National Taiwan University and Academia Sinica Joint Program Office

AUGUST 2024

NO. 2 Issue

NEWSLETTER

TOPIC

The NTU/AS Innovative Joint Program has been implemented for several years, and lots of PIs achieved excellent outcomes.

In this Issue, we have 3 articles sharing the recent research results in the field of "**Physics**" and "**Applied Science**".

國立臺灣大學 National Taiwan University

中央研究院 ACADEMIA SINICA

https://jpoas.ntu.edu.tw/
ntujpoas@ntu.edu.tw
R.1301, CCMS & Physics Building, National Taiwan University

Continuous polymerase chain reaction microfluidics integrated with a gold-capped nanoslit sensing chip for Epstein-Barr virus detection

Pei-Kuen Wei[1], Horn-Jiunn Sheen[2,], Yu-Jui Fan[3], Hao-Lun Hung[2], and Wei-Chieh Tseng[2]

A joint research team led by Academia Sinica Professor Wei Pei-Kuen and National Taiwan University Professor Sheen Horn-Jiunn has successfully developed a microfluidic platform that combines DNA replication and detection. This device can amplify gene fragments at the front end and detect them at the back end, reducing the time required for analysis without compromising accuracy or sensitivity.

Epstein-Barr Virus (EBV) is a human herpesvirus associated with various cancers such as nasopharyngeal carcinoma, Burkitt's lymphoma, and Hodgkin's lymphoma. Studies have shown that latent membrane protein 1 (LMP1) is present in most EBV-related malignancies and is considered a prognostic biomarker for these diseases. Therefore, developing a sensitive and efficient method to detect LMP1 DNA fragments is crucial for early cancer diagnosis.

Professor Sheen Horn-Jiunn's team connected the flow channel to the detection chip through the channel design (Figure 1). By utilizing different heating zones corresponding to PCR temperatures, this design allows the sample to be repeatedly heated and cooled between 95°C and 60°C, achieving effective thermal cycling. It also significantly increases the contact area between the PCR solution and the heating source, ensuring more precise temperature control and thereby shortening the PCR reaction time. Additionally, LMP1 DNA probes are modified on the detection chip through electrostatic interactions. By optimizing the modification time and the flow rate in the channel, the detection efficiency is improved.

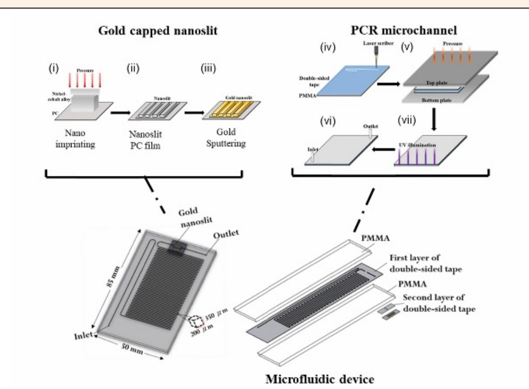


Figure 1. The microfluidic device involves two parts : a polymerase chain reaction (PCR) microchannel and a nanoslit surface plasmon resonance (SPR) chip.

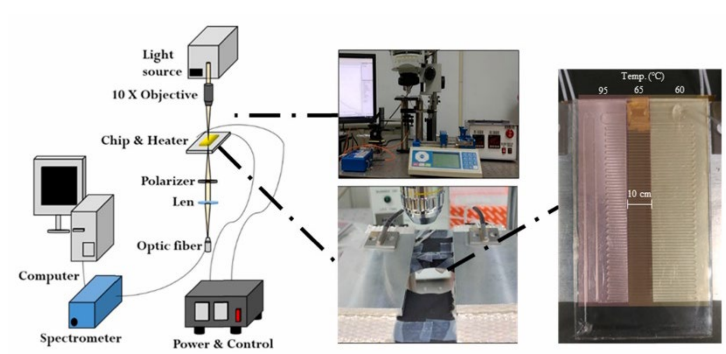


Figure 2. Heating and optical setup for the microfluidic device. Three temperature regions were used in the microfluidic device : 95°C for denaturation, 60°C for annealing/extension, and 65°C for detection.

Professor Wei Pei-Kuen's laboratory fabricated the SPR nanoslit chip using hot-embossing nanoimprinting lithography and integrated it with a transmission resonance spectroscopy optical path design (Figure 2). When broadband white light passes through the nanoslit SPR chip, a polarizer located on the other side of the SPR chip filters out the resonance wavelengths in the transverse magnetic (TM) direction. The transmitted light is collected through a fiber optic lens and then measured and analyzed using a spectrometer.

In the actual tests, four EBV-positive cell lines (NPC43, Akata, P3HR1, and NAMALWA) and one EBV-negative cell line (DB) were used. To demonstrate the device's capability to handle low-concentration samples, actual samples were diluted to 10μg/mL for DNA detection (Figure 3A). The results showed that all EBV-positive cells tested positive, while the EBV-negative cell tested negative. Gel electrophoresis revealed that the fluorescence signal of samples amplified by traditional PCR (initial concentration of 10μg/mL) appeared at the corresponding positions (Figure 3B). This not only indicates that these EBV-positive cells contain LMP1 but also demonstrates that the primers designed in this study successfully replicated LMP1. The intensity of the fluorescent bands also corresponds to the detection results in Figure 3A.

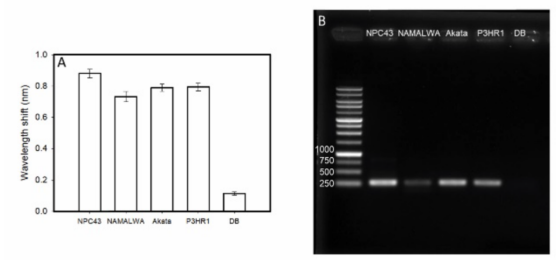


Figure 3. Detection of DNA from real specimens via the microfluidic device. The DNA sequence replicated by the microfluidic PCR was confirmed with (A) the surface plasmon resonance (SPR) chip and (B) gel electrophoresis. The initial DNA concentrations of all specimens are 10 μg/mL (Error bars denote the standard deviation (n = 3).

This device not only reduces the amplification time through microfluidic PCR (to approximately 36 minutes) but also simultaneously transfers the PCR amplification products to the SPR detection chip without sacrificing accuracy or sensitivity. The low-cost manufacturing method makes this device suitable for large-scale production. Moreover, the device can be adjusted to target different DNA sequences. Once the required DNA sequence is determined, the corresponding PCR primers and DNA probes can be prepared and used in the device for further applications.

Han-Yun Hsieh, Ray Chang, Yung-Yu Huang, Po-Han Juan, Hidetoshi Tahara, Kuan-Yi Lee, Ming-Han Tsai, **Pei-Kuen Wei***, **Horn-Jiunn Sheen***, and Yu-Jui Fan*, "Continuous polymerase chain reaction microfluidics integrated with a gold-capped nanoslit sensing chip for Epstein-Barr virus detection." ***Biosensors and Bioelectronics***, Vol. 195, p. 113672, 2022. (SCI IF= 13.39) [citation: 40]

1. Research Center for Applied Sciences, Academia Sinica
2. Institute of Applied Mechanics, National Taiwan University
3. School of Biomedical Engineering, Taipei Medical University

◆Information◆

Click or Scan the QR code to read the original journal article

Principal Investigators

Dr. Horn-Jiunn Sheen, Professor
Institute of Applied Mechanics, NTU
sheenh@ntu.edu.tw

Dr. Pei-Kuen Wei, Director of RCAS / Research Fellow
Research Center for Applied Sciences, AS
pkwei@gate.sinica.edu.tw

Joint Program Title

Development of microscale PCR high-throughput rapid test device by integrating microfluidic and surface plasma resonance chip

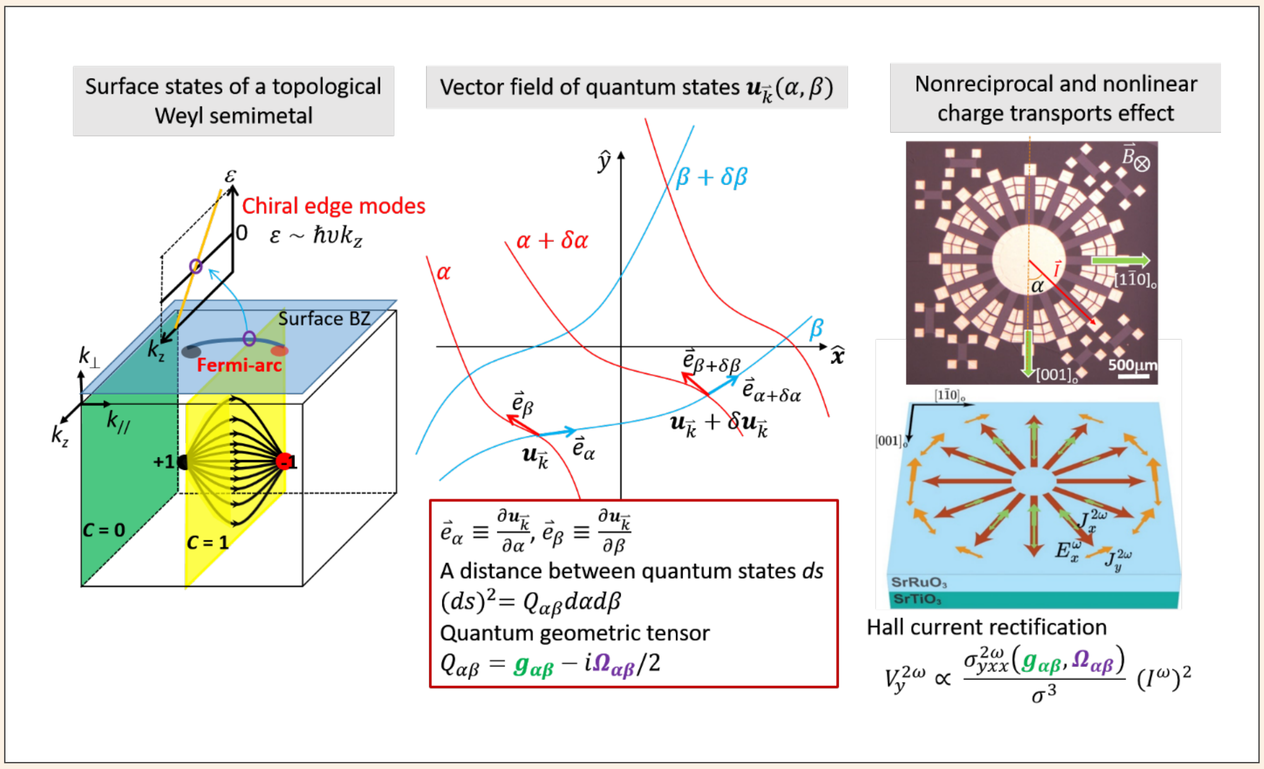
Program Duration

2021.01.01 - 2022.12.31

Revealing topological surface states via nonreciprocal and nonlinear transport effects

Wei-Li Lee[1], and I-Chun Cheng[2]

One of the challenging subjects in topological systems is to identify the charge transport signatures associated with the unusual surface states due to nontrivial bulk band topology. In a topological Weyl semimetal, there exist unique Fermi-arc surface states connecting non-overlapping bulk Weyl-node pair projected on a surface, and the corresponding "vector field" may give rise to nontrivial quantum geometric tensor terms of $Q_{\alpha\beta}=g_{\alpha\beta}-i\Omega_{\alpha\beta}/2$, where $g_{\alpha\beta}$ and $\Omega_{\alpha\beta}$ are the metric tensor and Berry curvature, respectively, associated with quantum electronic states. In latest studies, such quantum geometric quantities may lead to nonreciprocal and nonlinear charge transport effects (NRTE) in a single phase of matter, which thus provides a practical method to determine these quantum geometric quantities from NRTE measurements.



In a recent international collaborating work partly funded by a joint program between Academia Sinica and National Taiwan University, unusually large NRTE in both longitudinal and transverse channels were discovered in epitaxial thin films of topological ferromagnetic Weyl metal $SrRuO_3$ (SRO). These behaviors align with a proposed scenario of an effective Berry curvature dipole originating from Fermi-arc surface states accompanied by 1D chiral edge modes, which is supported by theoretical electronic band structure calculations. Our findings not only highlight the significance of NRTE as a charge transport probe for topological surface states with a broken inversion symmetry but also feature potential applications in nonreciprocal electronics and nonlinear optics using topological materials. The complete data and analyses have been recently published in **Physical Review X 14, 011022 (2024)**.

The SRO thin film growth, device fabrication, and transport measurements were carried out jointly by Dr. Wei-Li Lee's group at IoPAS and Prof. I-Chun Cheng's group at NTU supported by an NTU-AS joint program. The electronic band structure calculations were performed by Prof. Guan-Yu Guo's group at NTU and Prof. Wei-Cheng Lee's group at SUNY Binghamton. The optical SHG measurements were performed by Prof. David Hsieh's group at Caltech. The SRO thin film structural characterizations were performed by Director Chia-Hung Hsu's group at NSRRC.

Uddipta Kar, Elisha Cho-Hao Lu, Akhilesh Kr. Singh, P. V. Sreenivasa Reddy, Youngjoon Han, Xinwei Li, Cheng-Tung Cheng, Song Yang, Chun-Yen Lin, I-Chun Cheng, Chia-Hung Hsu, David Hsieh, Wei-Cheng Lee, Guang-Yu Guo, and Wei-Li Lee, "Nonlinear and Nonreciprocal Transport Effects in Untwinned Thin Films of Ferromagnetic Weyl Metal $SrRuO_3$", ***Physical Review X*** 14, 011022 (2024).

1. Institute of Physics, Academia Sinica
2. Graduate Institute of Photonics and Optoelectronics, National Taiwan University

Information

Click or Scan the QR code to read the original journal article

Principal Investigators

Dr. I-Chun Cheng, Professor
Grad. Institute of Photonics and Optoelectronics, NTU
iccheng@ntu.edu.tw

Dr. Wei-Li Lee, Research Fellow
Institute of Physics, AS
wlee@phys.sinica.edu.tw

Co-Principal Investigator

Dr. Jian-Zhang Chen, Professor
Institute of Applied Mechanics, NTU
jian@iam.ntu.edu.tw

Joint Program Title

Fabrication and characterization of two dimensional electronic devices

Program Duration

2021.01.01 - 2022.12.31

Realizing high-quality interfaces in 2D material spin valves

Ting-Chun Huang[1], Cheng-Tien Chiang[2,1], Chi-Feng Pai[3], Ya-Ping Hsieh[2], and Mario Hofmann[1]

Spintronics is a developing technology that uses the electron's spin and magnetic moment to revolutionize electronic devices. This technology aims to boost future electronics' performance, efficiency, and scalability. A crucial component in spintronic devices is the spin valve, which consists of a nonmagnetic spacer between two ferromagnetic layers. The alignment of these layers in an external magnetic field alters the device's resistance, a phenomenon known as magnetoresistance. A high magnetoresistance ratio enhances the sensitivity and performance of spintronic devices.

Two-dimensional materials like graphene are ideal for nonmagnetic spacers in spin valves due to their thin structure and excellent electronic properties. However, practical implementation faces challenges, primarily in achieving contamination-free and high-quality interfaces with ferromagnetic contacts. Contaminants and imperfections at these interfaces can degrade spin transport properties and reduce device performance.

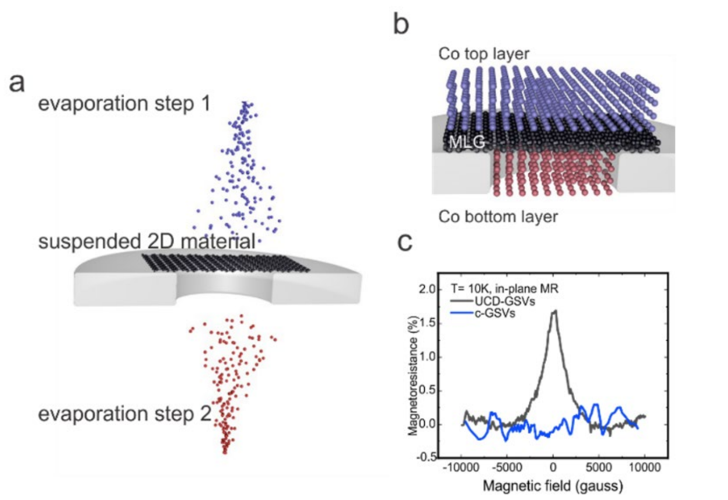


Figure a) the schematic of the UCD method, **b)** the schematic of a multilayer graphene spin valve, and **c)** the magnetoresistance of UCD-GSVs and c-GSVs.

We developed a novel uninterrupted contact deposition (UCD) approach to address interface issues. (Figure a) The UCD method deposits ferromagnetic contacts on both sides of a suspended 2D material in a single vacuum cycle, preventing contamination and oxidation without exposing it to the ambient environment. The UCD approach was demonstrated by depositing Co electrodes on both sides of suspended graphene (UCD-GSVs).

To perform the UCD method, we acquired high-quality graphene, capable of being suspended in micro-sized holes, from Prof. Hsieh. Prof. Hofmann utilized his expertise in microfabrication to produce a novel chip design. Professor Pai assisted in constructing homemade magnetic measurement equipment, and Professor Chiang provided some insights for our magnetotransport analysis.

Our UCD-GSVs showed much better electrical performance compared to c-GSVs (made by the conventional method). When we measured their magnetotransport properties, UCD-GSVs demonstrated clear magnetoresistance, whereas c-GSVs showed none. (Figure c) Additionally, our UCD-GSVs achieved the highest magnetoresistance ratio (~1.7%) reported in similar scientific studies.

These results demonstrate that our UCD method is highly effective in producing ultraclean interfaces and facilitating spin transport in 2D materials-based spin valves. The UCD method was also applied to multilayer graphene spin valves, elucidating the tunneling mechanism due to spin-lattice scattering.

Conclusion

The UCD approach significantly advances high-quality interface fabrication in 2D material spin valves, resulting in enhanced device performance. This method paves the way for more efficient and robust spintronic devices, emphasizing the crucial role of interface quality and offering a universal solution for improving spin transport properties in 2D materials.

Ting-Chun Huang, Wen-Hua Wu, Meng-Ting Wu, Chiashain Chuang, Chi-Feng Pai, Ya-Ping Hsieh and Mario Hofmann , "Realizing High-Quality Interfaces in Two-Dimensional Material Spin Valves", **ACS Materials Letters** 6, 1, 94 (2024) (IF:11.4)

1. Department of Physics, National Taiwan University, Taipei 106, Taiwan
2. Institute of Atomic and Molecular Sciences, Academia Sinica, Taipei 115, Taiwan
3. Department of Materials Science and Engineering, National Taiwan University , Taipei 106, Taiwan

◆ Information ◆

Click or Scan the QR code to read the original journal article

Principal Investigators

Dr. Mario Hofmann, Professor
Department of Physics, NTU
mario@phys.ntu.edu.tw

Dr. Cheng-Tien Chiang, Assistant Research Fellow
Institute of Atomic and Molecular Sciences, AS
ctchiang@pub.iams.sinica.edu.tw

Co-Principal Investigators

Dr. Chi-Feng Pai, Associate Professor
Dept. of Materials Science and Engineering, NTU
cfpai@ntu.edu.tw

Dr. Ya-Ping Hsieh, Associate Research Fellow
Institute of Atomic and Molecular Sciences, AS
yphsieh@gate.sinica.edu.tw

Joint Program Title

Direct probes at the interface between magnetic metals and two-dimensional materials

Program Duration

2023.01.01 - 2024.12.31