Ultra Light-sheet Macro Photography for Iteratively Expanded Drosophila Connectome

Professor Fu-Jen Kao

The initiative in imaging a hugely expanded Drosophila brain via iterative expansion microscopy (ExM) will be discussed. Through ExM, 100X expansion of Drosophila brain has been demonstrated by enlarging the typically 0.6x0.3x0.2 mm sized brain to 60x30x20 mm, promising electron microscopy-like resolution (~3 nm) with optical microscopy (~300 nm) to resolve the synapse connection.

The rapid and ultra-large-scale imaging of large tissue samples will revolutionize our understanding of the relationship between biological function and structure. Currently, commercially available imaging platforms, such as SmartSPIM, can acquire images with more than 100 million pixels at a data throughput rate of several GB per second (acquisition rate ~0.417 mm3 /s with a 4X lens). Taking the 100X expanded Drosophila brain as an example, its volume is approximately 15,000 mm3, and the expected 3D scanning is estimated to be approximately 36,000 seconds (~10 hours). As a comparison, the imaging speed of a spinning disk confocal microscope is only ~0.0058mm3 /s with a 10X lens, making it very challenging to image the whole 100X expanded brain.

We estimate that our ultra Lightsheet-based macro photography platform can achieve a 3D image rate of ~4 mm3/s with a 2X lens, an order of magnitude faster than SmartSPIM.

Curriculum Vitae

General details

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Education

- Doctor of Philosophy (PhD) in Physics at Cornell University (August, 1993)
- Master of Science (MA) in Physics at Cornell University (August, 1988)
- Bachelor of Science (BA) in Physics at the National Taiwan University (June, 1983)

Academic qualifications

- Fellow of TPS (The Physical Society of Taiwan) since 2016
- Fellow of SPIE since 2015
- Fellow of Royal Microscopy Society since 2005
- Distinguished Professor, Institute of Biophotonics, National Yang-Ming University (since August, 2019)
- Professor, Institute of Biophotonics, National Yang-Ming University (since August, 2004)
- Director, Incubation Center, National Yang-Ming University (August, 2010 July, 2011)
- Associate Dean, Office of Research and Development, National Yang-Ming University (August, 2006 July, 2011)
- Director, Institute of Biophotonics, National Yang-Ming University (August, 2004-January, 2011)
- Chief of Research and Planning, Office of Research Affair, National Sun Yat-sen University (May, 2003 July, 2004)
- Professor, Institute of Electro-Optical Engineering, National Sun Yat-sen University (since August, 2003)
- Professor, Department of Physics, National Sun Yat-sen University (August, 2002-July, 2003)
- Associate Professor, Department of Physics, National Sun Yat-sen University (August, 1993-July, 2002)

Professional qualifications and services

- 1. Associate Editor, IEEE TBME.
- 2. 2000 Session co-chair Scanning 2000, San Antonio, USA.
- 3. 2000 International committee member, Focus on Microscopy 2000, Shirahama, Japan.
- 4. 2000 Program Committee member, SPIE Photonics Taiwan 2000, Taipei, Taiwan.
- 5. 2000 **Organizer and co-Chair**, 2nd Asia Pacific Symposium on Confocal Microscopy and Related Technologies (Multidimensional Microscopy 2000), Kaohsiung, Taiwan.
- 6. 2001 International committee member, Focus on Microscopy 2001, Amsterdam, Netherlands.

- 7. 2001 International committee member, Multidimensional Microscopy 2001, Melbourne, Australia.
- 8. 2002 Organizer and co-Chair, Focus on Microscopy 2002, Kaohsiung, Taiwan.
- 9. 2002 **Organizer and co-Chair**, 2nd Japan-Taiwan Nanophotonic Symposium, Osaka University, Osaka, Japan
- 10.2004 International committee member and Session Chair, Photonics Asia, Beijing, China.
- 11.2004 The Second Asian and Pacific Rim Symposium on Biophotonics (APBP 2004), Session Chair, Taipei, Taiwan.
- 12.2003-2014 International committee member and session chair, Focus on Microscopy.
- 13.2005, 2007, 2008, 2009 Biophotonics at Yang-Ming, **Organizer and Chair**, Photophore 2009: IV International Biophotonics Meeting, National Yang-Ming University, Taipei, Taiwan.
- 14.2005-2016 Board member, The Physics Society of ROC, Taiwan.
- 15.2011-2013 **Director** of International Affairs and Standing Committee Member of the Physics Society of ROC, Taiwan.
- 16.2012-2013 **President**, Taiwan Local Section of Optical Society of America
- 17. Vice President and the Director of International Affairs of the Physics Society of ROC, Taiwan (Jan. 2012- Jan. 2014)
- 18. President of the Taiwan Physics Society (Jan. 2014-Jan. 2016)
- 19.2013-2022 Council Member, Association of Asia-Pacific Physical Societies (AAPPS)
- 20. Vice President of the Association of Asia-Pacific Physical Societies (2016-2019)
- 21. Chair of the CN Yang Award of the Association of Asia-Pacific Physical Societies (2018-2021)
- 22. Chief Editor, Chinese Journal of Physics (IF:3.957) (2022-2023)
- 23. Referee for journal papers in Optics Letter, Optics Express, Applied Physics Letters, Optics Communications, Applied Optics, J. of Biomedical Optics, etc.

List of recent publications and work

 Book: 1. Fu-Jen Kao, Gerd Kaiser, Ankur Gogoi (Eds.), Advanced Optical Methods for Brain Imaging, Springer, 2018. ISBN:978-981-10-9019-6



2. Peter Török and Fu-Jen Kao (Eds.), Optical Imaging and Microscopy-Techniques and Advanced Systems, Springer, Berlin, 2007.



ISBN-10: 354069563X **ISBN-13:** 978-3540695639

2. Hanry Yu, Ping-Chin Cheng, Pao-Chun Lin, and Fu-Jen Kao (Eds.), Multi-modality Microscopy, World Scientific Publishing Company, 1st edition (May 8, 2006).



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- 1. Over 100 SCI Journal Papers (Appendix 1)
- 2. Book Chapters (Appendix 2)
- 3. 3 Other Referred Journal Papers (Appendix 3)
- 4. Over 100 International Conference Presentations and Proceedings (Appendix 4)
- 5. 4 US Patent and 17 domestic patents (Appendix 5)
- 6. Technical reports and domestic publications (Appendix 6)

Honors and Award

- 1. 2002-2020, NSC Grant Fellowship (as a replacement for NSC Class A award)
- 2. 1994, 2000, 2001 NSC Class A award (the award is cancelled since 2002 as a policy change of NSC)
- 3. 1998, Excellence Award on Academic-Industrial Collaboration for "Small Frame Solid State Laser", Ministry of Education.
- 4. As an advisor for:
 - (1) 2000 International Science Affair, Ting-Fan Wu, Class 4 Award of Intel.
 - (2) 2001 Optics and Photonics Taiwan, Division of Optical Engineering, Student Award, Jian-Cheng Chen.
 - (3) 2002 Annual Meeting of Physics Society of Taiwan, Student Award, Sheng-Chih Shih.
 - (4) 2002 Optics and Photonics Taiwan, Division of Optical Engineering, Student Award, Jian-Cheng Chen.
 - (5) 2002 Optics and Photonics Taiwan, Division of Optical Engineering, Student Award, Der-Cheng Yang.
 - (6) 2004 Annual Meeting of Mechanics Society of Taiwan, Division of Thermal Fluid Dynamics/Energy, the 2nd Place Student Award, Yu-Sheng Jean.
 - (7) 2005 Optics and Photonics Taiwan, Division of Optical Engineering, Student Award, Yu-Chi Liao.
 - (8) 2007 Optics and Photonics Taiwan, Division of Optical Engineering, Student Award, Po-Yen Lin.
 - (9) 2009 Annual Meeting of Physics Society of Taiwan, Student Poster Award, Po-Yen Lin.
 - (10) 2009 Donahue Wu, National Yang Ming University Graduate Symposium, poster award
 - (11) 2010 Po-Yen Lin, International Conference on Optics and Photonics in Taiwan, Best student paper awards (oral presentation)
 - (12) 2010 Trista Wan, The 15th Joint Biophysics Conference, Poster award
 - (13) 2010 Gitanjal Deka, International Conference on Optics and Photonics in Taiwan, Poster award
 - (14) 2011 Kenny Lin , Annual Meeting of Physics Society of Taiwan, Poster award
 - (15) 2011 Nirmal Mazumder, Asian Biophysics Association Symposium, Travel award
 - (16) 2011 Emma Lin, The 16th Biophysics Conference, May18-21, in National Dong Hwa University, Hualien, Taiwan
 - (17) 2012 Henny Tsai, Annual Meeting of Physics Society of Taiwan, Poster award
 - (18) 2012 Shin-Hsien Lee, Annual Meeting of Physics Society of Taiwan, Poster award
 - (19) 2012 Po-Yen Lin, Photonics West, Jen Lab Best Poster Award
 - (20) 2012 Jerry Hu, Jimmy Lin, Yun-Xiang Lu, Wen-Tse Wang, Chia-Hui Deng, National Yang-Ming University Technology & Business Model Creativity Contest, First Prize, Wireless Induction Lighting
 - (21) 2012 Henry Tsai, Symposium on Single Molecule/Nanoparticle Spectroscopy and Imaging, National Chiao-Tung University, Best Poster award
 - (22) 2012 Nirmal Mazumder, the 5th Prize in PicoQuant Application Gallery contest

Exhibition

1. Fu-Jen Kao and Sheng-Lung Huang, International Photonics Exhibition, International Trade Center, Taipei, July 25~28, 1996.

- 2. Fu-Jen Kao and Sheng-Lung Huang, The 2nd APEC Technomart, Taipei, January 21~25, 1998.
- 3. Fu-Jen Kao and Sheng-Lung Huang, International Photonics Exhibition, International Trade Center, Taipei, July 11~14, 1998.
- 4. Fu-Jen Kao, Special Exhibition of the 20th Anniversary of National Sun Yat-sen University, Two-photon based laser scanning microscopy, 2000.
- 5. Sheng-Lung Huang, Fu-Jen Kao, Tze-Sheng Hong, Yi-Chin Ho, and Woodhi Cheng, Special Exhibition of the 20th Anniversary of National Sun Yat-sen University, Small Frame Solid State Laser, 2000.

Research Projects

- 1. NSC projects (Appendix 7)
- Excellence Project of Academic, Ministry of Education, 89-B-FA08-1-4 Southern Taiwan Center of Excellence in Neuroscience (In charge of the Advanced Bio-photonic Facilities), 1999-2003, NT\$4,000,000
- 3. Technology and Methodology developed (Appendix 8)
- 4. Advising over 50 master theses and

Domestic Services

- 1. 1999~2002 Topic Lecturer for the Graduate Class of Clinical Medical Institute, Chang Gong University.
- 2. 1998.3 Chair of "Southern Taiwan Confocal Microscopy Workshop".
- 3. 1998, 2000 Referee for the National High School Science Exhibition.
- 4. 2000 Editor of Physics Bi-monthly.
- 5. 2000 Referee of the Optical Engineering Society of Taiwan
- 6. 2003 Referee for the International Physics Olympia, Taipei.
- 7. 1999~2006 Committee member of Optical Engineering Division, Photonics Society of Taiwan.
- 8. 2007~2012 Committee member of Biophotonics Division, Photonics Society of Taiwan.

Teaching Experience

- 1. Lecturing courses on "Fundamentals of Optics", "Fundamentals of Modern Physics", "Electromagnetism", "Special topics in Photonics", "Thermal Dynamics", "Statistical Physics", "Applied Optics", "Photonics Techniques and Materials".
- 2. Tutorials and laboratory demonstration in 'Applications of gas, semiconductor and solid state lasers in optical science'

Appendix 1: SCI Journal Papers

- S.K. So, F.-J Kao, and W. Ho, 1988, Summary Abstract: Mechanisms of Laser Interaction with NO adsorbed on GaAs(110), J. Vac. Sci. Technol. A6, 1435.
- F.-J Kao, D.G. Busch, D. Gomes da Costa, and W. Ho, 1993, Femtosecond versus Nanosecond Surface Photochemistry: O2+CO on Pt(111) at 80K, Phys. Rev. Lett. 70, 4098.
- 3. F.-J Kao, D.G. Busch, D. Cohen, D. Gomes da Costa, and W. Ho, 1993, Femtosecond Desorption of Molecularly Adsorbed Oxygen from Pt(111), Phys. Rev. Lett. 71, 2094.
- 4. J. Yu, W.-S Fann, F.J. Kao, D.-Y Yang, and S.-H Lin, 1994, Molecular Orbital Calculations of Electronic Excited States in Poly(p-phenylene vinylene), Synthetic Metals 66, 143.
- 5. J. Yu, J. H. Hsu, K. R. Chuang, C. L. Chao, S. A. Chen, F. J. Kao, W. S. Fann, and S. H. Lin, 1995, Experimental and Theoretical Studies of Absorption and Photoluminescence Excitation Spectra of Poly(p-phenylene vinylene), Synthetic Metals, 74, 7.
- 6. K. H. Chen, Y.L. Lai, L.C Chen, J.Y. Wu, and F.J. Kao, 1995, High-temperature Raman study in CVD diamond, Thin Solid Films 270 (1-2): 143-147.
- 7. J.L. Chern, F.J. Kao, and I.M. Jiang, 1996, Transition between Nonstationary and Stationary Chaos, Phys. Lett. A 218, p268-274.
- 8. S.L. Huang, F.J. Kao, L.R. Liu, and C.S. Hsu, 1997, Frequency-Offset cavity-length control loop in a diode-laserpumped and actively mode-locked Nd:YLF laser, Optics Communications 134, p171-174.
- 9. S.L. Huang, F.J. Kao, H.S. Hsieh, and C.S. Hsu, 1998, Polarization-dependent periodic pulse oscillation in a diodepumped and intracavity-frequency-doubled Nd:YVO4, Applied Optics 37, p2397-2401.
- 10. F.J. Kao, S.Y. Chou, S.L. Huang, S.A. Chen, K.R. Chuang, and W.S. Fann, 1998, Imaging photo-induced reaction of PPV thin films by a spectrally resolved laser scanning microscope, Jpn. J. Appl. Phys. 37, p4409-4411.
- P. Mach, C.C. Huang, T. Stoebe, E.D. Wedell, T. Nguyen, W.H. de Jeu, F. Guittard, J. Naciri, R. Shashidhar, N. Clark, I.M. Jiang. F.J. Kao, H. Liu, and H. Nohira, 1998, Surface tension obtained from various smectic free standing films: The molecular origin of surface tension, Langmuir 14, p4330-4341.
- 12. C.F. Kuo, J.J.Wu, P.J. Tsai, F.J. Kao, H.Y. Lei, M.T. Lin, and Y.S. Lin, 1999, Streptococcal pyrogenic exotoxin B induces apoptosis and reduces phagocytic activity in U937 cells, Infection and Immunity 67, p126-130.
- 13. J.W. Lin, S.L. Huang, and F.J. Kao, 1999, Self-phase modulation and fast switching enhanced pulse generation in an actively mode-locked Nd:YLF laser, Optics Communications 161, p37-41.
- 14. S.L. Huang, T.Y. Tsui, C.H. Wang, and F.J. Kao, 1999, Timing jitter reduction of a passively Q-switched laser, Jpn. J. Appl. Phys. 38, L239-241.
- 15. F.J. Kao, M.K. Huang, Y.S. Wang, S.L. Huang, M.K. Lee, and C.K. Sun, 1999, Two-photon Optical Beam Induced Current Imaging of InGaN Blue LEDs, Opt. Lett. 24, p1407-1409.
- 16. C.K. Sun, J.C. Liang, J.C. Wang, F.J. Kao, S. Keller, M.P. Mack, U. Mishra, and S.P. DenBaars, 2000, Twophoton absorption study of GaN, Appl. Phys. Lett. 76, p439-441
- C.K. Sun, Y.L. Huang, J.C. Liang, J.C. Wang, K.G. Gan, F.J. Kao, S. Keller, M.P. Mack, U. Mishra, and S.P. DenBaars, 2000, Large near resonance third order nonlinearity in GaN, Optical and Quantum Electronics, 32, p619-640.
- 18. F.J. Kao, B.L. Lin, P.C. Cheng, 2000, Time-lapse two-photon fluorescence micro-spectroscopy of a single chloroplast, Scanning, 22, No.4, cover.
- 19. H.Z. Cheng, P.L. Huang, S.L. Huang, and F.J. Kao, 2000, Reentrant two-mirror ring resonator for generation of a single-frequency green laser, Opt. Lett. 25, p542-544.
- 20. P.C. Cheng, B.L. Lin, F.J. Kao, M. Gu, M.G. Xu, X. Gan, M.-K Huang, Y.-S. Wang, 2001, Multi-photon fluorescence microscopy –the response of plant cells to high intensity illumination, Micron 32, p 661-669.
- 21. A.Y.W. Chang, J.Y.H. Chan, F.J. Kao, C.M. Huang, and S. Chan, 2001, Engagement of iNOS at rostral ventrolateral medulla during mevinphos intoxication in the rat, J. of Biomedical Science, 8, p475-483.
- 22. C.K. Lee, F.J. Kao, S.C. Wang, and C.L. Pan, 2001, Simultaneous observation of second harmonic generation and three-photon excited photoluminescence from hybrid vapor phase epitaxy-grown GaN film, Jpn. J. Appl. Phys. 40, p6805-6806.
- 23. F.J. Kao, Y.M. Wang, J.C. Chen, P.C. Cheng, R.W. Chen and B.L. Lin, 2002, Photobleaching under single photon and multi-photon excitation: chloroplasts in protoplasts from Arabidopsis thaliana, Optics Communications 201, p85-91.
- 24. F.J. Kao, Y.M. Wang, J.C. Chen, P.C. Cheng, R.W. Chen and B.L. Lin, 2002, Micro-spectroscopy of chloroplasts in protoplasts from Arabidopsis thaliana under single photon and multi-photon excitation, J. of Luminescence 98, p107-114.
- 25. F.J. Kao, J.C. Chen, S.C. Shih, A. Wei, S.L. Huang, T.S. Horng, and P. Török, 2002, Optical beam induced current microscopy at DC and Radio Frequency, Optics Communications 211, p39-45.
- 26. P. Török, and F.J. Kao (corresponding author), 2002, Point spread function reconstruction in high aperture lenses focusing ultra-short laser pulses, Optics Communications 213, p99-104.
- 27. F.J. Kao, The Use of Optical Parametric Oscillator for Harmonic Generation and Two-photon UV Fluorescence Microscopy, 2004, Microscopy Research and Techniques 63, p175-181. (10/62 Biology)

- 28. Elena V. Perevedentseva, Artashes V. Karmenyan¹, Fu-Jen Kao, Arthur Chiou, 2004, Second Harmonic Generation of Biotin and Biotin Ester Microcrystals trapped in Optical Tweezers with a Mode-locked Ti:sapphire Laser, Scanning 26 (5): I78-I82 Suppl. 1, SEP-OCT 2004.
- Chung-Yuan Mou, Te-Chen Yang, Hong-ping Lin and Fu-Jen Kao (corresponding author), 2004, Visualization of Topological Microstructures of Mesoporous Silicate Hollow Sphere with Confocal Microscopy, Jpn. J. Appl. Phys. 43, p1525-1526. (27/71 Applied Physics).
- 30. Xin Hong and Fu-Jen Kao (corresponding author), 2004, Micro-Surface Plasmon Resonance Biosensing Based on Gold Nanoparticle Film, Applied Optics 43, p2868-2873. (16/54 Optics)
- 31. Sun C, Kuan C, Kao FJ, Wang YM, Chen JC, Chang CC, Shen P, 2004, On the nucleation, growth and impingement of plate like a-Zn2SiO4 spherrulites in glaze layer: a confocal and electron microscopic study, Materials Science and Engineering A. 379 (1-2): 327-333 AUG 15, 2004. (50/173 Material Science, Multidisciplinary)
- 32. Jian-Cheng Chen, Chia-Yao Lo, Kuang-Yao Huang, **Fu-Jen Kao**, Shih-Yu Tu, Sheng-Lung Huang, 2005, Fluorescence mapping of oxidation states of Cr ions in YAG crystal fibers, **Journal of Crystal Growth** 274, p522-529.
- 33. Stanciu GA, Sandulescu I, Boyer G, **Kao FJ**, 2005, Investigations on the SiC polytypes by using different techniques based on scanning laser microscopy, **Scanning** 27, p104-104.
- 34. Ji JY, Shen P, Chen JC, Kao FJ, Huang SL, Lo CY, 2005, Journal of Crystal Growth 282, p343-352.
- 35. Cheng-Chung Chang, Jen-Fei Chu, **Fu-Jen Kao**, Yi-Chun Chiu, Pei-Jen Lou, Huei-Chin Chen, Ta-Chau Chang, 2006, Verification of Antiparallel G-Quadruplex Structure in Human Telomeres by Using Two-Photon Excitation Fluorescence Lifetime Imaging Microscopy of the 3,6-Bis(1-methyl-4-vinylpyridinium)carbazole Diiodide Molecule, **Analytical Chemistry**, 78, 2810-15.
- Jian-Cheng Chen, Kuang-Yao Huang, Cheng-Nan Tsai, Yen-Sheng Lin, Chien-Chih Lai, Geng-Yu Liu, Fu-Jen Kao, and Sheng-Lung Huang, 2006, Composition dependence of the micro-spectroscopy of Cr ions in double-clad Cr:YAG crystal fiber. J. Appl. Phys. 99, 093113.
- Yu-Sheng Chien, Che-Hsin Lin, Fu-Jen Kao, and Cheng-Wen Ko, 2006, A Fully Integrated system for Cell/Particle Sorting in a Microfluidic Device Utilizing an Optical Tweezing and DIP Recognition Approach, Materials Science Forum Vols. 505-507, pp. 643-648.
- Yu-Sheng Chien, Che-Hsin Lin, Fu-Jen Kao, and Cheng-Wen Ko, 2007, Micro-Flow-Cytometer Integrated with Optical Tweezer and DIP Technique for Cell/Particle Sorting and Manipulation, Solid State Phenomena Vols. 121-123, pp. 1351-1354.
- Vladimir Ghukasyan, Yueh-Ying Hsu and Szu-Hao Kung and Fu-Jen Kao*, 2007, Application of fluorescence resonance energy transfer resolved by fluorescence lifetime imaging microscopy for the detection of enterovirus 71 infection in cells, J. Biomedical Optics, Vols. 12, pp. 024016 -23.
- 40. Elric Esposito, **Fu-Jen Kao**, Gail McConnell, Confocal optical beam induced current microscopy of light-emitting diodes with a white-light supercontinuum source, 2007, Applied Physics B, Vols 88, 551-555.
- 41. Yueh-Ying Hsu, Yu-Ning Liu, Wenyen Wang, **Fu-Jen Kao**, and Szu-Hao Kung, 2007, *In vivo* dynamics of enterovirus protease revealed by fluorescence resonance emission transfer (FRET) based on a novel FRET pair, Biochemical and Biophysical Research Communications, Vols. 353, pp. 939-945.
- Hsin-Ying Lee, Ke-Hao Pan, Chih-Chien Lin, Yun-Chorng Chang, Fu-Jen Kao, Ching-Ting Lee, 2007, Current spreading of III-nitride light-emitting diodes using plasma treatment, Journal of Vacuum Science & Technology B: Microelectronics and Nanometer Structures, Vols. 25, pp. 1280-1283.
- Yu-Fen Chang, Hsiao-Chuan Teng, Sha-Yen Cheng, Chin-Tien Wang, Ph. D.; Chiou Shi-Hwa, Lung-Sen Kao, Fu-Jen Kao, Arthur Chiou, De-Ming Yang, 2008, Orai1-STIM1 formed Store-Operated Ca2+ Channels (SOCs) as the Molecular Components needed for Pb2+ Entry in Living Cells, Toxicology and Applied Pharmacology, 227: 430-439. (IF: 4.722, P: 4/76)
- 44. Jiung-De Lee, Yu-Fen Chang, **Fu-Jen Kao**, Lung-Sen Kao, Chung-Chih Lin, Ai-Chu Lu, Bai-Chuang Shyu, Shih-Hwa Chiou, De-Ming Yang, 2008, Detection of the interaction between SNAP25 and rabphilin in neuroendocrine PC12 cells using the FLIM/FRET technique. *Microsco. Res. Tech.* 71: 26-34. (IF: 1.68, P: 5/15)
- 45. Hsing-Wen Wang, Vladimir Gukassyan, Chien-Tsun Chen, Yau-Huei Wei, Han-Wen Guo, Jia-Sin Yu, and Fu-Jen Kao, 2008, Differentiation of Apoptosis from Necrosis by Dynamic Changes of Reduced Nicotinamide Adenine Dinucleotide (NADH) Fluorescence Lifetime in Live Cells, Journal of Biomedical Optics 13, 054011.
- 46. Jiung-De Lee, Ping-Chun Huang, Yi-Cheng Lin, Lung-Sen Kao, Chien-Chang Huang, Fu-Jen Kao, Chung-Chih Lin, and De-Ming Yang, 2008, In-Depth Fluorescence Lifetime Imaging Analysis Revealing SNAP25A-Rabphilin 3A Interactions, Microscopy and Microanalysis 14:507-518. (IF: 2.18, P: 2/9)
- 47. Han-Wen Guo, Chien-Tsun Chen, Yau-Huei Wei, Oscar K. Lee, Vladimir Gukassyan, **Fu-Jen Kao**, and Hsing-Wen Wang, 2008, Reduced nicotinamide adenine dinucleotide fluorescence lifetime separates human mesenchymal stem cells from differentiated progenies, Journal of Biomedical Optics 13, 050505.
- 48. Yung-Hsiang Yi, Pei-Yun Ho, Tung-Wei Chen, Wen-Jie Lin, Vladimir Gukassyan, Tsung-Heng Tsai, Da-Wei Wang, Tien-Shen Lew, Chih-Yung Tang, Szechng J. Lo, Tsung-Yu Chen, **Fu-Jen Kao**, and Chi-Hung Lin, 2009,

Membrane targeting and coupling of NHE1/integrin α IIb β 3/NCX1 by lipid rafts following integrin-ligand interactions trigger Ca²+ oscillations, Journal of Biological Chemistry 10, 1024. (IF: 7.385).

- 49. Vladimir Ghukasyan and **Fu-Jen Kao***, 2009, Monitoring Cellular Metabolism with Fluorescence Lifetime of Reduced Nicotinamide Adenine Dinucleotide, Journal of Physical Chemistry C (accepted for publications).
- 50. TY Tzung, CY Chen, **FJ Kao**, WC Chen, Infrared irradiation as an adjuvant therapy in recalcitrant alopecia areata, Dermatologic surgery **35**, p721-3 (2009). (IF: 2.102)
- 51. Tien-Yi Tzung, Chia-Yi Yang, Yung-Chang Huang and **Fu-Jen Kao**, Colorimetry provides a rapid objective measurement of *de novo* hair growth rate in mice, Skin Research and Technology 2009, 15, p459-463. (IF: 1.348)
- Tai-Yu Chiu, Hsiao-Chuan Teng, Ping-Chun Huang, Fu-Jen Kao, and De-Ming Yang, Dominant Role of Orai1 with STIM1 on the Cytosolic Entry and Cytotoxicity of Lead Ions, Toxicological Sciences, 2009, 110, p353-362.(IF:4.443)
- S. C. Pei, T. S. Ho, T. M. Tai, L. M. Lee, J. C. Chen, A. H. Kung, F. J. Kao and S. L. Huang, Drawing of singlecrystal and glass-clad lithium tantalate fibers by the laser-heated pedestal growth method, Journal of Applied Crystallography, 2009, 43, p48-52. (IF 4.871)
- 54. Kate Hsu, Derek Lin, Tsung-Lin Kuo, Huei-Ning Wan, Nai-Wen Chi, and Fu-Jen Kao, Resolving the Structural-Functional Interaction Between HIV-1 Vpu and TASK Channels by FLIM/FRET, *Biophysical Journal*, Volume 96, P 175a.
- 55. Wen-Jie Lin, Chih-Yung Yang, Ying-Chih Lin, Meng-Chun Tsai, Chu-Wen Yang, Chien-Yi Tung, Pei-Yun Ho, Fu-Jen Kao and Chi-Hung Lin, Phafin2 modulates the structure and function of endosomes by a Rab5-dependent mechanism, Biochemical and Biophysical Research Communications, 2010, **391**, p1043-1048. (IF:2.648)
- Vladimir Ghukasyan, Chih-Chun Hsu, Chia-Rung Liu, Fu-Jen Kao* and Tzu-Hao Cheng, Fluorescence lifetime dynamics of eGFP in protein aggregates with expanded polyQ, J. Biomedical Optics, J. Biomed. Opt., 2010, 15, 016008. (IF:2.970)
- 57. Ping-Chun Huang, Tai-Yu Chiu, Li-Chun Wang, Hsiao-Chuan Teng, Fu-Jen Kao and De-Ming Yang, Visualization of the Orai1 Homodimer and the Functional Coupling of Orai1-STIM1 by Live-Cell Fluorescence Lifetime Imaging, Microscopy and Microanalysis, 2010 (accepted) (IF:2.992)
- 58. Xin Li, **Fu-Jen Kao***, Chien-Chin Chuang, and Sailing He, "Enhancing fluorescence of quantum dots by silicacoated gold nanorods under one- and two-photon excitation," Opt. Express **18**, 11335-11346 (2010) (IF:4.187)
- Aaron D. Slepkov, Andrew Ridsdale, Trista Ning, Joe Wang, Adrian F. Pegoraro, Douglas J. Moffatt, John P. Pezacki, Fu-Jen Kao and Albert Stolow, Forward-Collected FLIM-CARS Microscopy, J. Biomed. Opt., 2010. (IF:2.970)
- Tatyana Buryakina, Pin-Tzu Su, Vladimir Gukassyan, Wan-Jr Syu, and Fu-Jen Kao*, "Monitoring cellular metabolism of 3T3 upon wild type E. coli infection by mapping NADH with FLIM ", Chinese Opt. Lett. 8, 931-933 (2010)
- 61. Thilo Dellwig, Matthew R. Foreman, and **Fu-Jen Kao**^{*}, "Coherent Long-distance Signal Detection Using Stimulated Emission: a Feasibility Study", Chinese Journal of Physics **48**, 873-884 (2010).
- 62. Po-Yen Lin, Hong-Chou Lyu, Chin-Ying Stephen Hsu, Chia-Seng Chang, and Fu-Jen Kao, Imaging carious dental tissues with multiphoton fluorescence lifetime imaging microscopy, Biomedical Optics Express 2, pp. 149-158 (2011). <u>http://www.opticsinfobase.org/boe/abstract.cfm?uri=boe-2-1-149</u>.
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- 62. (**Invited Speaker**) Fu-Jen Kao, Cellular Molecular Dynamics Revealed through Autofluorescence and Multichannel FLIM, International Symposium on Advanced Techniques for Molecular Imaging, December 15-16, 2007, NCHU, Taichung, Taiwan.
- 63. (Invited Speaker) Fu-Jen Kao, Implementing Time-Resolved Microscopy for Molecular Dynamics, The 5th Asian Conference on Ultrafast Phenomena in Singapore, 6~9 January 2008, Singapore.
- 64. (**Invited**) Fu-Jen Kao, Cellular Molecular Dynamics Revealed through Autofluorescence and FLIM, February 15, 2008, Swinburne University, Melbourne, Australia.
- 65. (Invited) Fu-Jen Kao, Cellular Molecular Dynamics Revealed through Autofluorescence and FLIM, March 5, 2008, University of Ottawa, Ottawa, Canada.
- 66. (**Invited**) Fu-Jen Kao, Cellular Molecular Dynamics Revealed through Autofluorescence and Fluorescence Lifetime Imaging Microscopy (FLIM), March 6, 2008, National Research Council, Ottawa, Canada.
- 67. (Invited Speaker) Fu-Jen Kao, Cellular Molecular Dynamics Revealed through Autofluorescence and FLIM, Focus on Microscopy 2008, April 13~16, 2008, Awaji, Japan.
- 68. Fu-Jen Kao, Vladimir Gukkasyan, and Po-Yen Lin, Cellular Molecular Dynamics Revealed through Autofluorescence and Fluorescence Lifetime Imaging Microscopy, ICWIP of IUPAP, October 8-10, 2008, Seoul, Korea.
- 69. (Invited Speaker) Fu-Jen Kao, Vladimir Gukkasyan, and Po-Yen Lin, Correlating Cellular Metabolic Status with the Lifetime of Autofluorescence from NADH, AOE 2008, Oct. 30 to Nov. 2, Shanghai, China.
- 70. (Invited Speaker) Fu-Jen Kao, Autofluorescence and Second Harmonic Microscopy Imaging with Time-resolved Photon Counting, 6th Advanced Imaging Methods Workshop, Jan. 21~23, 2009, UC Berkeley, California, USA.
- 71. (Invited Speaker) Fu-Jen Kao, Imaging dental sections with polarization-resolved SHG and time-resolved autofluorescence, Photonics West 2009, Jan. 24~29, 2009, San Jose, USA.
- 72. (Invited Committee Member) Fu-Jen Kao, Monitoring Cellular Metabolism with Fluorescence Lifetime of Reduced Nicotinamide Adenine Dinucleotide, Focus on Microscopy 2009, April 4~8, 2009, Krakow, Poland.
- 73. (Invited Speaker) Fu-Jen Kao, Monitoring Cellular Metabolism with Fluorescence Lifetime of Reduced Nicotinamide Adenine Dinucleotide, the 8th International Conference on Photonics and Imaging in Biology and Medicine, Aug. 8-10, 2009, Wuhan, China.
- 74. (Invited Speaker) AOE
- 75. (**Invited Speaker**) Fu-Jen Kao, Visualizing Cellular Metabolism with Fluorescence Lifetime of Reduced Nicotinamide Adenine Dinucleotide, Molecular Imaging for Systems Biology, Nov. 6, 2009, Okazaki, Japan.
- 76. (Invited Speaker) Fu-Jen Kao, Microscopy for Molecular Dynamics, Dept. of Chemistry, University of Tokyo, Nov. 9, 2009, Tokyo, Japan.
- (Invited Speaker) Fu-Jen Kao, Multiphoton Polarization Microscopy: Pushing the limits, 9th Annual Workshop on FRET Microscopy W. M. Keck Center for Cellular Imaging (KCCI) University of Virginia, Charlottesville, Mar. 8-12, 2010.
- 78. (Invited Committee Member) Fu-Jen Kao, Cellular Metabolism Revealed with Polarization Resolved Fluorescence Lifetime of NADH, Focus on Microscopy 2010, Mar. 26~28, 2010, Shanghai, China.
- 79. (Invited Speaker) Fu-Jen Kao, Monitoring Cellular Metabolism with Polarization Resolved Autofluorescence Lifetime of NADH the 4th Advanced Optical Methods Workshop, May 19~21, 2010, Shenzhen, China.

- 80. (Invited Speaker) Fu-Jen Kao, Long-distance Fluorescence Lifetime Imaging Using Stimulated Emission_ a Feasibility Study W. M. Keck Center For Cellular Imaging (Kcci) University of Virginia, Charlottesville, Mar. 8-13, 2011.
- 81. (Invited Committee Member) Fu-Jen Kao, Long-distance Fluorescence Detection Using Stimulated Emission, Focus on Microscopy 2011, Apr. 17~20, 2011, Konstanz, Germany.
- (Invited Speaker) Fu-Jen Kao, Coming opportunities for nonlinear optical microscopy with focus on molecular dynamics imaging, 2011 International Conference on Functional Optical Imaging (FOI '11), Ningbo, China, Dec. 3-4, 2011
- 83. (Invited Committee Member) Fu-Jen Kao, Long Working Distance Fluorescence Lifetime Imaging through Stimulated Emission, Focus on Microscopy 2012, Apr. 1~4, 2012, Singapore.
- 84. (Invited Speaker) Fu-Jen Kao, Long working distance fluorescence lifetime imaging through stimulated emission, the 5th Advanced Optical Methods Workshop, May 9~11, 2012, Shenzhen, China.
- 85. (Invited Speakers) Fu-Jen Kao, Fluorescence Lifetime Imaging at Long Working Distance through Stimulated Emission, The International Summer Course and Workshop on Single Molecule/Nanoparticle Spectroscopy and Imaging, NTHU/NCTU Frontier Research Center on Fundamental and Applied Sciences of Matters, June 25-28, 2012.
- 86. (Invited Speaker) Fu-Jen Kao, Long Working Distance Fluorescence Lifetime Imaging through Stimulated Emission, Biomedical Molecular Imaging 2012 & The Second Molecular Imaging Center Symposium, Naluwan Resort Hotel, Wulai Dist., New Taipei City, Taiwan, Dec. 10-11, 2012.
- (Invited Speaker) Fu-Jen Kao, Pump-probe based FLIM revisited, 12th Annual Workshop on FRET Microscopy W. M. Keck Center for Cellular Imaging (KCCI), University of Virginia, Charlottesville, USA, Mar. 11-16, 2013.
- 88. (**Invited Speaker**) Fu-Jen Kao, Enhancing Stimulated Emission based Fluorescence Detection with Interferometric Setup, The 1st Taiwan-Korea Bilateral Biophysics Conference, Jun. 26, 2013.
- 89. (**Program Chari**) Fu-Jen Kao, The 2nd BioPhotonics Conference, National Taiwan University, Taipei, Taiwan, July 16-19, 2013.
- 90. (Invited Speaker) Fu-Jen Kao, 生醫影像科技推進現代科學新里程, 次世代細胞分子影像產業發展趨勢研討 會 by ITRI, Taipei, Taiwan, Sep. 11, 2013.
- 91. (**Invited Speaker**) Fu-Jen Kao, Enhancing Stimulated Emission based Fluorescence Detection with Interferometric Setup JSAP-OSA Joint Symposium, Kyoto, Japan, Sep. 16-19 2013.
- 92. (**Invited Speaker**) Fu-Jen Kao, Stokes' vector based polarization resolved second harmonic generation microscopy, 第三届海峡两岸生物医学光学/生医光电学术研讨会, Shenzhen, China, Sep. 23-24, 2013.
- 93. (Invited Speaker) Fu-Jen Kao, Long Working Distance Fluorescence Lifetime Imaging through Stimulated Emission, Annual Symposium on Biomedical Engineering and Technology, National Tsing Hwa University, Hsin-Chu, Taiwan, Nov. 15-16, 2013.
- 94. (Invited Speaker) Fu-Jen Kao, Enhancing Stimulated Emission based Fluorescence Detection with Interferometry2nd DYCE-ASIA Workshop / ISSP International Workshop on "Life Science and Photonics", The University of Tokyo, Kashiwa, Chiba, Japan, Dec. 17-18, 2013.
- 95. (Invited Speaker) Fu-Jen Kao, Enhancing stimulated emission-based fluorescence detection with interferometric setup, BiOS, Photonics West, San Francisco, USA, Feb. 1-6, 2014.
- 96. (Invited Speaker and Session Chair) Fu-Jen Kao, Recent development in endoscopic surgery at NYMU, Japan Taiwan Bilateral Conference on Biomedical and Plasmonic Imaging, NTU, Taipei, Taiwan, Apr. 13~16, 2014.
- 97. (Invited Committee Member) Fu-Jen Kao, Stimulated emission-based fluorescence detection enhanced with interferometric setup, Focus on Microscopy 2014, Sydney, Australia, Apr. 13~16, 2014.
- 98. (Invited Speaker) Fu-Jen Kao, LED lighting for Video-Assisted Thoracic Surgery, 2014 Biomedical Electronics EMC Workshop, Taipei, Taiwan, May 23, 2014.
- 99. (**Invited Speaker**) Fu-Jen Kao, Stimulated Emission based Fluorescence Detection, Advanced Imaging Workshop in Shenzhen, Shenzhen, China, Jul. 14-16, 2014.
- 100.(**Invited Speaker**) Fu-Jen Kao, On how to interact with male colleagues_ a male's point of view, 5th IUPAP International Conference On Women In Physics, Waterloo, Canada, Aug. 5-8, 2014.
- 101.(**Invited Speaker**) Fu-Jen Kao, Stimulated Emission Based Fluorescence Detection, The 15th RIES International Symposium 'Hibiki', Hokkaido University, Sapporo, Japan, Dec. 15-16, 2014.
- 102.(**Invited Speaker**) Fu-Jen Kao, Recent Developments in Endoscopy at NYMU, RSE-MOST Bilateral Workshop, Edinburgh, Scotland, UK, Jan. 7-8, 2015.
- 103.(Fellow) Fu-Jen Kao, Revealing starch denaturation with SHG microscopy, BiOS, Photonics West, San Francisco, USA, Feb. 7-12, 2015.
- 104.(Invited Speaker) Fu-Jen Kao, Stimulated emission based fluorescence detection, International Symposium on Frontiers in Bioimaging" at the Institute of Atomic and Molecular Sciences (IAMS), Academia Sinica, October 26-27th, 2015, Taipei, Taiwan.
- 105.(Chair and Organizer) Fu-Jen Kao, Focus on Microscopy 2016, Taipei, Taiwan, Mar. 23-26, 2016.
- 106.(**Invited Speaker**) Fu-Jen Kao, Stimulated emission based fluorescence detection, BIOMATSEN2016, İstanbul, Turkey, Jun. 1-3, 2016.

- 107.(Committee Member) Fu-Jen Kao, Fiber Based Illumination for Miniature Endoscopy, The 77th Autumn Meeting of JSAP, Niigata, Japan, Sep. 13~16, 2016.
- 108.(Invited Speaker) Fu-Jen Kao, Stimulated emission based fluorescence detection, IWAMSN2016, Halong Bay, Vietnam, Nov. 8~12, 2016.
- 109.(Keynote Speaker) Fu-Jen Kao, Stimulated Emission and Pump-Probe Microscopy, International Conference on Light and Light based technologies, Tezpur University, Assam, India, Nov. 26~28, 2016.
- 110.(**Invited Speaker**) Fu-Jen Kao, Stimulated emission based fluorescence detection, Asia Student Photonics Conference, Manipal University, Manipal, India, Dec. 12-14, 2016.
- 111.(Committee Member) Fu-Jen Kao, Fiber Based Illumination for Miniature Endoscopy, Focus on Microscopy 2017, Apr. 9~12, 2017.
- 112.(**Plenary Speaker**) Fu-Jen Kao, Stimulated Gain and Spontaneous Loss Imaging in Pump-Probe Microscopy, The 2nd International Forum on Surface and Microscopy, Harbin, China, Aug. 8-9, 2017.
- 113.(**Invited Speaker**) Fu-Jen Kao, A Flashback on Pump-Probe Microscopy, International Nanophotomics Symposium (IP2017), Ito, Japan, Aug. 25-27, 2017.
- 114.(**Plenary Speaker**) Fu-Jen Kao, Pump-Probe Microscopy with Stimulated Emission Modulation, Fifth International Meeting on Frontiers of Physics (IMFP2017), Kuala Lumpur, Malaysia, Dec. 3-7, 2017.
- 115. (Committee Member) Fu-Jen Kao, Polarization resolved second harmonic microscopy, Photonics West 2018, Jan. 26-Feb.2, 2018.
- 116. (Committee Member) Fu-Jen Kao, Fiber Based Illumination for Miniature Endoscopy, Focus on Microscopy 2018, Apr. 9~12, 2018.
- 117.(**Plenary Speaker**) Fu-Jen Kao, Conceiving the Future of Optical Microscopy, International Symposium on Advances in Biomedical Optics and Applications, Manipal, India, Mar. 21-22, 2018.
- 118.(Invited Speaker) Fu-Jen Kao, Time resolved imaging with stimulated Emission in Pump-Probe Microscopy, 12th Workshop And Conference On Advanced Multiphoton And Fluorescence Lifetime Imaging Techniques: Flim 2018, Max Born Institute, Berlin-Adlershof, Germany, June 15 – 16, 2018.
- 119. (Invited Speaker) Fu-Jen Kao, Time resolved imaging with stimulated Emission in Pump-Probe Microscopy, 20th Anniversary International Conference on Transparent Optical Networks ICTON 2018, Bucharest, Romania, July 1-5, 2018
- 120. (Plenary Speaker) Fu-Jen Kao, Coherent narrow-band light source for ultraslim endoscopes, 10th International Symposium on Precision Engineering Measurements and Instrumentation, Kunming, China, Aug 8-10, 2018.
- 121. (Special Lecture Speaker) Fu-Jen Kao, Stimulated emission, a novel modality for fluorophore detection, 2018 NAIST Symposium, Nara, Japan, Nov. 26-27, 2018.
- 122. (Plenary Speaker) Fu-Jen Kao, Stimulated emission, a novel method for fluorophore detection, IONS@School of Life Sciences, MAHE, Manipal, India, January 11-14, 2019
- 123. (Invited Speaker) Fu-Jen Kao, OTG based mobile endoscopy, COST meeting "Multimodality in laser scanning microscopy based on far field and near field", Polytechnic University of Bucharest, Bucharest, Romania, Apr. 10-11, 2019.
- 124. (Invited Committee Member) Fu-Jen Kao, Definition Stimulated Emission Microscopy with Synchronized Subharmonic Modulation, Focus on Microscopy 2019, London, United Kingdom, April 14-17, 2019.
- 125. (Invited Speaker) Fu-Jen Kao, Mobile (phone based) Endoscopy and Microscopy, The 8th International Summer Course on Nano Material Discovery, NCTU, Hsin-Chu, Taiwan, June 24-26, 2019.
- 126. (Invited Speaker) Fu-Jen Kao, Pump-probe Microscopy with Stimulated Emission, The 9th WACBE World Congress in Bioengineering, National Taiwan University, Taipei, Taiwan, August 16-19, 2019.
- 127. (Keynote Speaker)) Fu-Jen Kao, Synchronized Subharmonic Modulation in Stimulated Emission Microscopy, International Forum on Microscopy 2019, Beijing, China, September 6-8, 2019.
- 128. (Invited Speaker) Fu-Jen Kao, Synchronized Subharmonic Modulation in Stimulated Emission Microscopy, BioPhotonics 2019: The 4th International Conference on Biophotonics, National Taiwan University, Taipei, Taiwan, Sep. 15-18, 2019.
- 129. (Invited Speaker) Fu-Jen Kao, Synchronized Subharmonic Modulation in Stimulated Emission Microscopy TOIN Biomedical Engineering Symposium, TOIN, Yokohama, Japan, November 15-16, 2019.
- 130. (Invited Speaker) Fu-Jen Kao, Pump-probe Microscopy with Stimulated Emission, APPC 2019:14th Asia-Pacific Physics Conference, Kuching, Malaysia, November 16-21, 2019.
- 131.(**Invited Speaker**) Fu-Jen Kao, Synchronized subharmonic modulation in stimulated emission microscopy, Photonics West 2020 of SPIE, San Francisco, USA, February 1-6, 2020.
- 132.(**Invited Speaker**) Fu-Jen Kao, Synchronized subharmonic modulation in stimulated emission microscopy, ACS Fall 2020 National Meeting & Exposition in San Francisco, CA, August 17-20, 2020. Online
- 133.(**Invited Speaker**) Fu-Jen Kao, Advances in nonlinear optical microscopy, Webinar on Light-Matter Interaction for Biophysics Research, Manipal, India, December 22, 2020. Online
- 134.(Committee Member) Fu-Jen Kao, Microcirculation Diagnosis with Synchronous Electrocardiography Capturing and Contrast Enhancing Illumination, Focus on Microscopy 2021, Amsterdam, Netherland, March 28~31, 2021. Online

135.(Inaugural Talk) Fu-Jen Kao, Shedding light on Photonics Materials and Devices, Workshop on "Applications of Laser Based Imaging in Material Science (ALBIMS)", Jagannath Baruah College, Assam, India, 11-12 March, 2022. Online

Appendix 5: Patents

- 1. 00388575 of Taiwan, ROC, pulsed green light laser pointer, NSC86-2622-E-110-006, 2000/04/21.(Model patent)
- 2. <u>00424354</u> of Taiwan, ROC, Frequency stabilized passive Q-switch laser, 2001/03/01.(Invention)
- 3. <u>00425740</u> of Taiwan, ROC, Two-mirror stereo ring resonant cavity, NSC86-2622-E-110-006, 2001/03/11. (Invention)
- 4. US Patent 6,335,942 B1, Frequency stabilized passively Q-switched laser, Jan 1, 2002.
- 5. New invention I222539 of Taiwan, ROC, Confocal fiber coupling for micro-spectroscopy, 2004/10/21.
- 6. -I222539- A confocal microscopic fiber coupling system, 2004/10/21
- 7. -I252312- Realtime microparticle sorting/manipulation system, 2006/04/01
- 8. -I257204- Weak signal scanning microscopy, 2006/06/21
- 9. -I257268- Time-resolved electro-luminescence mapping microscopy, 2006/06/21
- 10. -I266892- Variable scanning rate optical beam induced current microscopy, 2006/11/21
- 11.-M331881- A multi-function lighting and warning mosquito expeller, 2008/05/11
- 12. -M340042- Micro-heatpipe based cold and hot pad, 2008/09/11
- 13. -M345495- Clothe having temperature-controlling device based on solar energy, 2008/12/01
- 14. -I306949- Methods and instruments for carrier diffusion measurement in semiconducting photonics devices, 2009/03/01
- 15. -M357865- Laser emission device, 2009/06/01
- 16. -I315690- A confocal plane imaging feedback optical system and method for laser engraving, 2009/10/11
- 17. -I329207- Modulation differential confocal microscopy, 2010/08/21
- 18. -I329010- Micro heat pipe based hot pad, 2010/08/21
- 19. -I338117- Oven based on diode with function of partial heating, 2011/03/01,097110306
- 20. -I348889- Pest collection device 2011/09/21 097144337
- 21. -M414765- Micro generator system 2011/10/21 100209411
- 22. -I355259- Confocally coupled fiber based spectrometer attachment for slit lamp, 2012/01/01 097146129
- 23. -I376080- Magnetic induction and energy storage system, apparatus and use thereof, 2012/11/01 097119497
- 24. -I385251- Transfection with micro explosion enacted by coated dry ice particles 2013/02/11 099124780
- 25. -I415007- Induction charged RFID system and execute method thereof 2013/11/11 098131503
- 26. -I463131- Optical detection system, 2014/12/01, 100134854

Appendix 6: Technical Reports and Domestics Journals

- 1. Fu-Jen Kao, Introduction to Optical Parametric Oscillator, Physics BiMonthly, 16 (4), p445-452, 1994.
- 2. Fu-Jen Kao, Applications of Ultrafast Laser in Confocal Microscopy, Instruments Today 17(6), p19-24, 1996.
- 3. Sheng-Lung Huang, Fu-Jen Kao, and Hong-Sheng Hsieh, Small Frame Green Laser, Engineering Communiqué, Vol.21, 1996.
- 4. Yung-Shun Wang, Cheng-Yu Wang, and Fu-Jen Kao, Nonlinear Optics in Confocal Microscopy, Physics BiMonthly, 20 (6), p632-639, 1998.
- 5. Fu-Jen Kao and Yung-Shun Wang, Introduction to Two-Photon Confocal Microscopy, Optics News, 76, p14-19, 1999.
- 6. Mou-Kuo Huang, Yung-Shun Wang, Cheng-Yu Tsai, and Fu-Jen Kao, Characteristics and Applications of Twophoton confocal microscopy, Vol 21(2), p56,-66, 1999.
- 7. Fu-Jen Kao, Two-photon micro-spectroscopy, Engineering Communiqué, Vol.47 (Cover), 2000.
- 8. Yi-Ming Wang, Liang-An Wei, and Fu-Jen Kao, Notes on Recent Developments of Confocal Microscopy, BiMonthly, 23 (2), p329-334, 2001.
- Fu-Jen Kao and Chia-Li Yeh, Applications of Confocal Microscopy on Bio-Medical Related Studies I, Optics News, Vol. 96, p10-13, 2002.
- 10. Fu-Jen Kao and Chia-Li Yeh, Applications of Confocal Microscopy on Bio-Medical Related Studies II, Optics News, Vol. 98, p34-39, 2002.
- 11. Fu-Jen Kao and He-Che Kuo, Micro-spectroscopy of Single Cells under 1-photon and Two-photon Excitation, Instruments Today, Vol.25 (5), p22-31, 2004.

Appendix 7: NSC Projects

NSC83-0208-M-110-050 Time-resolved scanning probe microscopy

- NSC84-2216-E-110-018 Investigation of the fundamental photonics properties of conjugated polymer: Subproject 4, 84-631.
- NSC85-2112-M-110-003 Observation of quantum confined structures with spectrally resolved microscopy, 85-656.

NSC85-2216-E-110-020 Investigation of the fundamental photonics properties of conjugated polymer: Subproject 5, optical probing of conjugated polymer based devices' interfaces, 85-671.

NSC86-2112-M-110-010 Probing of thin films with confocal microscopy and fiber based light sources, 85-652.

NSC86-2216-E-110-006 Investigation of the fundamental photonics properties of conjugated polymer: Subproject 5, optical probing of conjugated polymer based devices' interfaces and defects, 86-612

NSC86-2622-E-110-006 Development of small frame diode pumped solid state laser (2/3), Co-PI.

NSC87-2622-E-110-002 Development of small frame diode pumped solid state laser (2/3), Co-PI.

NSC87-2112-M-110-016 Investigation of thin film based micro-structure with confocal microscopy and ultrafast laser (1/3)

NSC88-2112-M-110-002 Investigation of thin film based micro-structure with confocal microscopy and ultrafast laser (2/3)

NSC88-2216-E-110-002 Investigation of the fundamental photonics properties of conjugated polymer: Subproject 5, OBIC microscopy of conjugated polymer based devices as a function of temperature.

NSC89-2112-M-110-016 Investigation of thin film based micro-structure with confocal microscopy and ultrafast laser

(3/3) NT\$784.400

NSC89-2216-E-110-003 Investigation of the fundamental photonics properties of conjugated polymer: Subproject 5, OBIC microscopy of conjugated polymer based devices as a function of temperature. NT\$608,400

NSC89-2112-M-110-027 RF OBIC and two-photon induced photo-damage

NSC90-2112-M-110-010 SH microscopy, NT\$1,572,400

NSC91-2736-L-110-001 Localized SPR based microscopic bio-sensing, NT\$2,246,900

NSC91-2112-M-110-009 Development and applications of advanced laser scanning microscopy (1/3), NT\$2,366,400

NSC92-2112-M-110-004 Development and applications of advanced laser scanning microscopy (2/3), NT\$2,016,400

NSC93-2112-M-110-002 Development and applications of advanced laser scanning microscopy (3/3), NT\$1,465,600

NSC93-2622-E-110-015-CC3 Non-contact and variable scan rate OBIC microscopy, NT\$337,900

NSC94-2112-M-110-017- Development of time-resolved microscopy (1/3), NT\$4,342,000

NSC95-2112-M-010-001- Development of time-resolved microscopy (2/3), NT\$1,964,000

NSC 96-2112-M-010-001- Development of time-resolved microscopy (3/3), NT\$1,917,000

NSC95-3112-B-010-015- Multiple modality microscopy imaging platform (1/3), NT\$4,001,000

NSC96-3112-B-010-008- Multiple modality microscopy imaging platform (2/3), NT\$3.862.000

NSC97-3112-B-010-006- Multiple modality microscopy imaging platform (3/3), NT\$1,223,000

NSC97-2112-M-010-002-MY3- A unified ultrasensitive multiphoton multidimensional imaging platform for autofluorescence based diagnosis and imagingNT\$5,816,000

NSC98-2112-M-010-001-MY3, Digital FLIM-CARS Microscopy: Elucidating Hepatitis C Host-Virus Dynamics, NT\$10,138,000

MOST101-2321-B-075-003-,以感應驅動 LED 為腔體微創手術之背景照明光源, 2012/03/01~2013/02/28, Co-I, NT\$1,000,000

MOST101-2627-M-010-002-整合分子影像與生物科技研發以 VEGF-EGF 融合蛋白為基礎之腫瘤診斷與治療藥物 -血管内皮生長因子與表皮生長因子融合蛋白的分子動力研究與結構分析(子計畫二)(3/3),

2012/08/01~2013/07/31, PI, NT\$1,302,000

MOST102-2622-M-010-001-CC2 多功能數位顯微鏡(1/2), 2013/02/01~2014/05/31, PI, NT\$667,000

MOST102-2112-M-010-003-MY3 同調螢光偵測與生命期影像, 2013/08/01~2016/07/31, PI, NT\$5,438,000

MOST103-2114-M-174-001-全國性學術團體辦理學術推廣業務計畫(中華民國物理學會), PI,

2014/01/01~2014/12/31, NT\$2,700,000

MOST104-2911-I-010-510-分子指紋顯微鏡用於生物和地質光子學(1/1),龍門計畫(補助任務導向型團隊赴國外 研習)

MOST104-2114-M-174-001-全國性學術團體辦理學術推廣業務計畫(中華民國物理學會), 2015/01/01~2015/12/31, PI. NT\$2.700.000

MOST105-2112-M-010-001-MY3 激發放射之深層與共軛焦成像, 2016/08/01~2019/07/31, PI, NT\$6,348,000

MOST106-2911-I-010-505-雙邊研究計畫(科技部與英國愛丁堡皇家學院國際合作人員交流計畫), 高成本效益之 光譜解析醫學影像 2016/04/01 ~ 2018/03/31, PI, NT\$480,000

MOST108-2112-M-010-001-受激放射光子計數顯微術, 2019/08/01~2022/07/31

MOST109-2927-I-010-502先端之海洋顏色遙感技術於濕地測繪和基於自發螢光與受激發射的葉綠素濃度監測 109/04/01~111/3/31, PI, NT\$480,000

Appendix 8: Technology and Methodology developed

- 1991 CPM based high power femtosecond amplified dye laser system, Cornell University, U.S.A.
- 1992 Time-of-flight pulse counting mass spectrometer, Cornell University, U.S.A.
- 1994 Picosecond KTP based optical parametric oscillator synchronously pumped by mode-locked Ti:sapphire laser, IAMS, Academia Sinica, Taiwan.

- 1994 Actively mode-locked diode-pumped Nd:YLF laser, National Sun Yat-sen University, Taiwan.
- 1995 CW diode-pumped Nd:YVO4 laser, National Sun Yat-sen University, Taiwan.
- 1995 Spectrally resolved confocal microscope, National Sun Yat-sen University, Taiwan.
- 1996 Pulse counting based and spectrally resolved confocal microscope, National Sun Yat-sen University, Taiwan.
- 1996 Optical beam induced contrast (OBIC) imaging by laser scanning microscope, National Sun Yat-sen University, Taiwan.
- 1996 Coherent bundled-fiber based endoscope for oral imaging, National Sun Yat-sen University, Taiwan.
- 1997 High extinction ratio polarization sensitive laser scanning microscope, National Sun Yat-sen University, Taiwan.
- 1997 Green (532 nm) battery powered laser pointer, National Sun Yat-sen University, Taiwan.
- 1998 A high performance two-photon confocal microscope, National Sun Yat-sen University, Taiwan. (The first successful installation in Taiwan)
- 1998 Ultrahigh sensitivity laser fluorescence microscope with liquid nitrogen cooled CCD camera, National Sun Yat-sen University, Taiwan.
- 1999 Two-photon photocurrent laser scanning microscope, National Sun Yat-sen University, Taiwan. (The first successful installation in Taiwan)
- 2000 Two-photon excitation micro-spectroscopy, National Sun Yat-sen University, Taiwan.
- 2001 Optical beam induced current microscopy at radio frequency, National Sun Yat-sen University, Taiwan.

(The first successful installation in the world)

- 2002 Dithered beam differential microscopy, National Sun Yat-sen University, Taiwan.
- 2003 Harmonic generation microscopy, National Sun Yat-sen University, Taiwan.
- 2004 Fluorescence Lifetime Imaging Microscopy, National Yang Ming University, Taiwan (**The first successful installation in Taiwan**)
- 2005 RF OBIC microscopy with frequency domain technique, National Sun Yat-sen University, Taiwan.
- 2006 Modulation differential confocal microscopy, National Yang-Ming University, Taiwan.
- 2007 Micro-laser incision and welding platform, National Yang-Ming University, Taiwan.
- 2008 Four-channel Fluorescence Lifetime Imaging Microscope, National Yang-Ming University, Taiwan.
- 2009 CARS-FLIM platform, National Yang-Ming University, Taiwan.
- 2010 Lifetime Resolved Stimulated Emission Depletion Microscope, National Yang-Ming University, Taiwan.
- 2011 Stokes' Vector based Multiphoton Polarization Microscope, National Yang-Ming University, Taiwan.
- 2012 Long Working Distance Stimulated Fluorescence Imaging, National Yang-Ming University, Taiwan
- 2013 Induction LED lighting for endoscopic illumination, National Yang-Ming University, Taiwan
- 2014 Polarization Resolved Second Harmonic Microscopy, National Yang-Ming University, Taiwan
- 2015 Supercontinuum for endoscopy illumination, National Yang-Ming University, Taiwan
- 2016 Background free Long Working Distance Stimulated Fluorescence Imaging, National Yang-Ming University, Taiwan
- 2017 Coherent light source for endoscopy illumination, National Yang-Ming University, Taiwan
- 2018 Time-lapsed RGB illumination for ultrathin endoscopy, National Yang-Ming University, Taiwan
- 2019 Photon counting based stimulated emission, National Yang-Ming University, Taiwan
- 2020 Synchronized Schlieren imaging of pulsed ultrasound, National Yang-Ming University, Taiwan

Shedding new light on multiphoton microscopy in biomedical research Associate Professor Guan-Yu Zhuo

Abstract

Multiphoton microscopy (MPM) has transformed biomedical research by enabling unprecedented exploration of cellular and subcellular structures within live tissues and animals. The objective of this presentation is to offer fresh insights into the principles, applications, and advancements of MPM, underscoring its immense potential for illuminating the complexities of biological systems and biomedical fields. We will commence by elucidating the historical view of MPM development, encompassing the concept of multiphoton excitation and its superiorities over traditional imaging techniques. Subsequently, we will delve into the diverse biomedical applications of MPM in our laboratory, spanning the studies of precise tissue imaging with polarization-resolved second harmonic generation (P-SHG) microscopy, heterodimerization of receptor proteins in the cell membrane with multiphoton fluorescence microscopy, exploration of tumor microenvironments with multimodalities of MPM, etc. Furthermore, we will examine cutting-edge technological innovations and experimental techniques that have expanded the capabilities of MPM, including label-free imaging approaches, fiber optics, spectral filtering, and artificial intelligence (AI) technologies. By exploring the current challenges and future prospects of MPM, we will emphasize the significant impact of this imaging modality in comprehending complex biological phenomena and driving discoveries across various biomedicine domains. In summary, this presentation aims to deliver a comprehensive overview of multiphoton microscopy, underscoring its significance as a powerful tool for unraveling the intricacies of life at the microscopic scale and propelling breakthroughs in biomedical research.

Curriculum Vitae

Guan-Yu Zhuo (卓冠宇), Ph.D.

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2007-2012

EDUCATION

Ph.D. in Physics, National Taiwan University (Taiwan) Biomedical Optics Lab, Prof. Shi-Wei Chu

Ph.D. thesis: Observation of Molecular Information at Nanometer Scale by Polarization Resolved-Second Harmonic Generation Microscopy (PSHM)

2012 Dean of Science Award in National Taiwan University

Master in Physics, National Chung Cheng University (Taiwan)2005-2007Bachelor in Physics, National Chung Cheng University (Taiwan)2001-2005

RESEARCH INTERESTS

***** Development of the next generation microscopy imaging methods

- * Artificial intelligence (AI) in digital pathology for diagnosis and precision oncology
- * Quantum enhanced imaging: nonlinear optics combined with quantum interference
- * A wearable miniscope for multiregion neural circuit investigations
- Label-free multimodal nonlinear optical microscopy for biomedical applications
 - * This study provides comprehensive insight into the physiochemical properties related to 3D molecular orientation, inter- and intramolecular interactions and disease progression in biological tissues or organs.
- * Superresolution optical imaging by reversible and saturable molecular switch
 - * Seeking an efficient molecular switch to suppress the optical signal within a submicrometer spatial domain and to increase the spatial resolution. The working principle is similar to RESOLFT.
- * 3D label-free single-particle tracking in living cells
 - * Interferometric light scattering and ultrahigh-speed image acquisition are used to record the trajectories that account for a biological event taking place in a very short period of time, such as protein binding on the cell membrane, viral infection, and intracellular transport.

CURRENT APPOINTMENT AND WORK EXPERIENCE

Associate Professor in the Institute of Translational Medicine and New Drug Development, China Medical University, Taiwan 08/2022-present

Assistant Professor in the Institute of New Drug Development, China Medical University, Taiwan

08/2018-07-2022

Contracted Assistant Professor in the Institute of Medical Science and Technology, National Sun Yat-sen University, Taiwan 08/2016-07/2018

- * Study biomass and bioenergy by multimodal nonlinear optical microscopy (MOST 105-2112-M-110-015-MY2).
- * NSYSU-KMU JOINT RESEARCH PROJECT: Innovative optical detection of esophageal cancer and cancerous

cells (IV) (#NSYSUKMU 106-I005).

- NSYSU-KMU JOINT RESEARCH PROJECT: Innovative optical detection of esophageal cancer and cancerous cells (V) (#NSYSUKMU 107-I002).
- Biomedical applications of angle-resolved second harmonic light scattering system (MOST 107-2112-M-039-001).
- Polarization-resolved second harmonic generation (P-SHG) microscopy with a high discriminative power A new model for interpreting polarization-dependent SHG (MOST 108-2112-M-039-001, 109-2112-M-039-001).
- Multimodal nonlinear optical microscopy in studying articular cartilage regeneration and osteoarthritis (MOST 110-2923-M-039-001-MY3).
- Multimodal nonlinear endomicroscopy combined with deep learning for precision health of esophagus (MOST 110-2112-M-039-001-MY3).
- IncRNA XIST Elicited Cellular Adaptation Mechanisms Mediated by Opioid Receptors (DMR-111-060, CMUH project).
- * Potential target for treating opioid use disorders: focus on PRKAR1B (NSTC 111-2635-B-039-003).

Postdoctoral Researcher in Max Planck Institute for Polymer Research, Germany 07/2015-01/2016

* An angle-resolved second harmonic scattering system was constructed to study the enantioselective mechanism by chiral nanoparticles.

Postdoctoral Researcher at the Institute of Atomic and Molecular Sciences, Academia Sinica, Taiwan

06/2014-06/2015

 Improving optical instruments for 3D particle tracking with a localization accuracy as high as 1.6 nm in the lateral direction and 2.5 nm in the axial direction. A very fast acquisition rate on the order of GHz is implemented.

Postdoctoral Researcher in the Department of Bioengineering, California Institute of Technology, USA

11/2013-03/2014

 Multimodal nonlinear optical imaging was used to verify the structure and morphology of the self-organized long epithelial tubules when reducing cell-substrate contact dimensionality in cell-collagen interactions.

Specialties:

- * Biomedical optical imaging, microscopy system design and development
 - Multimodal nonlinear optical microscopy (Harmonic Generation microscopy, Multiphoton Fluorescence microscopy, Fluorescence Lifetime Imaging Microscopy (FLIM), Coherent Anti-Stokes Raman Scattering (CARS) microscopy, Stimulated Raman Scattering (SRS) microscopy, etc.)
 - * Confocal (Raman/fluorescence) microscopy and chromatic confocal microscopy
 - * Superresolution optical microscopy (STimulated Emission Depletion microscopy, STED and Structured Illumination Microscopy, SIM)
 - * Interferometric scattering (iSCAT) microscopy for single-particle tracking
 - * Pump-probe optical microscopy
 - * Angle-resolved second harmonic scattering system
- Biomedical image processing and analysis

Teaching experience:

- * For undergraduate and graduate courses at National Sun Yat-sen University and China Medical University
 - * Biomedical Optical Imaging Techniques
 - * Experimental Optoelectronics

- * Lasers for Medical Applications
- * Medical Imaging System
- * Introduction to Biophotonics/Medical Engineering
- * Biomedical imaging: principals & applications
- * Photonic instruments and systems
- * Biotechnology instrumentation and application
- * Instrumental analysis and application
- * Special topics on biotechnology/biophotonics/nanomedicine/biomedical engineering/biomedical materials
- * Frontiers of biomedical imaging and nuclear medicine
- * Current biotechnology application in pharmaceutical development
- * Medical physics
- * Advanced fluorescence microscopy: practice and analysis
- * Independent Studies in Instrumentation Systems
- * Seminar

Academic service:

- * Committee membership of
 - * Optics & Photonics Taiwan, the International Conference (OPTIC 2017)
 - * The 4th IEEE International Conference on Biophotonics (ICB 2019)
 - * 2020 Annual Meeting of the Physical Society of Taiwan
 - * 2021 Annual Conference of Taiwanese Society of Biomedical Engineering (TSBME 2021)
- Guest editor for the topic "Biophotonics for cancer diagnostics and treatment" in Frontiers in Physics, the Methods Collections "Design and development of multiphoton nonlinear optical microscopy" in Journal of Visualized Experiments (JoVE), the topic "Novel Light Sources and Luminescent Materials for Biophotonic Applications" in Frontiers in Photonics
- * Patent reviewer for Center of Industry-Academia Collaboration, National Taiwan University
- * Reviewer for the Physics Subject of the National High School Science Projects 2022
- Journal reviewer for ACS Photonics, Sensors and Actuators B: Chemical, Acta Biomaterialia, Journal of Materials Chemistry C, Optics Letters, Optics Express, Biomedical Optics Express, Applied Optics, Scientific Reports, Journal of Innovative Optical Health Sciences, Journal of Microscopy, Applied Spectroscopy, Optics Communications, Optik, Frontiers In Medical Technology, Molecules, Energies, Separations, Chemosensors, Applied Sciences, Reviews in Medical Virology, Chemical Papers, etc.
- Committee membership of thesis oral defense in National Yang Ming Chiao Tung University, National Sun Yat-sen University, China Medical University, Feng Chia University, Tunghai University
- Membership of the International Ph.D. Program for Synchrotron Radiation and Neutron Beam Applications, NSYSU

2016-Present

PUBLICATIONS

Journal Articles

- (Note that "Zong-Yan Zhuo" was my former name. It was changed into "Guan-Yu Zhuo" since 2011)
- 1. M.-X. Lee, W.-H. Wang, W.-L. Chen, M.-C. Chen, C.-Y. Chou, S.-T. Lin, C.-Y. Lin, F.-J. Kao, and <u>Guan-Yu</u> <u>Zhuo</u>*, "Calibrated $\chi^{(2)}$ -tensor polarization-resolved second harmonic generation microscopy for precise tissue imaging," (Submitted, Applied Physics Letters).
- M.-C. Chen, I. Govindaraju, W.-H. Wang, W.-L. Chen, K. Mumbrekar, B. Sarmah, V. Baruah, P. Srisungsitthisunti, N. Karunakara, N. Mazumder, and <u>Guan-Yu Zhuo</u>*, "Polarization-resolved second harmonic generation microscopy of starch granules modified by gamma radiation," (Accepted, Microscopy and Microanalysis).
- M.-C. Chan, Q.-X. Liu, A. Gogoi, W.-H. Wang, C.-Y. Lin, and <u>Guan-Yu Zhuo</u>*, "Second harmonic generation laser scanning microscopy with intrinsic first-order modulation," *Opt. Lasers Eng.* 167, 107602 (2023). [IF: 5.666, Ranking: 18/101]
- <u>Guan-Yu Zhuo</u>, M.-C. Chen, T.-Y. Lin, S.-T. Lin, T.-L. Chen, and W.-S. Lee*, "Opioid-Modulated Receptor Localization and Erk1/2 Phosphorylation in Cells Coexpressing μ-Opioid and Nociceptin Receptors," *Int. J. Mol. Sci.* 24(2), 1048 (2023). [IF: 6.208, Ranking: 69/297]
- <u>Guan-Yu Zhuo</u>, S. Banik, F.-J. Kao, G. A. Ahmed, N. M. Kakoty, N. Mazumder*, and A. Gogoi*, "Optical Beam Induced Current Microscopy: Recent Advances and Applications," *Microsc. Res. Tech.*, 85(11), 3495 (2022). [IF: 2.893, Ranking: 5/21]
- I. Chakraborty, S. Banik, I. Govindaraju, K. Das, S. S. Mal, <u>Guan-Yu Zhuo</u>, M. A. Rather, M. Mandal, A. Neog, R. Biswas, V. Managuli, A. Datta, K. K. Mahato, and N. Mazumder*, "Synthesis and detailed characterization of sustainable starch-based bioplastic," *J. Appl. Polym. Sci.* 139(39), e52924 (2022). [IF: 3.057, Ranking: 43/90]
- C.-C. Chang, H.-K. Tsou, H.-H. Chang, L.-Y. Chan, <u>Guan-Yu Zhuo</u>, T. Maeda, C.-Y. Lin*, "Runx1 Messenger RNA Delivered by Polyplex Nanomicelles Alleviate Spinal Disc Hydration Loss in a Rat Disc Degeneration Model," *Int. J. Mol. Sci.* 23(1), 565 (2022). [IF: 6.208, Ranking: 69/297]
- G. Indira, <u>Guan-Yu Zhuo</u>, I. Chakraborty, S. Melanthota, S. Mal, B. Sarmah, J. Baruah, K. Mahato, and N. Mazumder*, "Investigation of Structural and Physico-chemical Properties of Rice Starch with Varied Amylose Content: A Combined Microscopy, Spectroscopy, and Thermal study," *Food Hydrocoll.* 122, 107093 (2022). [IF: 11.504, Ranking: 5/143]
- S.-Y. Chen, Z.-T. Su, D.-J. Lin, M.-X. Lee, M.-C. Chan, S. Das, F.-J. Kao*, and <u>Guan-Yu Zhuo</u>*, "Optimizing imaging depth of anisotropic scattering tissues with polarization engineered second harmonic generation microscopy," *Results Phys.* 28, 104653 (2021). [IF: 4.476, Ranking: 18/86]
- C.-W. Hung, N. Mazumder, D.-J. Lin, W.-L. Chen, S.-T. Lin, M.-C. Chan, and <u>Guan-Yu Zhuo</u>*, "Label-free characterization of collagen crosslinking in bone-engineered materials using nonlinear optical microscopy," *Microsc. Microanal.* 27(3), 587 (2021). [IF: 4.127, Ranking: 2/9] Journal cover
- <u>Guan-Yu Zhuo</u>, K. U. Spandana, K. M. Sindhoora, Y. V. Kistenev, F.-J. Kao, V. V. Nikolaev, H. Zuhayri, N. A. Krivova, and N. Mazumder*, "Label-free Multimodal Nonlinear Optical Microscopy for Biomedical Applications," *J. Appl. Phys.* **129**(21), 214901 (2021) [IF: 2.546, Ranking: 79/160] Journal cover; featured article
- A. Gogoi, S. Konwer, and <u>Guan-Yu Zhuo</u>*, "Polarimetric measurements of surface chirality based on linear and nonlinear light scattering," *Front. Chem.* 8, 1311 (2021). [IF: 5.221, Ranking: 53/178]

- M.-C. Chan, T.-H. Liao, C.-S. Hsieh, S.-C. Jeng, and <u>Guan-Yu Zhuo</u>*, "Imaging of nanoscale birefringence using polarization-resolved chromatic confocal microscopy," *Opt. Express* 29(3), 3965 (2021). [IF: 3.894, Ranking: 20/99]
- Guan-Yu Zhuo, P.-L. Tsai, H.-Y. Wang, and M.-C. Chan*, "Wave-vector-encoded nonlinear endomicroscopy," Opt. Lett. 45(13), 3713 (2020). [IF: 3.714, Ranking: 18/97]
- W.-C. Chen, Y.-J. Chen, S.-T. Lin, W.-H. Hung, M.-C. Chan, I-C. Wu, M.-T. Wu, C.-T. Kuo, S. Das, F.-J. Kao, and <u>Guan-Yu Zhuo</u>*, "Label-free characterization of collagen fibers in cancerous esophagus tissues using ratiometric nonlinear optical microscopy," *Exp. Biol. Med.* 245(14), 1213 (2020). [IF: 3.139, Ranking: 70/139]
- S.-T. Lin, W.-K. Hung, <u>Guan-Yu Zhuo</u> (co-first author), and M.-C. Chan*, "Observation of dynamic thermal lensing in an end-pumped Nd:YVO4 laser by chromatic confocal method," *Appl. Phys. Lett.* **116**(21), 211105 (2020). [IF: 3.597, Ranking: 37/155]
- S. Das, K. Rehman, <u>Guan-Yu Zhuo</u>, and F.-J. Kao*, "Spontaneous loss versus stimulation gain in pump-probe microscopy: a proof of concept demonstration," *J. Biomed. Opt.* 25(3), 036501 (2020). [IF: 2.785, Ranking: 29/97]
- I. Govindaraju, S. Pallen, S. Umashankar, S. Mal, S. Melanthota, D. Mahato, <u>Guan-Yu Zhuo</u>, K. Mahato, and N. Mazumder*, "Microscopic and spectroscopic characterization of rice and corn starch," *Microsc. Res. Tech.* 83(5), 490 (2020). [IF: 2.117, Ranking: 5/21]
- S. Das, I.-C. Chen, K. Rehman, J.-L. Hsu, <u>Guan-Yu Zhuo</u>, and F.-J. Kao*, "Background Free Imaging in Stimulated Emission Fluorescence Microscopy," J. Opt. 21, 125301 (2019). [IF: 2.753, Ranking: 30/95]
- N. Mazumder*, N. Balla, <u>Guan-Yu Zhuo</u>, Y. Kistenev, R. Kumar, F.-J. Kao, S. Brasselet, V. Nikolaev, and N. Krivova, "Label-free nonlinear multimodal optical microscopy basics, development and applications," *Front. Phys.* 7, 170 (2019). [IF: 1.895, Ranking: 36/81]
- <u>Guan-Yu Zhuo</u>, S.-W. Huang, C.-H. Lin, and S.-H. Lin*, "Wide-angle lasing from photonic crystal nanostructures of liquid-crystalline blue phase," *J. Mater. Chem. C* 7, 6433 (2019). [IF: 6.641, Ranking: 20/148] Been selected in the themed collection: Photonics
- A. Gogoi, N. Mazumder, S. Konwer, H. Ranawat, N.-T. Chen, and <u>Guan-Yu Zhuo</u>*, "Enantiomeric recognition and separation by chiral nanoparticles," *Molecules* 24, 1007 (2019). [IF: 3.060, Ranking: 67/172]
- <u>Guan-Yu Zhuo</u>, C.-H. Hsu, Y.-H. Wang, and M.-C. Chan*, "Chromatic confocal microscopy to rapidly reveal nanoscale surface/interface topography by position-sensitive detection," *Appl. Phys. Lett.* **113**, 083106 (2018). [IF: 3.495, Ranking: 29/146]
- N. Mazumder*, G. Deka, W.-W. Wu, A. Gogoi, <u>Guan-Yu Zhuo</u>, and F.-J. Kao*, "Polarization Resolved Second Harmonic Microscopy," *Methods* 128, 105 (2017). [IF: 3.802, Ranking: 21/78] Invited
- <u>Guan-Yu Zhuo</u>, H.-C. Su, H.-Y. Wang, and M.-C. Chan*, "In-situ high-resolution thermal microscopy on integrated circuits," *Opt. Express* 25, 21548 (2017). [IF: 3.307, Ranking: 17/92] Been selected for an Editor's Pick
- Y.-F. Huang, <u>Guan-Yu Zhuo</u>, C.-Y. Chou, C.-H. Lin, and C.-L. Hsieh*, "Label-free, ultrahigh-speed, 3D observation of bidirectional and correlated intracellular cargo transport by coherent brightfield microscopy," *Nanoscale* 9, 6567 (2017). [IF: 7.367, Ranking: 13/148]
- Y.-F. Huang, <u>Guan-Yu Zhuo</u>, C.-Y. Chou, C.-H. Lin, W. Chang, and C.-L. Hsieh*, "Coherent Brightfield Microscopy Provides the Spatiotemporal Resolution To Study Early Stage Viral Infection in Live Cells," ACS Nano 11, 2575 (2017). [IF: 13.942, Ranking: 4/87]
- 28. Guan-Yu Zhuo*, M.-Y. Chen, C.-Y. Yeh, C.-L. Guo, and F.-J. Kao*, "Fast determination of three-dimensional

fibril orientation of type-I collagen via macroscopic chirality," *Appl. Phys. Lett.* **110**, 023702 (2017). [IF: 3.411, Ranking: 29/148]

- <u>Guan-Yu Zhuo</u>, K.-C. Chen, K.-W. Lai, C.-R. Wang, C.-Y. Chao, and S.-W. Chu*, "Reversible suppression of second harmonic generation in dye-doped liquid crystal by light-induced thermal phase transition on sub-micrometer scale," *J. Appl. Phys.* **117**, 083103 (2015). [IF: 2.183, Ranking: 42/144]
- M.-Y. Chen, <u>Guan-Yu Zhuo</u>, K.-C. Chen, P.-C. Wu, T.-Y. Hsieh, T.-M. Liu, and S.-W. Chu*, "Multiphoton imaging to identify grana, stroma thylakoid, and starch inside an intact leaf," *BMC Plant Biol.* 14, 175 (2014). [IF: 3.942, Ranking: 22/199] Reported by Life Science Weekly
- <u>Guan-Yu Zhuo</u>, H. Lee, K.-J. Hsu, M. J. Huttunen, M. Kauranen, Y.-Y. Lin, and S.-W. Chu*, "Three-dimensional structural imaging of starch granules by second-harmonic generation circular dichroism," *J. Microsc.* 253, 183 (2014). [IF: 2.150, Ranking: 4/11] Been selected to the Encyclopedia of Analytical Chemistry 2015
- S.-W. Chu*, T.-Y. Su, R. Oketani, Y.-T. Huang, H.-Y. Wu, Y. Yonemaru, M. Yamanaka, H. Lee, <u>Guan-Yu Zhuo</u>, M.-Y. Lee, S. Kawata, and K. Fujita, "Measurement of a Saturated Emission of Optical Radiation from Gold Nanoparticles: Application to an Ultrahigh Resolution Microscope," *Phys. Rev. Lett.* **112**, 017402 (2014). [IF: 7.728, Ranking: 6/78] Highlighted by APS Physics website
- H. Lee, M. J. Huttunen, K.-J. Hsu, M. Partanen, <u>Guan-Yu Zhuo</u>, M. Kauranen, and S.-W. Chu*, "Chiral imaging of collagen by second-harmonic generation circular dichroism," *Biomed. Opt. Express* 4, 909 (2013). [IF: 3.176, Ranking: 7/80] Cover; been selected for Virtual Journal for Biomedical Optics
- Guan-Yu Zhuo, K.-J. Hsu, T.-Y. Su, N.-H. Huang, Y.-F. Chen, and S.-W. Chu*, "Effect of Lorentz local field for optical second order nonlinear susceptibility in ZnO nanorod," *J. Appl. Phys.* 111, 103112 (2012). [IF: 2.168, Ranking: 37/125]
- 35. T.-Y. Su, C.-S. Liao, C.-Y. Yang, <u>Guan-Yu Zhuo</u>, S.-Y. Chen, and S.-W. Chu*, "On the possible origin of bulk third harmonic generation in skin cells," *Appl. Phys. Lett.* **99**, 113702 (2011). [IF: 3.841, Ranking: 15/118] **Been selected for Virtual Journal of Biological Physics Research 22(7), 2011; 台灣物理研究快報**
- 36. Y.-Y. Tzeng, <u>Zong-Yan Zhuo</u>, M.-Y. Lee, C.-S. Liao, P.-C. Wu, C.-J. Huang, M.-C. Chan, T.-M. Liu, Y.-Y. Lin, and S.-W. Chu*, "Observation of spontaneous polarization misalignments in periodically poled crystals using second-harmonic generation microscopy," *Opt. Express* **19**, 11106 (2011). [IF: 3.753, Ranking: 5/78] **Been selected for Virtual Journal for Biomedical Optics**
- C.-S. Liao, <u>Zong-Yan Zhuo</u>, J.-Y. Yu, Y.-Y. Tzeng, S.-W. Chu*, S.-F. Yu, and P.-H.G. Chao, "Decrimping: The first stage of collagen thermal denaturation unraveled by in situ second-harmonic-generation imaging," *Appl. Phys. Lett.* **98**, 153703 (2011). [IF: 3.841, Ranking: 15/118] Been selected for Virtual Journal of Biological Physics Research, **21(8)**, **2011**
- 38. Zong-Yan Zhuo, C.-S. Liao, C.-H. Huang, J.-Y. Yu, Y.-Y. Tzeng, W. Lo, C.-Y. Dong, H.-C. Chui, Y.-C. Huang, H.-M. Lai, and S.-W. Chu*, "Second harmonic generation imaging A new method for unraveling molecular information of starch," *J. Struct. Biol.* 171, 88 (2010). [IF: 3.673, Ranking: 19/74] Been selected to the Encyclopedia of Analytical Chemistry 2015
- J.-Y. Yu, C.-S. Liao, <u>Zong-Yan Zhuo</u>, C.-H. Huang, H.-C. Chui, and S.-W. Chu*, "A diffraction-limited scanning system providing broad spectral range for laser scanning microscopy," *Rev. Sci. Instrum.* 80, 113704 (2009). [IF: 1.738, Ranking: 16/56]

Book Chapters

- S.-T. Lin, M.-X. Lee and <u>Guan-Yu Zhuo</u>*, (2022) Investigation of Diatoms with Optical Microscopy in: *Diatom Microscopy* [DIMI, Volume in the series: Diatoms: Biology & Applications, series editors: Richard Gordon & Joseph Seckbach], Wiley-Scrivener, Beverly, MA, USA.
- P. Dhawan, Priyasha De, K. M. Sindhoora, N. Mazumder, and <u>Guan-Yu Zhuo</u>*, (2022) Plasmonic optical imaging of biological samples in: *Recent Advances in Plasmonic Probes - Theory and Practice*, Springer Nature, London, UK.
- 3. K. N. Makkithaya, S. Nadumane, <u>Guan-Yu Zhuo</u>, S. Chakrabarty, and N. Mazumder*, (2022) Nanoparticle based collagen biomaterials for wound healing in: *Collagen Biomaterial*, IntechOpen, London, UK.
- M.-C. Chen, W.-H. Wang, G. Raju, N. Mazumder, and <u>Guan-Yu Zhuo</u>*, (2022) Polarization resolved second harmonic generation for tissue imaging in: *Optical Polarimetric Modalities for Biomedical Research*, Springer Nature, London, UK. (In press).

Elucidating the pre- and post-natal growth in teeth using multiphoton microscopy

Associate Professor Stephen HSU Chin-Ying

The global pandemic of obesity and cardiometabolic diseases (OCD) is a growing problem worldwide. Focusing on optimizing early life development has great potential to improve the health of the next generation and ameliorate the pandemic of non-communicable diseases, since the development of OCD are to be found to begin in utero and poor fetal growth (FG) has been associated with increased obesity and cardiometabolic risk in adulthood. Like annual rings in trees, the enamel and dentine of teeth contain a daily registration of their development in utero and may serve as a time-specific "fixed"/mineralized record to assess utero growth in a detailed manner. This talk will share the dental biomarkers (DBs) revealed by using the conventional imaging modalities, the limitations and challenges, followed by the potential solution provided by using multiphoton microscopy.

Name: Stephen HSU Chin-Ying

Present Appointment: Associate Professor (Department of Dentistry, National University Health System (NUHS), Faculty of Dentistry (FOD), National University of Singapore (NUS), 9 Lower Kent Ridge Road, Singapore 119085) Tel: (65) 67726832; Fax: (65) 6778-5742; E-mail: <u>denhsus@nus.edu.sg</u>

Research Interests (as clinician-scientist @ NUHS and NUS-NGS):

Bio-photonic/laser application on caries diagnosis, prevention and treatment; caries risk assessment/prediction; physicochemical characterization of dental tissues; Oral-systemic link

Teaching Areas: Cariology, Biostatistics, Community Health Study

Academic/Professional Qualifications:

- 1987: DDS, School of Dental Medicine, National Yang-Ming Medical College (NYMMC), Taipei, Taiwan
- **1991: AEGD-GPR** training, Advanced Education in General Dentistry (AGED) and General Practice Residency (GPR) training in NYMMC and Veterans General Hospital, Taipei, Taiwan
- 1994: MSc/Cert-Pedo, in Pediatric Dentistry, University of Iowa (UI), USA
- 1996: Cert DPH, in Preventive Dentistry & Dental Public Health, UI, USA
- 1997: Ph.D. Oral Science (Cariology), Dows Institute for Dental Research, UI, USA
- 1998: Fellow, American Association of Pediatric Dentistry (AAPD), USA

Awards:

- 1992 National Dean's List (USA)
- 1998 IADR/Colgate Research Award in Prevention (International Association for Dental Research, USA)
- **1998** NUS Staff Achievement Award (Singapore)
- **1999** IADR/Colgate Research Award in Prevention (USA)
- 2001 "Foundation Research Award" (AAPD, USA)
- 2003 "AAPD Award for excellence in research enhancing the specialty of Pediatric Dentistry" (USA)
- 2011 "Williams J. Gies Award" for clinical research (IADR, USA)

Team/Student Awards:

- 2001 David Scott Student Research Fellowship/Award, IADR, USA (US\$2,500)
- 2005 & 2010 Singapore Science Engineering Fair (SSEF), Gold Award
- 2006 Hatton / Unilever Travel Award, IADR, Brisbane, Australia (US\$1000)
- 2007 Lion Dental Research Award, IADR, New Orleans, USA (US\$2000)
- 2008 & 2010 NUS Outstanding Undergraduate Research Award, Singapore (S\$5000)

Career History & Service:

- 2001 Present: Member, Faculty Research Committee
- 2017 Nov Present: Member, Faculty Promotion & Tenure Committee, FOD, NUS
- 2009 July-Dec: Acting Vice Dean for research, FOD, NUHS, NUS
- 2006-2010: Director, Dental Biophotonic and Biomaterials program
- 2001-2010: Member, the University Research Committee
- 2001-present: Associate Professor, FOD, NUS; 1998-2001: Assistant Professor, Department of Preventive Dentistry, NUS
- 1997-1998: Lecturer, Department of Preventive Dentistry, NUS
- 1995-1997: Adjunct Assistant Professor, Department of Pediatric Dentistry, UI, USA

Major Research Grants: (PI: 16 grants totaling \$3,284,574; Collaborator: 5 grants totaling \$1,531,783)

- PI of BIGHEART (Biomedical Institute for Global Health Research and Technology) Grant: BIG2017-33 (S\$200,000) "Novel Living Water to Save Dental Implants" Nov2017-Oct2019
- PI of NMRC (National Medical Research Council) Grant: CIRG12may049 (S\$929,966 +20% indirect costs) "Building Oral Microbiome to Identify Novel Biomarkers/Modulators for Early Childhood Caries and Oral-Systemic Link" 2012-2017
- PI of BMRC (Biomedical Research Council) Grant: R-222-000-015-305 (\$\$799,450): "Innovative non-invasive laser treatment for prevention of enamel demineralization (tooth decays)" 2003-2007

Selected Publications (65 international peer-reviewed journal articles, 2 book chapters): ORCID

- Tan, G.-R., <u>Hsu, C.-Y. S.*</u> & Zhang, Y. pH-Responsive Hybrid Nanoparticles for Imaging Spatiotemporal pH Changes in Biofilm-Dentin Microenvironments. ACS Applied Materials & Interfaces 13, 46247–46259 (2021). (IF 10.383)
- Kalhan, T. A., ..., <u>Hsu, C.-Y. S.*</u> Caries Risk Prediction Models in a Medical Health Care Setting. *Journal of Dental Research* 99, 787–796 (2020). (IF 8.924)
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