturing cells in encapsulated hydrogel blended with Functional Nano oxygen sensors for measuring oxygen in 3Dimensional alginate hydrogel environment

By observing temporal progression and Live and Dead Cell imaging in the hydrogel environment of insulin cells, exhibits exponential decay in cellular density with time and we found that the CaCl<sub>2</sub> hydrogels showed a viable microenvironment compared to SrCl<sub>2</sub>. By using a mathematical curve-fitting technique, a time constant ( $t_1$ :  $1/e$  of maximum cellular density), the change in the slope of the dissolved oxygen curve for CaCl<sub>2</sub> and SrCl<sub>2</sub> was calculated and is approximately 120 and 45 h, respectively. For SrCl<sub>2</sub> at a time instance, 170 h is approximately 4 time constants ( $4t_1$ :  $1/[e^4]$ ; i.e., 1.83 percent of maximum cellular density) slowly approaching to the maximum DO level that can be attained in the hydrogel (less oxygen consumption by cells). The same phenomenon of the oxygen gradient reversal was observed in the CaCl<sub>2</sub> environment with the approximate time constant of 120 h ( $t_1$ ).

For HeLa cells on the basis of both temporal and spatial oxygen distribution, it was suggested that SrCl<sub>2</sub> provided a more

The development of a functional nanoparticle-based oxygen sensor system that can be used to measure the oxygen concentration in 3D hydrogel tissue cultures using fluorescence microscopy has been demonstrated. RIN-m5F and HeLa cell lines were successfully cultured with FNOPs in calcium and strontium chloride gelation alginate hydrogel environments. In the experiments, the size of the alginate hydrogels generated using an electrospray technique was in the range of 700-1000  $\mu$ m in diameter. The oxygen concentration gradient tested the cellular viability within the calcium- and strontium-based gelation for RIN-m5F and HeLa cells and demonstrated that the two different gelation ions result in a significant difference in oxygen gradient in 3D hydrogel environments and various suitability' s for different cell types.

“ The nano breathing sensor system allows highly temporal and spatial oxygen measurement at cellular level for 3D tissue constructs. ”

suitable environment. The gradient of oxygen with time is approximated with  $8.71 \times (e^{-t/1.93}) + 3.10$  and  $O_2$  SrCl<sub>2</sub> (mg/L) =  $6.36 \times (e^{-t/1.32}) + 2.50$ , which showed a similar exponential decay but differed in the initial level of oxygen concentration with 2.95 mg/L. A confocal image at 84 h of the HeLa cellular hydrogel environment followed the sigmoidal curve in both the hydrogels. The diffusion coefficient of oxygen in HeLa cells incubated in hydrogels was calculated by using the Fick' s law of diffusion equation in considering the rate of time equation and concentration gradient and it was found to be  $1.3 \times 10^{-9}$  m<sup>2</sup>/s, which is in the range of the nominal value inside polymeric hydrogel. In addition to the oxygen tension and size of a hydrogel, the preferential respective cellular behavior in a hydrogel material can be attributed to the factors such as mechanical response and integrin conformational changes within hydrogel environment.

In mimicking the natural environment, the application of these highly temporal and spatial resolved monitoring approaches will greatly enhance the design efficiency in producing suitable 3D microenvironments, particularly in additive manufacturing and for different cellular applications. Which will increase the ease and rapid generation of complex and/or larger hydrogel structures.



(from left) Professor Fan Gang Tseng  
Manohar Prasad Koduri.

### Research Highlights

- This project in conjunction with University of Liverpool, UK team is currently working on Human Mesenchymal stem cells for 3D tissue engineering applications
- This work granted the student (Mr. Manohar Koduri) for Collaboration Challenge Award -Travel Grant and Biogelx™-Discovery kit of worth 2500 Pounds, 3D Bionet, UK
- This work was awarded RSC membership award for the third best presentation (Mr. Manohar Koduri), in RSC Biomaterials Chemistry Annual Conference 2019, University of Liverpool, Liverpool
- This work was awarded Travel Grant of worth 500 USD (for Mr. Manohar Koduri) from Chemical and Biological Microsystems Society in attending The 20th International Conference on Miniaturized Systems for Chemistry and Life Sciences, 9-13 October 2016, Dublin, Ireland

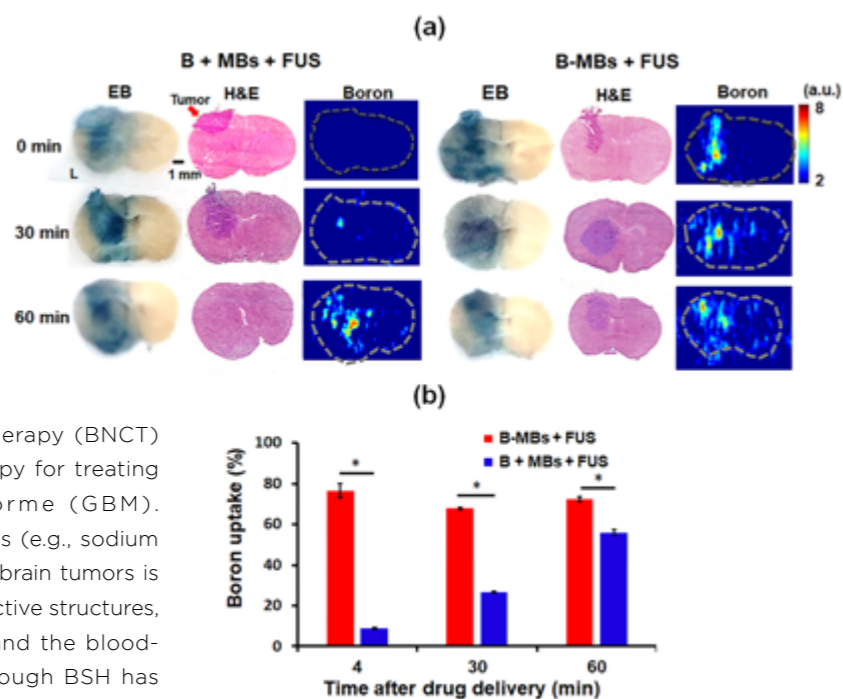
### Research Output

- Koduri, M.P., S. Goudar, V., Shao, Y.W., Hunt, J.A., Henstock, J.R., Curran, J. and Tseng, F.G., 2018. Fluorescence-Based Nano-Oxygen Particles for Spatiometric Monitoring of Cell Physiological Conditions. ACS applied materials & interfaces, 10(36), pp.30163-30171.
- Applied Taiwan patent 108105481
- Applied for US patent 16/441,036



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## Enhancing Boron Uptake in Brain Glioma by Boron-Polymer / Microbubble Complex with Focused Ultrasound



(a) Boron distribution and (b) boron cover rate in the tumor with different drug delivery protocols. (B+MBs+FUS: FUS sonication following administration of the MBs with PEG-b-PMBSH mixture; B-MBs+FUS: FUS sonication following administration of the B-MBs). This data suggested that after receiving the B-MB treatment with FUS, boron was immediately deposited into the tumor and its concentration did not decrease with time. However, in the B+MBs+FUS group, high boron uptake did not occur immediately after FUS treatment and instead gradually increased with time.

Boron neutron capture therapy (BNCT) is a promising radiotherapy for treating glioblastoma multiforme (GBM). However, the penetration of drugs (e.g., sodium borocaptate, BSH) for BNCT into brain tumors is limited by cerebral vesicular protective structures, the blood-brain barrier (BBB), and the blood-brain tumor barrier (BTB). Although BSH has been reported to be selectively taken up by tumors, it is rapidly excreted from the body and cannot achieve high tumor-to-normal brain ratio (T/N ratio) and tumor-to-blood ratio (T/B ratio). Despite the development of large-molecular-weight boron compounds, such as polymers and nanoparticles, to enhance permeation and retention effect, their effects remain insufficient for clinical use. To improve the efficiency of boron delivery to the tumor site, we propose combinations of self-assembled boron-containing

polyanion (PEG-b-PMBSH) nanoparticles ( $295 \pm 2.3$  nm in aqueous media) coupled with cationic microbubbles (B-MBs) assisted focused ultrasound (FUS) treatment. Upon FUS sonication (frequency = 1 MHz, pressure = 0.3–0.7 MPa, duty cycle = 0.5%, sonication = 1 min), B-MBs can simultaneously achieved safe BTB-opening and boron drug delivery into tumor tissue. Compared with the MBs of the PEG-b-PMBSH mixture group (B+MBs), B-MBs showed 3- and 2.3-fold improvements in the T/N ( $4.4 \pm 1.4$  vs  $1.3 \pm 0.1$ ) and T/B ratios ( $1.4 \pm 0.6$  vs  $0.1 \pm 0.1$ ) after 4 min of FUS sonication. The spatial distribution of PEG-b-PMBSH was also improved by the complex of PEG-b-PMBSH with MBs. The findings presented herein, in combination with the expanding clinical application of FUS, may provide improvements in BNCT and treatment of GBM.

### Research Output

- C. H. Fan, T. W. Wang, Y. K. Hsieh, C. F. Wang, Z. Gao, A. Kim, Y. Nagasaki, and C. K. Yeh\*, ACS Applied Materials & Interfaces, vol. 11, no. 12, pp. 11144-11156, 2019.



(from left)  
Professor Chih-Kuang Yeh  
Dr. Ching-Hsiang Fan.

“ This study provides a novel approach for delivering boron drugs to brain tumors for boron neutron capture therapy. ”



## ***Material Science***

- *Take a "Spin" onto the Next Generation MRAM*
- *Platinum-trimer Decorated Cobalt-palladium Core-shell Nanocatalyst with Promising Performance for Oxygen Reduction Reaction*
- *Generalizing the Effects of Chirality on Block Copolymer Assembly*

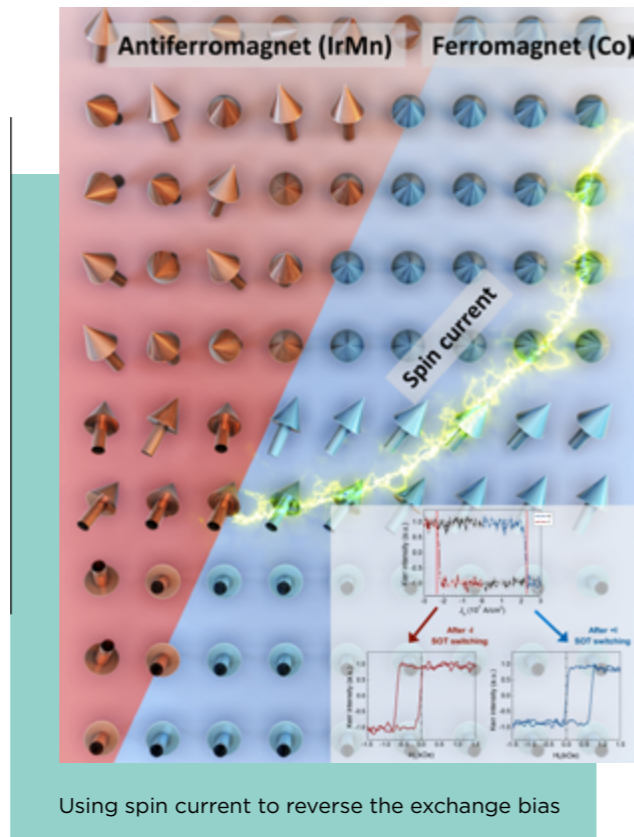


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## Take a "Spin" onto the Next Generation MRAM

Magneto-resistive random access memory (MRAM) is the forerunning candidate for the next generation digital technology. However, manipulating MRAM efficiently and effectively has been challenging. A revolutionary breakthrough was recently achieved by an interdisciplinary research team based at National Tsing Hua University (NTHU) in Taiwan, led by Prof. Chih-Huang Lai and Prof. Hsiu-Hau Lin. By adding a layer of platinum, only a few nanometers thick, it generates spin current to switch the pinned magnetic moments at will - a task that has never been accomplished before.

From mobile phones to computers, wearable devices, the Internet of Things, and smart city operations, data processing and storage are essential. To allow faster reading and writing, less power consumption and retaining data through a power outage, MRAM stands out in the keen competitions. Prof. Lai and Lin's breakthrough, published in Nature Materials recently, adds wings to MRAM technology and attracts attentions from both industry and academy.



### Steering spin currents in MRAM

At present, information processing in digital devices is mainly carried out using dynamic random access memory (DRAM), but it consumes significant power and faces serious hurdles when reduced in size. DRAM utilizes the charges of electrons. However, electrons have both charge and spin; therefore, Prof. Lai and Lin's team works with electron spins to manipulate MRAM.

The key structure in MRAM is like a sandwich. The upper layer consists of a freely flipping magnet, in charge of data computation, while the bottom layer consists of a fixed magnet, responsible for data storage; and these two layers are separated by an oxide layer. The challenge is to switch these layers of different natures by electrical means. After a long series of experiments, they found the key ingredient: a nanometer layer of platinum.

Due to spin-orbit interactions, the electric current drives the collective motion of electron spins first. The spin current then switches the pinned magnetic moment effectively and precisely.

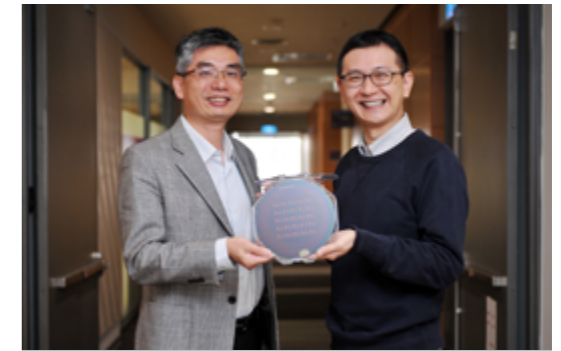
### Spintronics blazing hot

In recent years, NTHU has been promoting cross-disciplinary cooperation, such as the MRAM research conducted by the physicist Lin and the materials expert Lai, who have learned to work together seamlessly.

Major international companies all participate in the competition of MRAM development, including Samsung, Intel, and TSMC. The mass production of high-density MRAM begins this year, a development where the research team led by Prof. Lai and Lin has played a key role.

The research team is currently extending their groundbreaking discovery to other structures, and their ongoing findings are expected to have major impacts on the development of memory industry. In Prof. Lai's view, the development of MRAM technology is going to have a decisive influence on the future competitiveness of Taiwan's semiconductor industry.

“ *This implies that the FM magnetization and EB can be manipulated independently.* ”



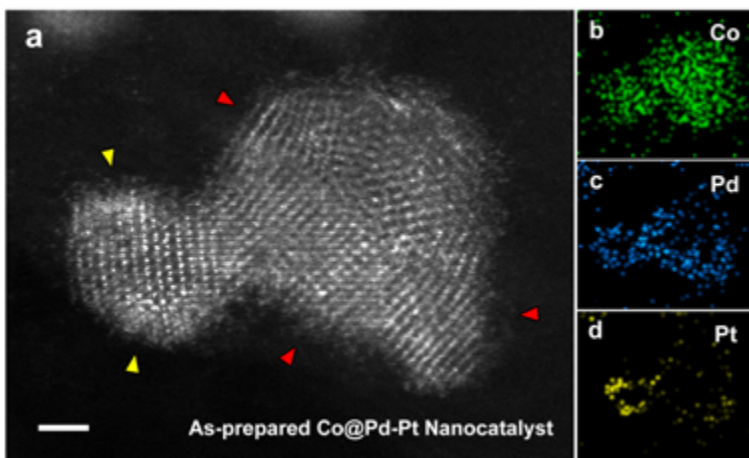
(from left)  
Professor Chih-Huang Lai  
Professor Hsiu-Hau Lin

### Research Highlights

- IEEE Fellow
- TECO Award (東元獎)
- HOU JIN-DUI Outstanding Honorary Award (侯金堆傑出榮譽獎)

### Research Output

- Manipulating exchange bias by spin-orbit torque, P.K. Lin, B. Y. Yang, M. H. Tsai, H. H. Lin, C.H. Lai, Nat. Mater. 18, 335, (2019)
- Initialization-Free Multilevel States Driven by Spin-Orbit Torque Switching K.F. Huang, D. S. Wang, M. H. Tsai., H. H. Lin, and C. H. Lai, Adv. Mater. 29, 1601575 (2017)



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## Platinum-trimer Decorated Cobalt-Palladium Core-shell Nanocatalyst with Promising Performance for Oxygen Reduction Reaction

Scanning transmission electron microscopy (STEM) of Pt-decorated Co-Pd. a Atomic-scale high angle annular dark field-STEM (HAADF-STEM) image of as-prepared Pt-decorated Co-Pd (Co@Pd-Pt) nanocatalyst. Yellow and red arrows indicate the decorated Pt species and the unconformable Pd shell regions, respectively. Scale bar: 1 nm. b-d EDS elemental maps of the Co@Pd-Pt nanocatalyst in a. reprinted from Sheng Dai and Chen T.-Y. et al. in "Platinum-trimer decorated cobalt-palladium core-shell nanocatalyst with promising performance for oxygen reduction reaction" Nature Communications | (2019) 10:440

Scientists have long been struggling to develop high-performance fuel cells as environmentally friendly power in electric vehicles. However, Prof. Chen Tsan-Yao of the Department of Engineering and System Science (National Tsing Hua University, Taiwan), has recently made a major breakthrough by using ultrasonic waves to make tiny grooves in the surface of various materials, which in conjunction with an atomic-scale platinum catalyst and can be used to double the alkaline fuel cells (AFCs) efficiency.

This atomic-scale catalyst increases the oxygen reduction (cathode reaction) current intensity by tenfold, with no degradation for eight months of continuous operation, while reducing the production cost by 90 percent; such cells have a lifespan of two or three years. This ground breaking research has been published and selected as focus paper of Energy Materials in the February issue of Nature Communications.

Exploring the atomic scale boundary

A fuel cell is a power generation device to convert chemical energy into electrical energy. AFC is safer and more efficient than acid batteries, and thus are widely used in spacecraft and satellites. Catalyst is the key component in fuel cell performance. Prof. Chen said that there are many factors affecting the efficiency of the catalyst, especially size. At the same volume, the smaller the catalyst particles, the larger the surface area, and the higher the performance. However, if the particles are too small, they become unstable and rapidly loss their efficiency. Thus Chen's challenge was to reduce the size to atomic scale and increase the stability.

Inspired from the love of coffee soda

Chen said that the coffee soda inspires him the strategies. At 2016, while chatting with the coffee shop owner, he discovered that depending on the order in which the coffee and soda are poured into the glass, the sweetness, taste, and amount of bubbles are very different. As a result, he had his research assistants reverse the order in crystal growth. Unlike traditional method, they add new materials every ten seconds and stop the reaction in only seconds which resulting in the Pt trimer catalysts.

“ They localize electrons from neighbouring atoms and boost activity of Co-Pd NP in ORR. ”

The dream of quantum-size-correlation to further reducing cost, increasing efficiency, and extending lifespan

Not surprisingly, Chen's students initially had some doubts about his unorthodox approach. With hundreds of failures, they finally made the Pt trimer catalysts which remained stable while maintaining high activity in AFCs. Chen said that the amount of platinum used in his atomic catalyst is only 1%, compared to 35% for the average commercial catalyst; and the mass current density is increased by 30 times. Prof. Chen said that he is currently developing a quantum-size-correlation in catalyst for making cells even cheaper and more efficient.



(from left)  
Wei-Hao Hsiung, Han-Ting Lin,  
Professor Tsan-Yao Chen, Che-Yen, Yu-Je Ciou

### Research Highlights

- Featured article in energy materials in Nature Communications in 2019.02 chosen by Associated Editor Prof. Jacilynn Brant

### Research Output

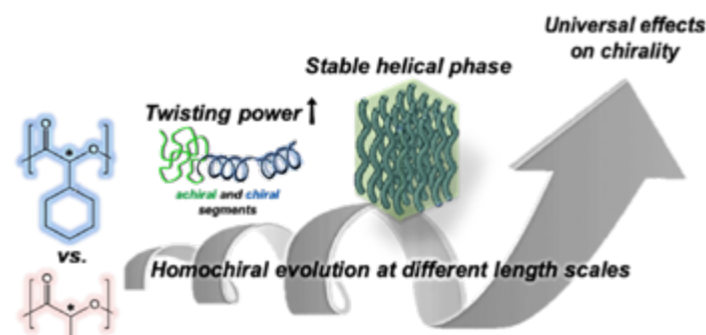
- Sheng Dai, Jyh-Pin Chou, Kuan-Wen Wang, Yang-Yang Hsu, Alice Hu, Xiaoqing Pan and Tsan-Yao Chen\* in Nature Communications 2019, 10, 440
- Yu Zhuang, Jyh-Pin Chou, Pang-Yu Liu, Tsan-Yao Chen, Ji-jung Kai, Alice Hu\* and Hsin-Yi Tiffany Chen\* Journal of Materials Chemistry A, 2018, 6, 23326 - 23335
- Yu Zhuang, Jyh-Pin Chou, Hsin-Yi Tiffany Chen, Yang-Yang Hsu, Chih-Wei Hu, Alice Hu\* and Tsan-Yao Chen\* Sustainable Energy Fuels 2018, 2, 946 - 957.



## Generalizing the Effects of Chirality on Block Copolymer Assembly

Professor Rong-Ming Ho  
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The homochiral evolution from monomeric, to conformational, and to mesodomain chirality was evidenced by probes of chiral structure in self-assembled PBnMA-PCG BCPs\* across multiple length scales. Higher rotational strength of chiral PCG chain as compared to chiral PLA chain was evidenced by the ECD g-factor at C=O absorption region, which is consistent with the observation of a thermodynamically stable helical phase (H\*). Indeed, oSCF studies of chiral diblock melts suggest that stronger inter-chain chirality enhances the stability of mesochiral H\*. Also, VCD spectra of chiral PCG in C-O-C absorption region point to the existence of inter-chain skew in the BCP\* morphology. Taken together, we postulate that the bulkier chiral side group of PCG may give rise to a more persistent helical bias, which in turn enhances the chiral anisotropy of inter-chain chiral interactions that favor the formation of self-assembled mesochiral morphologies.



Block copolymers comprising chiral entities, denoted as chiral block copolymers (BCP\*s), were designed to fabricate helical architectures from self-assembly. A helical phase (denoted H\* to distinguish its P622 symmetry) from that of the normal hexagonally packed cylinder phase was discovered in the self-assembly of polystyrene-b-poly(L-lactide) (PS-PLLA) BCPs\*. The phase behavior of the BCPs\* was systematically examined. Also, the mechanisms of chiral transfer at various length scales in the self-assembly of enantiomeric chiral block copolymers (BCPs\*) were studied. The evolution of homochirality from molecular chirality into hierarchical chirality in the self-assembly of the BCPs\* was found. Generalization of the chirality effects on the self-assembly of block copolymers was established recently. The operation of the self-assembly of the BCP\* may provide insights into morphological evolution from the molecular level via homochiral evolution, and give the appealing applications such as chiral metamaterials. As a result, methodologies for the understanding of the mechanisms of the chirality transfer at different length scales in the self-assembly of chiral homopolymers and block copolymers were proposed to provide the approaches to give supplementary information for disclosing the mysteries of the homochiral evolution from molecular level to hierarchical superstructures.

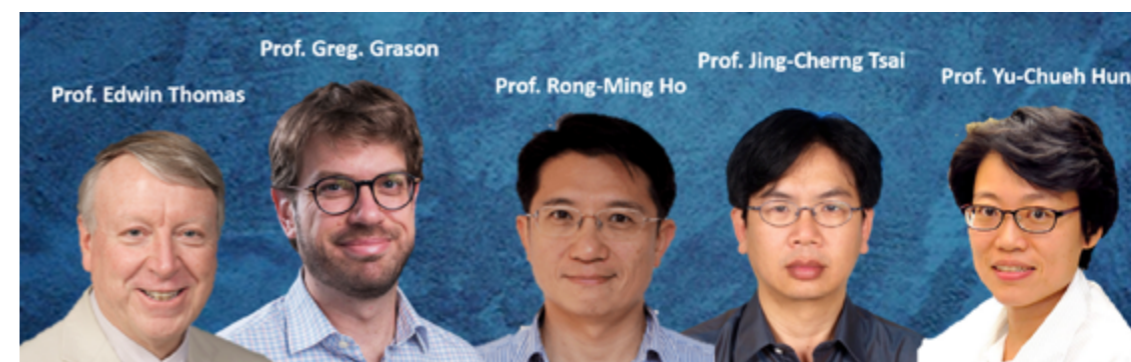
“The evolution of homochirality from molecular chirality into hierarchical chirality in the self-assembly of the BCPs\* was found.”

### Research Highlights

- 2015-2018 Ministry of Science and Technology National Project: Nanonetworks from Templating of Chiral Copolymers for Optical and Environmental Applications.
- 2015-2018 U.S. Department of Energy, Office of Science, Office of Basic Energy Sciences: Development and Application Mesogeometric Analysis and SCF Simulation of Triblock Assemblies.
- 2018-2021 Taiwan/USAF Program: From Molecular to Hierarchical Chirality for Chiroptics.

### Research Output

- Wang, H.-F.; Yang, K.-C.; Hsu, W.-C.; Lee, J.-Y.; Hsu, J.-T.; Grason, G. M.; Thomas, E. L.; Tsai, J.-C.; Ho, R.-M., Generalizing the effects of chirality on block copolymer assembly. *Proceedings of the National Academy of Sciences* 2019, 116, 4080.
- Wen, T.; Wang, H.-F.; Li, M.-C.; Ho, R.-M., Homochiral Evolution in Self-Assembled Chiral Polymers and Block Copolymers. *Accounts of Chemical Research* 2017, 50, 1011.
- Feng, X.; Burke, C. J.; Zhuo, M.; Guo, H.; Yang, K.; Reddy, A.; Prasad, I.; Ho, R.-M.; Avgeropoulos, A.; Grason, G. M.; Thomas, E. L., Seeing the Mesoatomic Distortions in Soft Matter Crystals. *Nature*, 2019, 575, 175.



(from left)  
Prof. Edwin Thomas, Prof. Greg. Grason, Prof. Rong Ming Ho,  
Prof. Jing-Cherng Tsai, and Prof. Yu-Chueh Hung



## ***Humanities and Social Science***

- 
- *Archaeological Investigations in Heping Dao, Keelung, Taiwan*
  - *What Leads to Prosocial Behaviors on Social Networking Services : A Tripartite Model*



Professor. Cheng-hwa Tsang  
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## Archaeological Investigations in Heping Dao, Keelung, Taiwan



Archaeological excavation at the Heping Dao B site, Keelung.

Archaeological work has been carried out in Heping Dao (Heping Island), Keelung, northern Taiwan since 2011. The site has revealed a rich archaeological record spanning a long-term sequence that comprehends most of the history of Taiwan.

The study of this long-term sequence of habitation in Heping Dao throughout prehistory to current times, allows us to attempt a historical archaeology of the longue duree of the place that in turn enables the establishment of comparisons between periods and raising of specific questions, among them: the general understanding of cultural transformation along the Neolithic and the Iron Age, and in turn the transition Iron Age/Aboriginal historic times in Taiwan, which in our view has to be observed as a history of continuity rather than of interruptions; the recognition of the Chinese presence in Taiwan in the pre-European period; the implantation of the European colony and its effects on the local populations; the differing material remains and impacts caused by the presence of pre-European Chinese and the Qing occupation; and the potential for a comparison between the European and the Japanese colonial projects as seen in the material record.



Professor Cheng-hwa Tsang (center of the second row) and his Taiwan-Spain binational team of archaeology

“ *The potential for a comparison between the European and the Japanese colonial projects as seen in the material record.* ”

### Research Highlights

- Stone foundations, which were uncovered from the Heping Dao site, have been proved to be the ruins of a 17th century Spanish church. These ruins are the most concrete material evidence of the Spanish colony so far found in Taiwan.

### Research Output

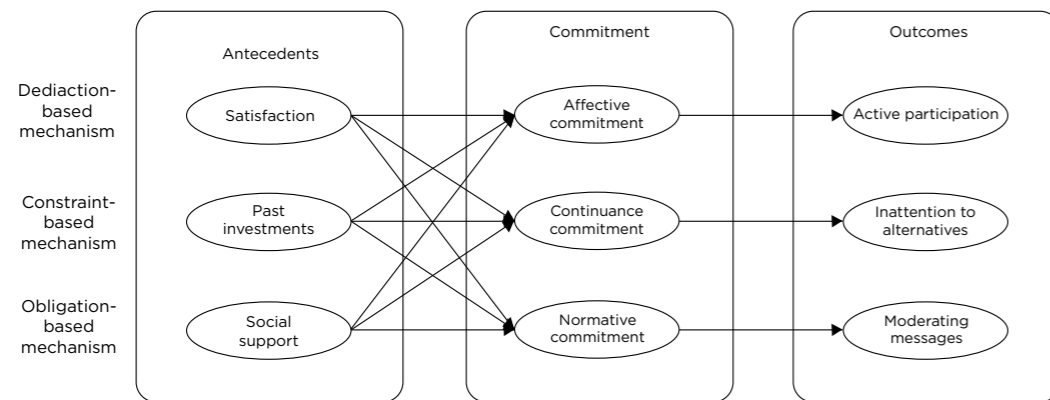
- Berrocal, María Cruz and Cheng-Hwa Tsang, eds, *Historical Archaeology of Early Modern Colonialism in Asia-pacific: The Asia-pacific Region*. University of Florida Press, 2017.
- María Cruz Berrocal, Cheng-hwa Tsang, et., *Comprised Archaeological History of Taiwan through the Long-Term Record of Heping Dao, Keelung*, *International Journal of Historical Archaeology*, 2018.





## What Leads to Prosocial Behaviors on Social Networking Services : A Tripartite Model

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Control variables: age, gender, SNS experience, number of SNS friends, and adiction

The objective of this study was to propose and empirically test a model of postadoption phenomena in the context of SNS. This model is specifically intended to show the underlying mechanisms of SNS members' behaviors that are managerially relevant and critical, namely, active participation, inattention to alternatives, and moderating messages. Consistent with previous efforts, our model posits that the dedication- and constraint-based mechanisms regulate online members' behaviors at the postadoption stage. Furthermore, we extended prior studies by adding the obligation-based mechanism so as to take into account the social aspect of online behavior in the context of SNS. In the tripartite model we propose, three types of commitment serve as mediating variables. In particular, affective commitment, continuance commitment, and normative commitment are expected to play central roles in, respectively, the dedication-, constraint-, and obligation-based mechanisms.

Our tripartite model proposes that each mechanism generally differs in its relationships between intervening variables (i.e., affective commitment, continuance commitment, and normative commitment) and behavioral outcomes (i.e., active participation, inattention to alternatives, and moderating messages). Accordingly, within this framework, intramechanism relationships between commitment and outcomes are shown

to be stronger than those of intermechanism relationships. However, the tripartite model posits that because of specific SNS characteristics, the complexity of the effects of the antecedents (i.e., satisfaction, past investments, and social support) on commitment exceed what the mechanisms imply. As a result, each antecedent is shown to have both intramechanism and intermechanism effects on commitment. Overall, we hope to demonstrate the applicability of the dual and commitment models to the context of SNS and, more important, highlight the enormous research potential in integrating their two distinctive perspectives and research traditions.

“The major challenge for social networking services (SNS) has been getting users to exhibit prosocial behavior by active participation in creating and sharing content.”



Professor Soumya Ray

### Research Highlights

- Distinguished Research Award - 2019 (Ministry of Science and Technology)
- Outstanding Teaching Award - 2019 (National Tsing Hua University)
- Wu Ta-You Award - 2012 (National Science Council)
- New Faculty Research Award - 2012 (National Tsing Hua University)

### Research Output

- Kuem, J., Ray, S., Siponen, M., and Kim, S. S. 2017. "What Leads to Prosocial Behaviors on Social Networking Services: A Tripartite Model." *Journal of Management Information Systems* (34:1), pp. 40-70 (doi: 10.1080/07421222.2017.1296744).
- Ray, S., Kim, S. S., and Morris, J. G. 2012. "Research Note-Online Users' Switching Costs: Their Nature and Formation," *Information Systems Research* (23:1), pp. 197-213 (doi: 10.1287/isre.1100.0340).
- Ray, S., Kim, S. S., and Morris, J. G. 2014. "The Central Role of Engagement in Online Communities," *Information Systems Research* (25:3), pp. 528-546 (doi: 10.1287/isre.2014.0525).
- Ray, S., Ow, T., and Kim, S. S. 2011. "Security Assurance: How Online Service Providers Can Influence Security Control Perceptions and Gain Trust," *Decision Sciences* (42:2), pp. 391-412.
- Shmueli, G., Ray, S., Estrada, J. M. V., and Chatla, S. B. 2016. "The elephant in the room: Predictive performance of PLS models," *Journal of Business Research* (69), Elsevier B.V., pp. 4552-4564 (doi: 10.1016/j.jbusres.2016.03.049).