2024 醫學應用化學系研討會

主題:醫學應用化學系與生醫工程跨域交流

日　　期:中華民國 113 年 3 月 16 日(星期六)

地　　點:中山醫學大學 正心樓 0211 教室

主辦單位:中山醫學大學 醫學應用化學系

中山醫學大學
2024 醫學應用化學研討會

目 錄

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議 程 表：

時間	主題	主持人
08:30~08:50	**報到**	
08:50~09:00	開幕式　長官致詞	中山醫學大學醫學應用化學系 萬金鳳副教授
09:00~10:00	講　題：生醫微流體的應用 演講者： 陽明交通大學生醫工程研究所 李博仁教授	中山醫學大學醫學應用化學系 朱智謙教授 萬金鳳副教授
10:00~10:20	**茶敘交流時間**	
10:20~11:20	講　題：細胞力學:3D 細胞微球組裝與應用 演講者： 清華大學生醫工程與環境科學系 陳之碩副教授兼系副主任/產學企劃組組長	中山醫學大學醫學應用化學系 朱智謙教授 萬金鳳副教授
11:20~12:00	綜合討論與交流時間	

中山醫學大學
2024 醫學應用化學研討會

生醫微流體的應用

陽明交通大學生醫工程研究所 李博仁教授

Microfluidic Marvels: Innovations Transforming Healthcare

Speaker: Bor-Ran Li

Abstract:

Recent developments in microfluidic applications have revolutionized various fields, including healthcare and biotechnology, by offering precise manipulation of fluids on a microscale. In the context of noninvasive health monitoring, microfluidic platforms play a crucial role in integrating sweat-based sensing technologies. For instance, a wearable hydrogel patch incorporating microfluidic channels enables the rapid sampling of natural perspiration for glucose monitoring. This microfluidic patch facilitates the collection of sweat without the need for external stimulation, ensuring seamless integration into daily routines.

Similarly, microfluidic devices have been instrumental in cancer diagnostics, particularly in isolating cancer cells from bodily fluids. The spiral microfluidic device designed for rapid isolation of cancer cells from pleural effusion demonstrates the potential of microfluidics in enhancing diagnostic accuracy. By efficiently separating cancer cells from background cells, this device aids in obtaining purer samples for downstream analysis, such as flow cytometry.

Furthermore, microfluidic technology has advanced assisted reproductive techniques, specifically in sperm sorting for infertility treatment. The Progressive Sperm Sorting Chip (PSSC) utilizes microfluidic principles to create a gradient flow field, enabling the isolation of high-quality sperm with progressive motility. This microfluidic approach ensures gentle sorting of healthy sperm, leading to improved fertilization rates.

In summary, microfluidic applications seamlessly integrate noninvasive health monitoring, cancer diagnostics, and fertility treatment by providing precise fluid manipulation at a microscale. These advancements highlight the versatility and potential of microfluidics in revolutionizing various aspects of healthcare and biotechnology.

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[1] Lab on a Chip 20 (21), 4007-4015 (2020)
[2] Talanta 241, 123187 (2022)
[3] iScience 26(8)107356 (2023)

中山醫學大學
2024 醫學應用化學研討會

李博仁教授 簡歷

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- **EDUCATION**

Ph.D., Department of Chemistry, University of dinburgh,UK.

(Dec. 2005 – Nov. 2009) Supervisor: *Prof. Steve Chapman*

M.Sc., Department of Applied Chemistry, National Chiao Tung University, Taiwan (Sep. 1999 – Jul. 2001) Supervisor: *Prof. Yaw-Kuen Li*

B.Sc., Department of Applied Chemistry, National Chiao Tung University, Taiwan (Sep. 1995 – Jul. 1999)

- **RESEARCH POSITIONS**

Professor, Institute of Biomedical Engineering, NYCU, Hsinchu, Taiwan (February 2024-current)

Associate Professor, Institute of Biomedical Engineering, NYCU, Hsinchu, Taiwan (August 2020- January 2024t) **Assistant Professor,** Institute of Biomedical Engineering, NYCU, Hsinchu, Taiwan (February 2015- July 2020) **Assistant Research Scholar,** Institute of Applied Chemistry, National Chiao Tung University, Hsinchu, Taiwan (August 2014 – January 2015)

Post-doctoral Research Fellow, Center for Interdisciplinary Science, National Chiao Tung University, Hsinchu, Taiwan (September 2013 – July 2013)

Post-doctoral Research Fellow, Nanoscale Materials and Bioanalytical Chemistry Lab, Institute of Atomic and Molecular Sciences, Academia Sinica, Taiwan (July 2012 – August 2013)

Post-doctoral Research Associate, Nanoscale Materials and Bioanalytical Chemistry Lab, Department of Chemistry, National Taiwan University, Taiwan (December 2009 – June 2012)

Research Assistant (Military Service), Cellular and Developmental Biology Lab, Institute of Biomedical Sciences, Taiwan (October 2001-October 2005)

AWARDS

- MOST FutureTech Demo and Breakthrough Award (2023)
- Outstanding Teaching Award (2020)
- National Innoaward Award (2019)
- MOST FutureTech Demo and Breakthrough Award (2019)

- MOST Assistant Researcher Scholar Fellowship (2014-2016)
- Academia Sinica Postdoctoral Fellowship (2012 – 2014)
- EaStCHEM Prize Postgraduate Full Studentship (2005 – 2008)

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- MOST FutureTech Demo and Breakthrough Award (2023)
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- MOST Assistant Researcher Scholar Fellowship (2014-2016)
- Academia Sinica Postdoctoral Fellowship (2012 – 2014)
- EaStCHEM Prize Postgraduate Full Studentship (2005 – 2008)

PUBLICATIONS

SCI Journal Article (2019-2024)：

1. Lin HP, Su H, Chen CW, **Li BR*** (*corresponding authors) (2024, Jan). Integration of a Micro-Transparent heater- integrated electrochemical (μTHE) cell for investigation of the thermal stability of cytochrome c redox variants. ***Microchemical Journal***
2. Huang CH, Chen CH, Huang TK, Lu F, Huang YJ, **Li BR*** (*corresponding authors) (2023, Aug). Design of a Gradient- Rheotaxis Microfluidic Chip for Sorting of High-quality Sperm with Progressive Motility. ***iScience***
3. Chang CH, Nien CL, **Li BR*** (*corresponding authors) (2023, Jul).Development of a Vertical Bubble Acoustic Microfluidic Sputum Liquefier for Improved Cancer Cell Detection. ***Sensors and Actuators B: Chemical.***
4. Chang CH, Wang CL, **Li BR*** (*corresponding authors) (2023, May). Rapid Detection of Live Bacteria in Water Using Nylon Filter Membrane-Integrated Centrifugal Microfluidics. ***Biosensors and Bioelectronics***.
5. Lin PH, Nien HH, **Li BR*** (*corresponding authors) (2023, Mar). WearableMicrofluidics for Continuous Assay.
   Annual Review of Analytical Chemistry, 16.
6. Kuo SH, Peraro A, Lin HP, Chang CH, and **Li BR*** (*corresponding authors) (2023, Jan). Hand-Powered Point-of- Care: Centrifugal Microfluidic Platform for Urine Routine Examination (μCUREX). ***Langmuir***.
7. Chen CW, Cho WH, Chang CY, Su CY, Chu NN, Kei CC*, **Li BR*** (*corresponding authors) (2022, Dec). CF4 Plasma-based Atomic Layer Etching of Al2O3 and Surface Smoothing Effect. ***Journal of Vacuum Science & Technology A***, 41, 012602.
8. Wang PG, **Li BR**, Wang YL, Wu CC, Chen JC (2022, Dec). Application of aminobenzoic acid electrodeposited screen- printed carbon electrode in the betaamyloid electrochemical impedance spectroscopy immunoassay. ***Talanta***, 124154.
9. Lin CF, Chang CH, Noël L, **Li BR**, Meng HF, Soppera O, Zan HW (2022, Nov). NIR Laser

Integration of Photodetector on 3D Printed Chamber for Colorimetric Biosensing. ***Advanced Materials Technologies***, 2201026.

10. Lin PH, Sheu SC, Chen CW, Huang SC, **Li BR*** (*corresponding authors) (2022, Jan). Wearable hydrogel patch with noninvasive, electrochemical glucose sensor for natural sweat detection. ***Talanta***, 123187. MOST 110-2113-M- 009-016.
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14. Lin HC, Wang YC, Yang JM, Huang CS, Kuo SH, **Li BR** (2020, Oct). Gradient Grating Period Guided-Mode Resonance for potential biosensing applications. ***IEEE Sensors Journal***.
15. Lin PH, Chang WL, Sheu SC, **Li BR*** (*corresponding authors) (2020, Oct). A noninvasive wearable device for real- time monitoring of secretion sweat pressure by digital display. iScience, 101658. MOST 109-2113-M-009-016.13. Tsou PH, Chiang PH, Lin ZT, Yang HC, Song HL, Li BR* (*corresponding authors) (2020, Sep). Rapid purification of lung cancer cells in pleural effusion through spiral microfluidic channels for diagnosis improvement. ***Lab on a Chip***.
16. Hsieh YL, Chen CW, Lin WH, **Li BR*** (*corresponding authors) (2020, Apr). Construction of Nickel Oxide Nano-coral Structure on Microscope Slides for Total Self-Assembly Oriented Probe Immobilization and Signal Enhancement. ***ACS Applied Bio Materials***, doi.org/10.1021/acsabm.0c00249.
17. Lin CT, Cuo SH, Lin PH, Chiang PH, Lin WH, Chang CH, Tsou PH, **Li BR*** (*corresponding authors) (2020, Apr). Hand- Powered Centrifugal Microfluidic Disc with Magnetic Chitosan Bead-Based ELISA for Antibody Quantitation. ***Sensors & Actuators: B. Chemical.*** MOST 108-2113-M-009-016.
18. Chang PH, Weng CC, **Li BR***, Li YK* (*corresponding authors) (2020, Mar). An antifouling peptide-based biosensor for determination of Streptococcus pneumonia markers in

human serum. ***Biosensors and Bioelectronics***, 151, 11969. (SCI). MOST 108-2113-M-009-016

19. Lin PH, **Li BR*** (*corresponding authors) (2020, Jan). Antifouling strategies in advanced electrochemical sensors and biosensors. ***Analyst***, DOI:10.1039/C9AN02017A. (SCI). MOST 108-2113-M-009-016.
20. Wu ST, Huang CY, Weng CC, Chang CC, **Li BR***, Hsu CS*(*corresponding authors) (2019, Sep). Rapid prototyping of open-surface microfluidic platform using wettability-patterned surfaces prepared by atmospheric-pressure plasma jet. ***ACS Omega***, 4(15), 16292-16299. MOST 108-2113-M-009-016.
21. Chiu PL, Chang CH, Lin YL, Tsou PH, **Li BR*** (*corresponding authors) (2019, May). Rapid and Safe Isolation of Human Peripheral Blood B and T Lymphocytes through Spiral Microfluidic Channels. ***Scientific Reports***, 9:8145. MOST 106-2113-M-009-013-MY2.
22. Yang CH, Hsieh YL, **Li BR*** (*corresponding authors) (2019, May). Design Integrated Microfluidic Chips for Clinical Applications. ECS Transactions, 89 (7), 37-41. MOST 106-2113-M-009-013-MY2.
23. Wu ST, Weng CC, **Li BR***, Hsu CS* (*corresponding authors) (2019, Apr). Fabrication of magnetic liquid marbles using superhydrophobic atmosphericpressure plasma-jet-formed fluorinated silica nanocomposites. ***Journal of Materials Science***, 54(14), 10179-10190. MOST 106-2113-M-009-013-MY2.
24. Yang CH, Hsieh YL, Tsou PH, **Li BR*** (*corresponding authors) (2019, Feb). Thermopneumatic suction integrated microfluidic blood analysis system. ***PLOS ONE***. MOST 106-2113-M-009-013-MY2.
25. Lin PH, Huang SC, Chen KP, **Li BR***, Li YK* (*corresponding authors) (2019, Jan). Effective Construction of a High- Capacity Boronic Acid Layer on a Quartz Crystal Microbalance Chip for High-Density Antibody Immobilization. ***Sensors***, 2019, 19(1), 28. (SCI, 16/61, Instruments & Instrumentation). MOST106-2113-M-009-013-MY2.

中山醫學大學
2024 醫學應用化學研討會

細胞力學:3D 細胞微球組裝與應用

清華大學生醫工程與環境科學系

陳之碩　副教授兼系副主任/產學企劃組組長

Abstract:

Mechanical interactions serve essential drive force for morphogenesis, tissue organization, and tumor metastasis. Cells can sense the mechanical force from the neighboring environments, through cell junctions and specific transmembrane proteins, to activate downstream physiological responses. Mechanotrusduction signals are investigated in many studies, however, the influences of cellular contacts in 3 dimension remain underexplored. In this study, using glioma spheroid with approximate 400 μm diameter, we examined the impacts of microglia on rheological properties of the multicellular structure. First, with soft-indentation, we found that even 5% of microglia around can effectively stiffen the glioma spheroids; the analysis of force-deformation curve revealed heterogeneous microstructures in glioma spheroid. Then, the creep measurement suggested an alteration of force-deformation transition in the presence of microglia attached on the periphery of spheroid. Applied with constant deformation, the bi-phase force response curve implied the different underlying mechanisms of the energy dispersion; with microglia, the change of force response characteristic suggested the reorganization of interior glioma spheroid. In summary, our findings suggested that the microglia, which highly associated with glioma progression, can modify the ensemble rheological properties of multiple-glioma structure. We speculate the long-range (few hundred microns) perturbation in mechanical properties can modulate the downstream mechanotrnasduction signals. More experiments regarding the cytoskeleton rearrangement and Rho/Rac expression will be performed to elucidate the potential impacts in detail.

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WORK EXPERIENCE

Associate Professor, 2021-Present

Department of Biomedical Engineering and Environmental Sciences National Tsing Hua University, Taiwan.

Assistant Professor, 2015-2021

Department of Biomedical Engineering and Environmental Sciences National Tsing Hua University, Taiwan.

Postdoctoral Fellow, 2013-2015

Department of Dermatology, Feinberg School of Medicine, Northwestern University

- Development of super-resolution microscopy and Total internal reflection microscopy
- The assembly of adherens junction and cytoskeleton dynamics of epithelia cells

EDUCATION

Ph.D., Biological Engineering and Small-scale Technologies, 2007-2012 University of California, Merced, CA, USA

M.S., Nuclear Science, 2002-2004 Molecular Biophotonics

National Tsing Hua University, Hsinchu, Taiwan

B.S., Nuclear Science, Graduation with highest honor, 1998-2002 National Tsing Hua University, Hsinchu, Taiwan

RESEARCH SUMMARY

The development of biophotonic technology highly facilitates the progression of biomedical researches. In our laboratory, by integrating with different molecular biology methods, we have developed few biophotonic platforms, such as cellular traction force microscopy, fluorescence activation microscopy, and magnetic tweezers system, to investigate various biomedical topics. Over the past few years, we have mainly focused on two interesting areas 1) Cell mechanics and 2) Bio-macromolecule assembly.

1) Cells can sense mechanical signaling and alter their physiology accordingly (mechanotransduction). Recently, the correlations between the physical cues

from microenvironment and the disease progressions have been appreciated. In our study, we noticed the inflammatory responses of macrophage is associated with the stiffness of surrounding environment. The alteration of substrate stiffness can change the NADPH oxidase activity and mitochondria ROS production; substrate stiffness also regulates downstream inflamosome signal and antimicrobial responses (*ACS Appl. Mat. Interfaces* 2020). In addition to inflammatory responses, we found the counterinfluence effect of two physical cues of desmoplasia, hypoxia and substrate stiffness, on glucose metabolism of colorectal cancer. However, high expression of aldolase B can reverse the counterinfluence into compounding effect, which significantly enhance the aerobic glycolysis of colorectal cancer cells (*Colloids Surf B Biointerfaces* 2020). From molecular level, we investigated the assembly dynamic of E-cadherin, one critical transmembrane protein in regulation of cancer metastasis, by using fluorescence activation microscopy and single-molecule localization light microscopy. We found that an adherens junction consists of several high-density cadherin clusters, and the rapid cycling of cadherin cluster is driven by actin assembly (*PANS*, 2018, 2021).

2)Macromolecule assembly serves essential role in various biological processes, such as protein-protein interactions and DNA hybridization. In the laboratory, we developed different biophotonic approaches to investigate macromolecular interactions. Using optical tweezers with nanometer resolution, we studied the impact of freezing process on the integrity of DNA structures. After regular freezing- thaw cycles, the reduced life time of DNA molecule under tensions (~ pN) indicates freezing can compromise the integrity of DNA structure (Journal of Biological Physics, 2017). In addition to studies of DNA molecule and cadherin clusters, we further extended the concept of molecular assembly to marine dissolved organic matter (DOM) and microbial extracellular polymeric substance (EPS). We constructed a customized magnetic tweezers to measure the stickiness of EPS collected from marine algae, which represent one of determining properties of marine organic particles. In contrast to indirect stickiness estimation, we take a step forward to directly assess the EPS stickiness and further discover the interactions among heterogeneous marine macromolecules

(Science of the Total Environment 2021). The assembly of marine DOM serves important roles in microbial community and carbon cycle in ocean. By using laser confocal microscopy and dynamic laser scatter, we demonstrated artificial nanoplastics significantly disturb the assembly of marine DOM (Science of the Total Environment 2018). Moreover, by applying the polymer assembly model, we can further disrupt the biofilm structure of Pseudomonas aeruginosa with aerosolized hypertonic saline, which can effectively enhance the efficacy of antibiotics (Scientific Reports,2020).

Over the past years, from biophysical perspective, we have explored cellular physiology and bio-molecular interactions using biophotonic approaches. Currently, we investigate the intercellular force propagation and planar polarization in cellular collective migration. Combing with Cellular Potts model simulation with in vitro intercellular force measurement, we propose an enthalpy-driven cell assembly model to interpret the organization and dynamics between heterogeneous cell populations. Since collective migration highly relates to tumor invasion and tissue development, the outcome of our current studies may provide insights of cellular dynamics and contribute to the development of alternative disease treatments.

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3. J Lo, C.C Liu, Y.S Li, P.Y Lee, P.L Liu, P.C Wu, T.C Lin, **C.S Chen**, C.C Chiu, Y.H Lai, Y.C Chang,H.E Wu, Y.R Chen , Y.K Huang, S.P Huang, S.C Wang, C.Y Li "Punicalagin Attenuates LPS-Induced Inflammation and ROS Production in Microglia by Inhibiting the MAPK/NF-kappaB Signaling Pathway and NLRP3 Inflammasome Activation" Journal of Inflammation Research,2022
4. C.R Chen, R.S Chang, **C.S Chen** "Identification of Prognostic Genes in

Gliomas Based on Increased Microenvironment Stiffness" Cancers, 2022

5. A Alias, S Mishra, G Pendharkar, **C.S Chen**, C.H Liu, Y.J Liu, and D.J Yao "Microfluidic Microalgae System: A Review" Molecules, 2022
6. Y.S Hsiao, S.C Yen, P.I Wu, Edgar Qui˜nones, S.T Hung, **C.S Chen**, S.M Tsai "Microfluidic organic bioelectronic chips for efficient isolation of trophoblast cells using a combination of rational catenation and electrically controllable refining" Materials Chemistry and Physics, 2022
7. H.L Lin, C.E Chiang, M.C Lin, M.L Kau, Y.T Lin, **C.S Chen** " Aerosolized Hypertonic Saline Hinders Biofilm Formation to Enhance Antibiotic Susceptibility of Multidrug-Resistant Acinetobacter baumannii" Antibiotics, 2021
8. L.S Yu, M Jhunjhunwala, S.Y Hong, L.Y Yu, W.R Lin, **C.S Chen** "Tissue Architecture Influences the Biological Effectiveness of Boron Neutron Capture Therapy in In Vitro/In Silico Three-Dimensional Self- Assembly Cell Models of Pancreatic Cancers" Cancers, 2021
9. S.Y Mao, H.W Peng, S.Y Wei, C.S Chen, Y.C Chen " Dynamically and spatially controllable albumin- based hydrogels for the prevention of post-operative adhesion" ACS Biomaterials Science & Engineering, 2021
10. R. B Troyanovsky, A Sergeeva, I Indra, C.S Chen, R Kato, L Shapiro, B Honig, S M Troyanovsky" Sorting of cadherin-catenin-associated proteins into individual clusters" Proceedings of the National Academy of Sciences of the United States of America,2021
11. S Mishra, Y. J. Lui, C.S. Chen*, D. J. Yao " An Easily Accessible Microfluidic Chip for High- Throughput Microalgae Screening for Biofuel Production" Energies, 2021
12. C.S Chen, R.F Shiu, Y.Y Hsieh, C Xu, C I. Vazquez, Y Cui, Ian C. Hsu, A Quigg, P H. Santschi, W.C Chin "Stickiness of extracellular polymeric substances on different surfaces via magnetic tweezers" Science of the Total Environment, 2021
13. Y.C Chuang, H.M Chang, C.Y Li, Y Cui, C.L Lee, C.S Chen "Reactive oxygen species and inflammatory responses of macrophages to substrates with physiological stiffness" ACS Applied Materials & Interfaces, 2020
14. H.L Lin, C.S Chen, J Fink, G.H Lee, C.W Huang, J.C Chen, Z.Y Chiang "In vitro evaluation of a vibrating-mesh nebulizer used repeatedly over 28 days" Pharmaceutics, 2020

15.M Jhunjhunwala, H. L Lin, G.Y Li, C.S Chen “Recognition of respiratory dysfunctions using algorithm- assisted portable airflow sensors” ECS Journal of Solid State Science and Technology, 2020

16.R.F Shiu, C. I Vazquez, Y.Y Tsai, G.V Torres, C.S Chen, P.H Santschi, A. Quigg, W.C Chin, “Nano- and microplastics trigger secretion of protein-rich extracellular polymeric substances from phytoplankton” Science of the Total Environment, 2020

17.R.S Chang, C.S Chen, C.L Lee, Y.C Cuia, W.J Chung, Ian C.Hsu “Heuristic self-photography approach for flat-top beam generation with arbitrary beam intensity distribution” Optik, 2020

18.H.C Huang, W.R Lin, S.N Lim, C.T Yeh, T.H Yen, M.R. Alison, C.S Chen, “Aldolase Triggers Metabolic Reprogramming in Colorectal Cancer in Hypoxia and Stiff Desmoplastic Microenvironments” Colloids and Surfaces B: Biointerfaces, 2020

19. H.L Lin, L.C Chiu, G.H Wan, C.C Huang, Z.T Lee, Y.T Lin, S.R Wu, C.S Chen, “Hypertonic saline enhances the efficacy of aerosolized gentamicin against Pseudomonas aeruginosa” Scientific Report, 2020

20.R.F Shiu, C. I Vazquez, Y.Y Tsai, G.V Torres, C.S Chen, P.H Santschi, A. Quigg, W.C Chin, “ Nano- plastics induce aquatic particulate organic matter (microgels) formation” Science of the Total Environment, 2019

21.R.F Shiu, C.L Lee, P.Y Hsieh, C.S Chen, Y.Y Kang, W.C Chin, N.H Tai “Superhydrophobic graphene- based sponge as a novel sorbent for crude oil removal under various environmental conditions” Chemosphere, 2018

22.I. Indra, J. Choi, C.S Chen, R.B. Troyanovsky,L Shapiro, B. Honig, S. M. Troyanovsky,”Spatial and Temporal Organization of Cadherin in Punctate Adherens Junctions” Proceeding of the National Academy of Science, 2018

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marine environments: importance of extracellular polymeric substances." Environmental Science & Technology, 2012.

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