BIOGRAPHICAL SKETCH

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NAME: Liu, Jonathan T.C.

eRA COMMONS USER NAME (credential, e.g., agency login): LIU.JONATHAN

POSITION TITLE: Professor of Pathology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Princeton University, Princeton, NJ	B.S.E.	06/1999	Mechanical Engineering
Stanford University, Stanford, CA	M.S.	06/2000	Mechanical Engineering
Stanford University, Stanford, CA	Ph.D.	01/2005	Mechanical Engineering & Laser Diagnostics
Molecular Imaging Program at Stanford (MIPS), Stanford, CA	Postdoctoral	08/2009	Biomedical Optics & Molecular Imaging

A. Personal Statement

The molecular biophotonics lab, directed by Dr. Liu, develops optical-imaging solutions to guide clinical decisions. This includes custom 3D microscopy devices and computational analysis strategies for early disease detection, risk stratification, and surgical guidance. These projects leverage Dr. Liu's multidisciplinary expertise in optical instrumentation, machine learning, spectroscopy, molecular imaging, tissue processing, and clinical translation. Dr. Liu is a co-founder and board member of Alpenglow Biosciences Inc., which has commercialized the 3D pathology technologies developed in his lab.

Relevant funded projects:

PSI-030 08/15/24 – 08/14/29
ARPA-H Precision Surgical Interventions (PSI) program
Comprehensive multi-resolution histology of surgical margin surfaces with volumetric co-registration
Our goal is to develop an intraoperative "flatbed scanner" located within the operating room to comprehensively image the margin surfaces of fresh surgical specimens within 15 min of excision. To realize this speed, an AI-guided multi-resolution imaging workflow will be developed. Clinical validation will be performed on breast lumpectomies and head & neck cancer resections.
Role: PI

R01 CA268207 (Liu, Grady, and Mahmood) 05/01/24 – 04/30/29
NIH / NIDDK
Computational 3D pathology for Barrett's esophagus risk stratification
Major goals are to develop computational 3D pathology assays for risk stratification of Barrett's esophagus patients based on examination of their endoscopic biopsies. Aim 1 (standardization and quality control) – to develop a 3D pathology pipeline to enable reproducible (>95% yield) generation of clinical grade 3D datasets; Aim 2 (AI triage to assist pathologists) – to develop weakly supervised deep-learning triage methods, based on annotated 2D image levels within 3D pathology datasets, for time-efficient pathologist interpretation of 3D pathology datasets; and Aim 3 (AI decision support) – to develop weakly supervised deep learning, based on patient outcomes, for fully computational risk stratification of putative low-grade patients.
Role: PI

R01 CA268207 (Liu and Madabhushi) 07/01/22 – 06/30/27
NIH / NCI
Prostate cancer risk stratification via computational 3D pathology
This collaborative project will develop foundational methods and machine classifiers based on hand-crafted 3D features (from tissues structures segmented in 3D) to guide clinical treatment decisions for patients with low- to intermediate-risk prostate cancer. In particular, the Prostate cancer Image Risk Score via 3D pathology (ProsIRiS3D) will be provide guidance for placing patients on active surveillance (Aim 2) and for treating patients with adjuvant therapy after prostatectomy (Aim 3).
Role: PI

R01 EB031002 (Liu) 07/01/21 – 06/30/25 (NCE to 2026)
NIH / NIBIB
Instrumentation platform for 3D pathology with open-top light-sheet (OTLS) microscopy
A combination of technologies will be developed to advance the nascent field of non-destructive 3D pathology. Innovations include (1) a multi-resolution hybrid OTLS microscope for time-efficient analyses of large clinical specimens, (2) tools for automation of tissue-labeling and clearing processes, and (3) post-imaging methods for image-guided macro-dissection of thick tissues for downstream genomics assays. Collectively, our project aims are designed to extend current 2D pathology workflows into 3D to minimize clinical-adoption barriers.
Role: PI

R01 CA244170-01 (Liu and Sanai) 06/01/20 – 05/31/25 (NCE to 2026)
NIH / NCI
In vivo dual-axis confocal microscopy of 5-ALA-induced PpIX to guide low-grade glioma resections
Academic-Industry Partnership (AIP) grant, with Leica Microsystems Inc. to develop a handheld surgical microscope to guide the resection of low-grade gliomas (LGG). In vivo images of 5-ALA-induced PpIX will be correlated to quantitative biological metrics of tumor burden and proliferative index. A clinical validation study will show that quantitative microscopy of PpIX in LGG patients is predictive of post-operative measurements of extent of resection.
Role: PI

W81XWH-20-1-0851 (Madabhushi) 09/01/20 – 8/31/25 (NCE)
DoD CDMRP Prostate Cancer Research Program (PCRP)
Race Specific 3D Computational Pathology Biomarkers for Predicting Prostate Cancer Specific Recurrence
Prostate cancer (PCa) is exceedingly prevalent in African American (AA) men compared to Caucasian American (CA) men, with incidence almost 60% higher and mortality rate two to three times greater. The risk of dying from low-grade prostate cancer is also double that of CA men. This project aims to develop race-specific PRISM3D models for predicting patient outcomes and also correlating them with genomic signatures.
Role: Co-I

B. Positions and Honors

Positions and Employment

2025 –	Professor, Dept. of Pathology, Stanford University
2025 –	Affiliate Professor, Dept. of Mechanical Engineering, University of Washington
2021-2025	Professor, Dept. of Mechanical Engineering, University of Washington
2019-2025	Adjunct Professor, Dept. of Bioengineering, University of Washington
2017-2025	Adjunct Professor, Dept. of Lab Med. & Pathology, University of Washington School of Medicine
2016-2021	Associate Professor, Dept. of Mechanical Engineering, University of Washington
2014-2016	Assistant Professor, Dept. of Mechanical Engineering, University of Washington
2010-2014	Assistant Professor, Dept. of Biomedical Engineering, SUNY Stony Brook
2009-2010	Instructor, Stanford University School of Medicine

Other Experience and Professional Service (selected)

2024, 2026 **Congress vice-chair (2024) / Congress chair (2026):** Optica/OSA Biophotonics Congress (BIOMED)
2022 **Associate editor:** *Biomedical Optics Express*
2020, 2022 **Program chair (2020) / Conference chair (2022):** Microscopy, Histopathology and Analytics (MHA) conference, Optica/OSA Biophotonics Congress (BIOMED)
2020-present **Associate Editor:** *BME Frontiers* - a *Science* Partner Journal
2019 **Associate Editor:** Frontiers in Oncology: cancer imaging and image-directed interventions
2018-present **Topical editor:** *Journal of Biomedical Optics*
2018 **Co-founder:** Alpenglow Biosciences, Seattle, WA
2017 **Conference co-chair:** Telluride Science Research Center (TSRC) "Frontiers and Challenges in Laser-Based Biological Microscopy," Telluride, CO
2014-present **Study section member**: Cancer Prevention and Research Institute of Texas (CPRIT) Research Programs, Imaging Technology and Informatics, ITI
2012-present **Program committees:** SPIE European Conferences in Biomedical Optics (ECBO), SPIE Photonics West, World Molecular Imaging Congress (WMIC), Telluride Science Research Center (TSRC) "Frontiers and Challenges in Laser-based Microscopy," OSA Biophotonics Congress (BIOMED), OSA Frontiers in Optics (FiO), IEEE Photonics Conference, CLEO Pacific Rim.
2007-present **Ad hoc reviewer:** NSF SBIR/STTR imaging panel, NSF SBIR panel for SARS-CoV-2 diagnostics, Beckman Foundation Light-Sheet Program (2020)
2013-present **Ad hoc NIH reviewer:** NIDCR special grants review committee (DSR), NCI special emphasis panel, SBIR contracts, Enabling Bioanalytical and Imaging Technologies (EBIT), Imaging and Biomarkers for Early Cancer Detection (DTCS-A), Imaging Technology & Development (ITD), Clinical Translational Imaging Sciences (CTIS), Biomedical Technology Development and Dissemination (BTDD), Cellular and Molecular Technologies (CMT)
2007-present **Ad hoc reviewer:** Proc. Natl. Acad. Sci USA (PNAS), Scientific Reports, Journal of Biomedical Optics, Optics Letters, Optics Express, Biomedical Optics Express, Annals of Biomedical Engineering, IEEE Transactions of Biomedical Engineering, IEEE Journal of Microelectromechanical Systems (JMEMS), IEEE Journal of Selected Topics in Quantum Electronics, Journal of Visualized Experiments, Molecular Imaging and Biology, PLoS ONE, Journal of Cancer Research and Clinical Oncology, Bioconjugate Chemistry (ACS), Lasers in Surgery and Medicine, Journal of Biophotonics, Theranostics, Nature Reviews Clinical Oncology, Nature Methods
2005-present **Member:** Society of Photo-Optical Instrumentation Engineers (SPIE); Optica / Optical Society of America (OSA); World Molecular Imaging Society (WMIS); American Association of Cancer Research (AACR)

Honors

2025 Elected Fellow of AIMBE
2025 Arvid and Marianne Peterson Endowed Professorship, Univ. of Washington
2024 Elected Fellow of SPIE
2023 Elected Fellow of Optica (formerly Optical Society of America)
2017-2020 Bryan T. McMinn Endowed Professorship, Univ. of Washington
2018 UW College of Engineering Team Award, Engineering Innovation in Health (EiH) biodesign Program
2013 Stony Brook BME department outstanding teacher award
2009-2013 NIH K99/R00 "Pathway to Independence" Award (through the NIBIB)
2009 Best Oral Presentation Award, Center for Biomedical Imaging at Stanford (CBIS) symposium
2007 Nominated by Stanford University for the Burroughs Wellcome Fund (BWF) Career Award at the Scientific Interface (2007)
2006-2008 NIH Loan Repayment Award for clinical researchers
2005-2008 Canary Foundation / American Cancer Society postdoctoral fellowship for early cancer detection
2004 AIAA Best Paper by the Ground Testing Technical Committee
2003 AIAA Foundation Wright Brothers Graduate Award
2003 Outstanding Paper Award, AIAA Ground Testing Technical Committee
1999-2002 NSF Graduate Fellowship Award
1999 Sigma Xi Book Award, Tau Beta Pi, Phi Beta Kappa, Princeton University

1999 Sau-Hai Lam *58 Prize as the top graduate in mechanical engineering, Princeton University

C. Contributions to Science (*equal contribution)

1. **Open-top light-sheet (OTLS) microscopy.** We have been developing OTLS microscopy systems for nondestructive slide-free 3D pathology of preclinical and clinical specimens that are optically cleared and fluorescently labeled.
    a. A.K. Glaser, K.W. Bishop, L.A. Barner, E.A. Susaki, S.I. Kubota, G. Gao, R.B. Serafin, P. Balaram, E. Turschak, P.R. Nicovich, H. Lai, L.A.G. Lucas, Y. Yi, E.K. Nichols, H. Huang, N.P. Reder, J.J. Wilson, R. Sivakumar, E. Shamskhou, C.R. Stoltzfus, X. Wei, A.K. Hempton, M. Pende, P. Murawala, H.U. Dodt, T. Imaizumi, J. Shendure, B.J. Beliveau, M.Y. Gerner, L. Xin, H. Zhao, L.D. True, R.C. Reid, J. Chandrashekar, H.R. Ueda, K. Svoboda, and **J.T.C. Liu,** "A hybrid open-top light-sheet microscope for multi-scale imaging of cleared tissues," *Nature Methods* 19, 613 (2022)
    b. L.A. Barner, A.K. Glaser, H. Huang, L.D. True, and **J.T.C. Liu**, "Multi-resolution open-top light-sheet microscopy to enable efficient 3D pathology workflows," *Biomed. Opt. Exp.* 11, 6605 (2020)
    c. A.K. Glaser, N.P. Reder, Y. Chen, C. Yin, P. Wei, S. Kang, L. Barner, W. Xie, E.F. McCarty, P.R. Nicovich, C. Stoltzfus, M. Gerner, C. Mao, A.R. Halpern, J.C. Vaughan, L.D. True, and **J.T.C. Liu**, "Multi-immersion open-top light-sheet microscope for high-throughput imaging of cleared tissues," *Nature Communications* 10, 2781 (2019).
    d. A.K. Glaser*, N.P. Reder*, Y. Chen, E.F. McCarty, C. Yin, Linpeng Wei, Y. Wang, L.D. True, and **J.T.C. Liu**, "Light-sheet microscopy for slide-free nondestructive pathology of large clinical specimens," *Nature Biomedical Engineering* 1, 0084 (2017).
2. **Nondestructive 3D pathology workflows.** We have developed a variety of tissue-preparation protocols, quality-control methods, and software tools to enable the reproducible generation of high-quality 3D pathology datasets from clinical specimens.
    a. H.C. Hsieh, Q. Han, D. Brenes, K.W. Bishop, R. Wang, Y. Wang, C. Poudel, A.K Glaser, B.S. Freedman, J.C. Vaughan, N.L. Allbritton, and **J.T.C. Liu**, "Imaging 3D cell cultures with optical microscopy," *Nature Methods* (2025)
    b. K.W. Bishop, L.A. Erion Barner, Q. Han, E. Baraznenok, L. Lan, C. Poudel, G. Gao, R.B. Serafin, S.S.L. Chow, A.K. Glaser, A. Janowczyk, D. Brenes, H. Huang, D. Miyasato, L.D. True, S. Kang, J.C. Vaughan, and **J.T.C. Liu**, "An end-to-end workflow for non-destructive 3D pathology," *Nature Protocols* (2024)
    c. M.Y. Lee, C. Mao, A.K. Glaser, M.A. Woodworth, A.R. Halpern, A. Ali, **J.T.C. Liu**, and J.C. Vaughan, "Fluorescent labeling of abundant reactive entities (FLARE) for cleared-tissue and super-resolution microscopy," *Nature Protocols* 17, 819 (2022)
    d. R. Serafin, W. Xie, A.K. Glaser, and **J.T.C. Liu**, "FalseColor-Python: a rapid intensity-leveling and digital-staining package for fluorescence-based slide-free digital pathology," *PLoS ONE* 15, e0233198 (2020)
3. **Clinical decision support with 3D pathology (ex vivo).** We are performing clinical studies to demonstrate the value of 3D vs. 2D pathology for improved prognostication and treatment stratification. We are developing workflows for both human interpretation and computational machine-learning analysis of our large 3D pathology datasets.
    a. A.H. Song, M. Williams, D.F.K. Williamson, S.S.L. Chow, G. Jaume, G. Gao, A. Zhang, B. Chen, R. Serafin, R. Colling, M.R. Downes, X. Farre, P. Humphrey, C. Verrill, L.D. True, A. Baras, A.V. Parwani, **J.T.C. Liu*** and F. Mahmood*, " Analysis of 3D pathology samples using weakly supervised AI," *Cell* 187, 2502 (2024) *Co-senior authorship
    b. L.A. Erion Barner*, G. Gao*, D.M. Reddi, L. Lan, W. Burke, F. Mahmood, W.M. Grady, and **J.T.C. Liu**, "AI-triaged 3D pathology to improve detection of esophageal neoplasia while reducing pathologist workloads," *Modern Pathology* 36, 100322 (2023)

c. W. Xie, N.P. Reder, C. Koyuncu, P. Leo, S. Hawley, H. Huang, C. Mao, N. Postupna, S. Kang, R. Serafin, G. Gao, Q. Han, K.W. Bishop, L.A. Barner, P. Fu, J.L. Wright, C.D. Keene, J.C. Vaughan, A. Janowczyk, A.K. Glaser, A. Madabhushi, and **J.T.C. Liu**, "Prostate cancer risk stratification via non-destructive 3D pathology with deep learning-assisted gland analysis," *Cancer Research* 82, 334 (2022)

d. **J.T.C. Liu**, A.K. Glaser, K. Bera, L.D. True, N.P. Reder, K.W. Eliceiri, and A. Madabhushi, "Harnessing nondestructive 3D pathology," *Nature Biomedical Engineering* 5, 203 (2021)

4. **Miniature optical-sectioning microscopes for non-invasive pathology (in vivo).** We have been developing endoscopic and handheld optical-sectioning microscopes to enable in vivo point-of-care pathology. Devices have been developed for oral-cancer detection and for neurosurgical guidance. These devices utilize MEMS scanners, precision machining, custom micro-optical components, and novel alignment methods.

   a. K.W. Bishop*, B. Hu*, R. Vyawhare*, Z. Yang*, D. Liang, G. Gao, E. Baraznenok, Q. Han, L. Lan, S.S.L. Chow, N. Sanai, and **J.T.C. Liu**, "A miniature line-scanned dual-axis confocal microscope for versatile clinical use," *Biomed. Opt. Exp.* 14, 6048 (2023).

   b. C. Yin, L. Wei, K. Kose, A.K. Glaser, G. Peterson, M. Rajadhyaksha, and **J.T.C. Liu**, "Real-time video mosaicking to guide handheld in vivo microscopy," *J. Biophotonics*, 13 (2020).

   c. L. Wei, C. Yin, Y. Fujita, N. Sanai, and **J.T.C. Liu**, "A handheld line-scanned dual-axis confocal microscope with pistoned MEMS actuation for flat-field fluorescence imaging," *Opt. Lett.* 33, 671 (2019).

   d. C. Yin, L. Wei, S. Abeytunge, G. Peterson, M. Rajadhyaksha, and **J.T.C. Liu**, "Label-free in vivo pathology of human epithelia with a high-speed handheld dual-axis confocal microscope," *J. Biomed. Opt.* 24, 030501 (2019).

5. **Optical imaging for surgical guidance.** We are developing high-resolution fluorescence imaging methods to guide tumor resection procedures in the brain, head & neck regions, and breast.

   a. G. Gao*, D. Miyasato*, L.A. Barner, R. Serafin, K.W. Bishop, W. Xie, A.K. Glaser, L.D. True, and **J.T.C. Liu**, "Comprehensive surface histology of fresh resection margins with rapid open-top light-sheet (OTLS) microscopy," *IEEE Trans. Biomed. Eng.* 70, 2160 (2023)

   b. Y. Fujita, L. Wei, P.J. Cimino, **J.T.C. Liu**, and N. Sanai, "Video-mosaicked handheld dual-axis confocal microscopy of gliomas: an ex vivo human study," *Frontiers in Oncology* 10, 1674 (2020)

   c. Y. Chen*, W. Xie*, A.K. Glaser, N.P. Reder, C. Mao, S.M. Dintzis, J.C. Vaughan, and **J.T.C. Liu,** "Rapid pathology of lumpectomy margins with open-top light-sheet (OTLS) microscopy," *Biomed. Opt. Exp.* 10, 1257 (2019).

   d. L. Wei, Y. Chen, C. Yin, S. Borwege, N. Sanai, and **J.T.C. Liu**, "Optical-sectioning microscopy of protoporphyrin IX fluorescence in human gliomas: standardization and quantitative comparison with histology," *J. Biomed. Opt.* 22, 046005 (2017)