

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF CELL AND DEVELOPMENTAL BIOLOGY
COLLEGE OF LITERATURE, SCIENCE, AND THE ARTS
DEPARTMENT OF BIOPHYSICS

Dawen Cai, Ph.D., assistant professor of cell and developmental biology, Department of Cell and Developmental Biology, Medical School, and assistant professor of biophysics, Department of Biophysics, College of Literature, Science, and the Arts, is recommended for promotion to associate professor of cell and developmental biology, with tenure, Department of Cell and Developmental Biology, Medical School, and associate professor of biophysics, without tenure, Department of Biophysics, College of Literature, Science, and the Arts.

Academic Degrees:

Ph.D.	2007	University of Michigan
B.S.	2000	Peking University

Professional Record:

2014-present	Assistant Professor of Biophysics, University of Michigan
2013-present	Assistant Professor of Cell and Developmental Biology, University of Michigan
2011-2013	Assistant Research Scientist of Physics, University of Michigan
2011-2012	Assistant Research Scientist of Microbiology and Immunology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Cai is actively involved in teaching. He regularly lectures in CDB530, a graduate-level course that covers cell biology in a broad fashion, and in CDB560, a graduate-level course that emphasizes quantitative and computational skills. Dr. Cai has served as a faculty evaluator and coordinator for the cell and developmental biology, neuroscience, and biophysics graduate student seminars. He has been teaching graduate students and post-doctoral fellows in the Research Responsibility and Ethics course, PIBS 503. Outside of the university, Dr. Cai teaches the microscopy and image analysis module for the Cold Spring Harbor Laboratory summer course on Advanced Techniques in Molecular Neuroscience.

Dr. Cai is very involved in teaching and mentoring in his own laboratory. He has mentored 23 undergraduate students, seven graduate students, seven fellows, and 11 visiting scholars. Two of his former post-doctoral fellows are now assistant professors at research universities within the United States. His graduate students have received many honors and awards, including giving platform presentations and receiving poster and paper awards at international conferences as well

as receiving prestigious fellowships from the NIH and other international funding agencies. Dr. Cai has served or continues to serve on 15 graduate dissertation committees.

Research: Dr. Cai's research program is focused on developing novel technologies to profile single neurons and to map their connections and functions within the entire brain. To enable the study of molecular heterogeneity in the brain, a highly complex tissue, he led an effort to develop a microfluidic (droplet-based) high-throughput and low-cost single-cell manipulation and profiling platform. Its applications include, but are not limited to, single-cell selective gene quantification and single-cell transcriptome profiling. Using this technology, novel marker genes have been identified to specify neuronal subtypes and define their lineages in the developing *Drosophila* brain. Moving forward, Dr. Cai will combine a novel spectral-spatial lineage barcoding tool developed in his laboratory to reveal the roles of lineage-specific transcription factors in determining terminal neuronal fates. In parallel, Dr. Cai has led the effort to establish a paradigm-shifting experimental pipeline that makes it possible to define the spatial distribution of functionally-distinct neurons in the brain, and to map the wiring connections between them. This light microscopy-based approach, termed *spectral connectomics*, enables multi-spectral image datasets to be obtained with nanoscale resolution, in which the molecular expression profile, morphology, and connectivity of densely-labeled neurons can be obtained in the same brain. In addition, Dr. Cai's laboratory develops computational tools to enable quantifying images acquired by spectral connectomics.

Dr. Cai's research addresses a very significant question – the development and functional organization of the brain. His program is trans-disciplinary, highly innovative and collaborative, and at the forefront of neuroscience. Dr. Cai's work is routinely published in high-impact journals, and has 33 peer-reviewed articles which has steadily led to invitations to speak at top-tier academic institutions and at national and international meetings. Dr. Cai's research program has received major external funding since 2013. He is the principal investigator of three RF1 NIH grants, one R01 NIH grant and one industry grant as well as a co-investigator of four additional grants.

Five Recent Significant Publications:

Shen FY, Harrington MM, Walker LA, Cheng HPJ, Boyden ES, Cai D: Light microscopy-based approach for mapping connectivity with molecular specificity. *Nature Communications*, *BioRxiv* doi:10.1101/2020.02.24.963538 (in press).

Veling MW, Li Y, Veling MT, Litts C, Michki N, Liu H, Ye B, Cai D: Identification of neuronal lineages in the *Drosophila* peripheral nervous system with a “digital” multi-spectral lineage tracing system. *Cell Reports* 29:3303-3312, 2019.

Roossien DH, Sadis BV, Yan Y, Webb JM, Min LY, Dizaji AS, Bogart LJ, Mazuski C, Huth RS, Stecher JS, Akula S, Shen F, Xiao T, Vandenbrink M, Lichtman JW, Hensch TK, Herzog ED, Cai D: Multispectral tracing in densely labeled mouse brain with nTracer. *Bioinformatics* 35:3544-3546, 2019.

Chung MT, Kurabayashi K, Cai D: Single-cell RT-LAMP mRNA detection by integrated droplet sorting and merging. *Lab on a Chip* 19:2425-2434. PMID: PM31187105, 2019.

Chung MT, Nunez D, Cai D, Kurabayashi K: Deterministic droplet-based co-encapsulation and pairing of microparticles via active sorting and downstream merging. *Lab on a Chip* (2017) 17:3664-3671, 2017.

Service: Dr. Cai is a long-standing member of the Cell and Developmental Biology (CDB) and Neuroscience Admission Committees. He is serving on the Biophysics Career Choice Committee, the CDB Infrastructure Committee, the University of Michigan Microscopy Core Advisory Committee, and the University of Michigan Medical School Basic Science Research IT Committee. He also serves as the CDB innovation officer to the Fast Forward Medical Initiative. Dr. Cai is a member of the American Biophysical Society, The American Society for Cell Biology, and the Society for Neuroscience. He has served as a member of five NIH study sections, and is a review editor for *Frontiers in Neuroscience* and *Neural Technology*, as well as a research topic editor for *Neuronal Tracking* and *Neural Circuit Reconstruction*.

External Reviewers:

Reviewer A: “Dr. Cai has had four current graduate students, with four more having graduated. He has also mentored six postdoctoral fellows, including two currently in the lab. This shows a vibrant and successful lab that can attract both graduate students and postdoctoral fellows. In addition, he has mentored 19 undergraduate students; this is very impressive and important for attracting students into STEM. By all accounts, Dr. Cai has had tremendous success in building and running a successful research lab... I support Dr. Cai for promotion. In particular, his funding and publications would be sufficient for tenure at [my institution]. I look forward to his continued success.”

Reviewer B: “Dr. Cai is that rare and powerful combination of inventor, engineer, and biomedical scientist, always seeking to equip the investigator with new tools to probe deeper and wider, to ask new kinds of questions, to expand what is feasible. Through his creativity and proficiency, Dawen is shifting the current manner of tracing neuronal lineages and circuit formation and plasticity. Moreover, the methodologies he has developed are practical and accessible. Thus, their impact will be broad. Dawen is unquestionably a leader. He is also a highly successful collaborator and generous colleague. I recommend Dr. Cai with much enthusiasm for promotion to Associate Professor with tenure. I believe he embodies the highest goals of the University of Michigan and brings distinction to the Department of Cell and Developmental Biology.”

Reviewer C: “Dawen is standing at the frontline of light microscopy and has participated in the development of several crucial technologies including Brainbow-based labeling methods. He is very productive and has published several high quality papers...Dawen is definitely an outstanding researcher and I would say he is among the top 5-10% in his peer group. I would also like to emphasize that his collaboration with Ed Boyden, and his ability to collaborate with other senior or junior PIs really makes him stand [sic] out from this peer group.”

Reviewer D: “I can say with little reservation that...Dr. Cai would be promoted to full professor in our Department at [my institution]. He has established himself as an impactful scholar, I know firsthand that he is a talented teacher, he has published over 30 peer reviewed papers, he has significant extramural funding for the next 2 years, and he shows no signs of decreased momentum in his research activities... I found his paper on a novel scRNAseq approach particularly exciting, and it clearly indicates his future direction of developing a combination bar-coded libraries with multispectral imaging and trans-synaptic labelling approaches to combine information about molecular identities with connectional maps and lineage relationships in the nervous system. This type of analysis could lead to the ultimate type of dataset for developmental neurobiology, and Dawen Cai might be the person to pull such a technical feat off.”

Reviewer E: “Professor Cai is among the most technically innovative scientists in the field of neuroscience today... I can say that not only is Professor Cai and [sic] outstanding scientist he is also an outstanding lecturer. His style in this small class setting of about 16 students is very conversational and engaging for everyone in the room. With this method of engagement, Professor Cai was able to consistently convey how to implement his methodologies and techniques so that everyone in the course is now able to replicate his experiments. This is not only a reflection on his ability to communicate scientifically but also his scientific integrity. To state this simply, his methodologies work well and are easily adopted. Further, his open and honest communication allows for this work to be passed onto the broader scientific community... Professor Cai has been instrumental in the development of expansion microscopy with Professor Ed Boyden. This has led to a series of high impact papers from both the Boyden and Cai laboratories.”

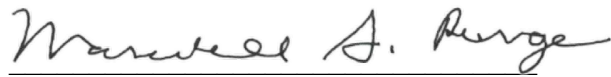
Reviewer F: “The positive impact of Dr. Cai’s work on his field, as well as to introduce potentially profound or transformative advances, is highly evident in the exemplary transcript of funded and submitted proposals described in Dr. Cai’s Candidates Packet. This is a striking testament to the influence of his existing body of work, the likely success of his current efforts, and in combination with the creativity he has already shown, the high probability that he will enjoy a long and successful career in the field.... Moreover, careful review of his work leaves me to think that Dr. Cai will remain on the frontline of the creative work and discoveries in his field in the future. Thus, I think Dr. Cai merits this appointment and I recommend him enthusiastically, I am confident that Dr. Cai would be an outstanding candidate for an equivalent promotion in many other leading institution, including [my institution].”

Reviewer G: “I believe that Dr. Cai has made an outstanding contribution to the field of connectomic neuroscience. His initial development of the viral Brainbow method, together with the production of a wide range of antibodies that are specific to different fluorescent proteins, has provided an excellent tool for revealing neural morphology within the nervous system. We have used this extensively in my laboratory... This technique, which is referred to as Spectral Connectomics is a *real tour de force*, allowing the synaptic connections between multiple neurons to be investigated in unprecedented details... Dr. Cai has an impressive publication record, with several papers in very high impact journals (including the Nature journals) and has been highly successful in obtaining grant funding. It is evident from the successes of his trainees

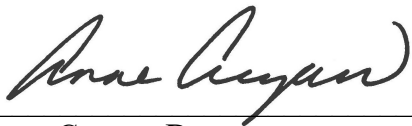
that he has also been a very effective mentor. He has made significant contributions to the discipline, by service on NIH study sections, Editorial boards as an *ad hoc* reviewer.”

Summary of Recommendation:

Dr. Cai is an outstanding researcher who is continuing in an upward trajectory through development of a unique niche in cell and developmental biology and neuroscience. He is an excellent educator, and important contributor to both departments. We are pleased to recommend Dawen Cai, Ph.D. for promotion to associate professor of cell and developmental biology, with tenure, Department of Cell and Developmental Biology, Medical School, and associate professor of biophysics, without tenure, Department of Biophysics, College of Literature, Science, and the Arts.



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May 2021