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PRINCIPAL INVESTIGATOR: Chris B. Schaffer

CONTRACTING ORGANIZATION: Cornell University, Ithaca, NY 14853

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Chris B. Schaffer
Rong Wang

E-Mail: cs385@cornell.edu

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Biomedical Engineering
Cornell University
115 Weill Hall
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14. ABSTRACT

The overall project focuses on elucidating the cell signaling that drives structural changes in brain blood vessels that lead to the formation of arterio-venous malformations, with Prof. Rong Wang (UCSF) as the scientific lead. Prof. Chris Schaffer's lab (Cornell) contributes to this work by helping Prof Wang's laboratory maintain the necessary in vivo imaging capabilities at UCSF and by developing more advanced imaging capabilities that would allow a finer dissection of the cellular interactions that underlie the vascular changes.

15. SUBJECT TERMS

Nonlinear microscopy, hyperspectral imaging, arterio-venous malformation

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Introduction:
This overall scientific project is led by Prof. Rong Wang at UCSF. Prof. Chris Schaffer's laboratory at Cornell has collaborated with Prof. Wang for more than 12 years, using high-resolution in vivo imaging methods to study the vascular changes that occur in the brain of mouse models of arterio-venous malformations, as well as how altered cellular signaling due to genetic knock-outs alters those vascular changes. This report describes the contributions of Prof. Schaffer's laboratory to this endeavor, which focuses primarily on two aspects of the work. First, Prof. Schaffer supports the in vivo imaging capabilities in Prof. Wang's laboratory. He guided the construction of the two-photon excited fluorescence microscope that is used there, and during this grant he has facilitated system maintenance, upgrades, repairs/alignment, as well as training of individuals in Prof. Wang's laboratory in the use of this instrument. He also contributed to the design of experiments using in vivo imaging and the analysis and interpretation of results. The second major activity on this grant in Prof. Schaffer's laboratory focuses on the creation of advanced nonlinear microscopes that would allow more complex cellular dynamics to be followed in vivo. This latter research has produced a working hyperspectral multiphoton microscope that acquires 48 channels of excitation/emission spectral information per pixel, enabling the imaging of ten or more fluorescent species simultaneously. This work was recently published in *Optica.* A new design that is under construction now will dramatically speed up the acquisition of this data, which is essential for the use of this tool in live animals.

Keywords:
Nonlinear microscopy, hyperspectral imaging, arterio-venous malformation

Accomplishments:
Major Goals of this Project:
Prof. Rong Wang's laboratory discovered more than 10 years ago an altered cell signaling pathway, involving constitutively active Notch4, that leads to the formation of arterio-venous malformations (AVMs) in the brain of mice. Brain AVMs can be devastating, as they are typically not diagnosed until they lead to an ischemic or hemorrhagic stroke and there are few treatment options beyond a highly-invasive and risky surgical removal. Prof. Wang's discovery that Notch4 over activity can produce brain AVMs provided one of the first viable animal models of AVMs, permitting detailed studies of the genetic and physiological underpinnings of this disease. Such studies require in vivo analysis of brain vascular structure and function, and the contributions of Prof. Schaffer's laboratory to this project center on developing and guiding the use of in vivo imaging tools to accomplish this analysis. Under this award, Prof. Schaffer's laboratory aimed to make two key contributions to this work. First, we continued to support the in vivo imaging work conducted in Prof. Wang's laboratory, including help with instrumentation, guiding experimental design and analysis of results, and training personnel. Second, we have sought to expand the complexity of biological phenomena that can be studied through in vivo imaging by building a hyperspectral multiphoton microscope, with the goal of enabling in vivo imaging of multiple distinct cell types simultaneously.

Accomplishments Toward these Goals:
Goal 1: Support in vivo imaging efforts in Prof. Wang's laboratory at UCSF
Prof. Wang's laboratory uses a two-photon excited fluorescence (2EPF) microscope that was designed by Prof. Schaffer's laboratory and constructed by a jointly advised PhD student about 10 years ago. Briefly, 2PEF imaging enables fluorescently-labeled structures to be imaged with micrometer resolution, in three-dimensions, and at depths of several hundred micrometers into optically scattering samples, such as tissue. This 2PEF imaging has been an essential tool in Prof. Wang's exploration of the genetic and physiological (e.g. blood flow mediated vascular remodeling) underpinnings of AVM formation and regression in her Notch4-based AVM mouse models. Prof. Schaffer's laboratory has supported these efforts by first designing and guiding the construction of the 2PEF microscope and, since then, guiding the maintenance and repair of the instrument, advising on the use of the instrument and the processing of the resulting images, helping with experimental design and the analysis of results, and training of new members of Prof. Wang's laboratory on the use of this tool. This expert support role has been accomplished through several different mechanisms. First, Prof. Schaffer visits Prof. Wang's laboratory 1-2 times a year for a couple of days. During these visits, he personally maintains the microscope, trains new users and answers instrumentation questions, and participates in meetings to discuss progress, plan experiments, and analyze results. Prof. Schaffer did not visit Prof. Wang's laboratory in 2020 or 2021 due to the COVID pandemic. Second, members of Prof. Schaffer's laboratory frequently consult by email and videoconference with members of Prof. Wang's laboratory to deal with technical problems with the microscope, to advise on the design and execution of in vivo imaging experiments, to guide quantitative image processing and data analysis, and to answer general questions. These two

mechanisms have led to a more than 12 year run of Prof. Wang's laboratory having world-class in vivo imaging capabilities that have enabled her AVM studies. This award has supported the efforts of Prof. Schaffer's lab to sustain these capabilities in Prof. Wang's laboratory from the Fall of 2016 through the Fall of 2020.

Goal 2: Develop hyperspectral multiphoton microscopy

Studies of both normal and disease-state physiology in animal models would benefit from the capability to simultaneously visualize and distinguish a broad variety of cell types in vivo. Poor spectral resolution and/or sensitivity to optical scattering hinders the application of current microscopies to in vivo imaging of many fluorescent markers in scattering samples. 2PEF microscopy has become the technique of choice for visualization of fluorescently-labeled features deep into scattering samples (~0.5 mm in mouse cortex), at subcellular resolution. However, typical 2PEF systems have just two to four different wavelength detection channels, which limits measurements to just a few fluorescent markers. Spectral resolution has been improved in 2PEF using detection systems based on dispersive optics, but this approach becomes counter-productive in scattering samples, where scattered light leads to spectral blurring and poor spectral resolution in angle-dependent systems for separating wavelengths. Confocal detection can reduce this spectral blurring, but eliminates much of the benefit of 2PEF for deep imaging. Other approaches to increasing the number of fluorescent species that can be imaged simultaneously with 2PEF have focused on increasing the number of detector channels and/or using multiple excitation laser wavelengths.

We have attacked this problem through the design and construction of a hyperspectral multiphoton microscope (HMM) to address the challenge of achieving clear separation of multiple fluorescent species while maintaining the deep imaging capability of 2PEF. The first version of this instrument used three different wavelength excitation lasers to differentially excite different fluorescent dyes on successive image frames. In addition, the four channel fluorescence detection system had angle-tuned bandpass filters in front of each detector, which could be rotated to shift the detected wavelength in each channel. With four different angles of these angle-tuned filters, we could detect fluorescence over the 400 – 700-nm wavelength range with ~25-nm spectral resolution, requiring four successive frames. Thus 12 successive frames (4 angles X 3 lasers) produced a 48-channel hyperspectral image. We then linearly unmixed this 48 channel image to obtain pure images of each fluorescent marker. We demonstrated imaging of ten different color fluorescent beads with strong overlap, imaging of up to eight different color fusion proteins that linked different color fluorescent proteins to different intracellular structural proteins, and imaging of up to eight distinct biological structures in vivo using harmonic generation, fluorescent protein expression, and exogenous dyes and fluorescently-labeled antibodies to highlight specific structures. This work was published in *Optica* in 2020.

A major problem with this first-stage instrument, however, is the slow imaging speed. Our instrument requires about 30 s to acquire a full 48-channel hyperspectral image, so three-dimensional image stacks can require tens of minutes to acquire. This slow imaging limits experimental throughput on the instrument and sets a lower limit on the time resolution at which we can follow dynamic events. An additional challenge is the impact of motion artifact on the accuracy of the linear unmixing. When imaging in live animals, there is some unavoidable motion of the tissue due to heart beat and respiration. In the brain, we typically have 1-3 μm of motion, mostly due to respiration. Because this motion will occur between successive image frames taken with different excitation colors and detecting different emission wavelengths, the images that are used to linearly unmix and extract "pure" images of each fluorescent marker will be slightly shifted relative to each other, leading to poor unmixing at the boundaries of objects. Although we correct for some of this motion artifact with post-processing, there remains some regions of poor unmixing, especially at the edges of smaller objects. We also note that this microscope is somewhat wasteful in terms of the utilization of emitted fluorescence. In any given image, we are rejecting (and not detecting) about three-fourths of the potential emitted light.

We are now improving on our design for the HMM to create an instrument that would be more robust for in vivo imaging experiments. This new design will address the issues of imaging speed, sensitivity to motion artifact, and inefficient use of emitted fluorescence. In a collaboration led by Prof. Frank Wise (Applied Physics, Cornell), we have designed femtosecond laser sources that produce synchronized femtosecond duration laser pulses at multiple different wavelengths. We will capitalize on the unique capabilities of this synchronized multi-color laser source to create a hyperspectral multiphoton microscope that dramatically increases the density of fluorescence information that is obtained. By switching pulse-by-pulse between the three generated colors and, additionally, driving non-degenerate two-photon absorption by simultaneously irradiating with combinations of colors, we create five different excitation conditions. Imaging the fluorescence emission across eight simultaneous detection channels that span the visible wavelength range will yield a 40 channel hyperspectral image that will allow fine separation of fluorescent dyes based on two-photon excitation and fluorescence

emission spectra. This new system will acquire 40-channel images at about three frames per second, a speed up of about two orders of magnitude compared to our current instrument. Because the excitation conditions are switched pulse-to-pulse and the emission channels are detected simultaneously, motion artifact will not lead to distortions between the 40 different channels of the image. Finally, because we are using an 8 PMT system and dropping the use of angle-tuned bandpass filters, we detect all available fluorescence at all times, making more efficient use of the fluorescence that is generated.

We have made progress in two critical ways and anticipate finishing the final construction and begin demonstrating use of this instrument later this year. First, we have finalized the complex electronics and software required to synchronize the fluorescence detected with the individual excitation pulse that excited it. This required the use of field programmable gate arrays to appropriately route the data at the ~10 MHz rate of excitation pulses. Second, we demonstrated non-degenerate two-photon excitation using synchronized femtosecond pulses of different colors from a fiber laser built by the Wise lab. This latter work was published in *Biomedical Optics Express* in 2021.

Opportunities for Training and Professional Development:
This proposal has provided the primary source of support for a PhD student, Mr. Menansili Mejooli. Mr. Mejooli has a background in electrical and computer engineering and his PhD has focused on developing advanced optical microscopy tools. Mr. Mejooli was the second author on our *Optica* paper on the HMM and was also second author on our collaborative *Biomedical Optics Express* paper on fiber laser non-degenerate two photon imaging. I anticipate he will finalize the construction of the next-generation HMM this summer and complete demonstration experiments this Fall. He will complete his PhD toward the end of 2021.

Impact:
Impact on discipline:
Our support of Dr. Wang's lab in the use of 2PEF for in vivo studies directly impacts the field of AVM studies by enabling her lab to use these methods. In the field of optics and microscopy, the first generation HMM is, frankly, a somewhat brute force approach to increasing the spectral discrimination capability of nonlinear microscopy, but it does represent the largest number of excitation/emission imaging channels that has been demonstrated. Our second generation HMM makes clever use of pulse train engineering and detection systems to gain a dramatic amount of additional spectral information with the only real tradeoff being laser and microscope complexity.

Impact on other disciplines:
The greatest impact of multiphoton microscopy in biomedical research has been the ability to directly observe and quantify the behavior of, and interactions between, cells in living organisms. This has been used primarily as a tool for hypothesis testing, where cell types of interest are labeled using genetic strategies or exogenous dyes and are imaged on microscopes that feature 2–4 simultaneous fluorescence detection channels. In these kinds of experiments, "red" and "green" labeled cells (or other structures) stand out against a black background. That black space is not empty, however, but is densely filled with other cell types that are not seen and whose role, therefore, cannot be examined. Modern genetic labeling strategies, such as the various Brainbow constructs, are approaching the point where every cell in a volume can be labeled with a unique combination of fluorescent proteins. Clearly differentiating these color combinations and thus delineating the cells, however, requires much more information than can be acquired on current microscopes that image well *in vivo*. Use of these powerful labeling strategies has been limited primarily to post-mortem imaging of tissue using confocal microscopes, which are too sensitive to optical scattering for robust *in vivo* use. The HMM will overcome this challenge and enable us to image many fluorescent species simultaneously in scattering samples, and should transform *in vivo* imaging from a tool used primarily for hypothesis testing to a more general technique that could be used for unbiased biological discovery. The instrument could enable experiments where the dynamic interactions of *all* cells in the imaged volume can be tracked over time to *generate* hypotheses about the cellular interactions that drive normal- and disease-state physiological processes. As an example of this impact, our lab is part of an NIH-funded P01 program project grant focused on imaging the response of T-cells to tissue injury. Our role is to help with instrumentation to enable the simultaneous imaging of multiple classes of cells to better understand the cell interactions that lead to T-cell mediated immunity or tolerance.

Impact on technology transfer:
We partnering with ThorLabs on the development of the second-generation HMM. So far, this partnership has focused on them providing some custom optical and opto-mechanical design and fabrication for us at steeply

discounted rates. If the instrument proves to work as well as we hope and if the laser technology from Prof. Wise's lab proves reasonable to replicate, I believe ThorLabs will be interested in pursuing commercialization of the microscope. We were recently awarded a patent on some of the key technology and ideas that underlie the first and second generation HMM designs.

Impact on society:
If successful, this instrument development could provide a powerful new tool to elucidate the cellular interactions that drive disease processes, potentially revealing new mechanisms that could be targeted therapeutically.

Changes/Problems:
Changes in approach:
The reduced quality of the linear unmixing due to uncompensated motion artifact in the first-generation HMM was more severe than we had hoped and this, coupled with the slow imaging speed, has really decreased my enthusiasm for this as a design that could be broadly used, especially for in vivo applications. So, rather than moving forward with animal experiments using the first-generation design, we focused on the second-generation HMM, which I believe will solve the primary problems, but at the expense of a more complicated laser and microscope design. This trade-off currently seems very much worth it.

Products:
Publications:
M.L. Buttolph, M.A. Mejooli, P. Sidorenko, C.-Y. Eom, C.B. Schaffer, and F.W. Wise, "Synchronously pumped Raman laser for simultaneous degenerate and nondegenerate two-photon microscopy," *Biomedical Optics Express* **12**, 2496 (2021).
A.J. Bares, M.A. Mejooli, M.A. Pender, S.A. Leddon, S. Tilley, K. Lin, J. Dong, M. Kim, D.J. Fowell, N. Nishimura, C.B. Schaffer, "Hyperspectral multiphoton microscopy for in vivo visualization of multiple, spectrally overlapped fluorescent labels," *Optica* **7**, 1587 (2020).

Patents:
A.J. Bares, C.B. Schaffer, S. Tilley, "Hyperspectral multiphoton microscope for biomedical applications," 10,394,008.

Participants:

Name:	Chris B. Schaffer
Project Role:	PI
Research ID:	ORCID: 0000-0002-7800-9596
Months:	1
Contribution:	Oversee the design, construction, and testing of HMM. Visit Prof. Wang to consult, maintain microscope and train users.
Funding:	Cornell salary and this award

Name:	Menansili Mejooli
Project Role:	Graduate student
Researcher ID:	??
Months:	12
Contribution:	Performed work on the design, construction, and testing of generation one and two HMM, as well as created linear unmixing and image analysis code.
Funding:	Cornell TA and fellowship awards, as well as this grant.

Other support:
An updated current and pending support document is appended for Prof. Schaffer.

PHS 398 OTHER SUPPORT

Schaffer, Chris

Active

3R01AG049952-05S1 (Schaffer, C)	15-May-2015 to 30-Apr-2021	Cal: 0.00 Acad: 1.35 Sumr: 0.00

National Institutes of Health

STALLED CAPILLARY FLOW: A NOVEL MECHANISM FOR HYPOPERFUSION IN ALZHEIMER DISEASE

The major goals of this project: This proposal tests the idea that reactive oxygen species produced in the Alzheimer brain leads to upregulation of cell adhesion markers in the endothelium, causing leukocyte adhesion in a subset of brain capillaries, thereby causing a global decrease in blood flow.

Role: PI

5R01EB002019-19 (Wise, F)	01-Sep-2016 to 31-May-2021	Cal: 0.00 Acad: 0.75 Sumr: 0.00

National Institutes of Health

LASER AND MICROSCOPE DEVELOPMENT FOR MULTICOLOR NONLINEAR IMAGING DEEP IN TISSUE

The major goals of this project: The major goals are the development of practical sources of high-energy ultrashort light pulses, along with novel microscope designs that will dramatically increase penetration depth and information density, which will enable novel studies of health and disease.

Role: CO

IIP-1635712 (Butcher, J)	01-Sep-2016 to 28-Feb-2021	Cal: 0.00 Acad: 0.38 Sumr: 0.00

NSF Directorate for Engineering

BLOOD FLOW REGULATION OF PHARYNGEAL ARCH ARTERY MORPHOGENESIS

The major goals of this project: The major goal of this project is to test the overall hypothesis that conserved hemodynamic signatures within the pharyngeal arch arteries (PAA) network control its local remodeling and maturation.

Role: CO

5R01NS100447-05 (Iadecola, C)	30-Sep-2016 to 30-Jun-2021	Cal: 0.00 Acad: 0.68 Sumr: 0.00

Weill Cornell Medicine / NIH NINDS

APOE4 AND MECHANISMS OF DIFFUSE WHITE MATTER INJURY

The major goals of this project: Prof. Schaffer’s laboratory will conduct all experiments in this proposal involving three-photon excited fluorescence imaging of vascular structure and reactivity in the white matter of mice as well as of myelin degeneration following carotid artery obstruction. Prof. Schaffer will guide the planning, execution, and analysis of these experiments. He will also coordinate with Prof. Iadecola and members of his team at Weill Cornell Medical.

Role: Cornell sub-contract PI

DBI-1707312 (Xu, C) 01-Sep-2017 to 31-Aug-2021 Cal: 0.00 Acad: 0.00 Sumr: 1.50

National Science Foundation

CORNELL NEUROTECHNOLOGY HUB FOR LARGE SCALE, NONINVASIVE RECORDING OF NEURAL ACTIVITY

The major goals of this project: Large scale, noninvasive recording of neural activity in awake and behaving animals is essential to understand the function of the central nervous system. Optical imaging is non-invasive and provides the high spatial resolution necessary to resolve individual neurons, while at the same time allowing many cells in a neural circuit to be observed simultaneously as they compute sensory or motor information

Role: CO

CBET-1706761 (Nishimura, N) 15-Jul-2017 to 30-Jun-2021 Cal: 0.00 Acad: 0.00 Sumr: 0.25

National Science Foundation

NEUROPHOTONIC STRATEGIES FOR CELL-RESOLVED, NON-INVASIVE BRAIN MACHINE INTERFACES: MULTICOLOR BIOLUMINESCENCE DELIVERED BY GENE THERAPY

The major goals of this project: This project is to develop an novel brain machine interface technology based on unmixing of multicolor bioluiminescence.

Role: CO

5R01NS099568-02 (Jhong, J) 15-Jul-2017 to 30-Jun-2022 Cal: 0.00 Acad: 0.25 Sumr: 0.00

Burke Medical Research Institute / National Institutes of Health

ENGAGING NEURON-INTRINSIC SIGNALING FOR AXON GROWTH AFTER SPINAL CORD INJURY

The major goals of this project: We aim to use in vivo three-photon excited fluorescence microscopy to visualize axon growth and neural activity in the spinal cord of mice after spinal cord injury and in response to proposed therapeutic strategies, in coordination with Prof. Jhong at the Burke Institute.

Role: Cornell sub-contract PI

DOH01-C32240GG-3450000 (Schaffer, C) 01-Mar-2017 to 28-Feb-2022 Cal: 0.00 Acad: 0.00 Sumr: 0.38

New York State Department of Health

ADAPTIVE OPTICS FOR DEEP IMAGING IN SPINAL CORD AFTER INJURY

The major goals of this project: We will install a deformable mirror that will enable us to correct for wavefront aberrations induced by focusing through the spinal cord and evaluate the extent to which this improves our signal strength, spatial resolution, and imaging depth.

Role: PI

5R01NS104350-03 (Vartanian, T) 01-Dec-2017 to 30-Nov-2022 Cal: 0.00 Acad: 0.00 Sumr: 0.38

Weill Cornell Medicine / NIH NINDS

Damage Associated Molecular Patterns and Regenerative Failure in MS

The major goals of this project: The Schaffer laboratory will conduct assessments of the myelin content of cerebellar slices and other central nervous system tissue samples using third harmonic generation microscopy as well as contribute to the planning and interpretation of experiments analyzing the underlying mechanisms and possible treatments for the demyelination of axons that underlies multiple sclerosis and to aid myelin visualization by Prof. Vartanian and his group.

Role: Cornell sub-contract PI

5R01NS108472-03 (Boas, D) 01-Sep-2018 to 31-May-2023 Cal: 0.05 Acad: 0.00 Sumr: 0.00

Boston University / NIH NINDS

The impact of microvascular (dys)regulation on cerebral flow and oxygen heterogeneity

The major goals of this project: Prof. Schaffer's laboratory will be responsible for conducting many of the two-photon imaging experiments to elucidate the mechanisms and consequences of stalled blood flow in brain capillaries.

Role: PI (MPI award - Cornell subaward)

5P01AI102851-07 (Fowell, D) 01-Sep-2019 to 31-Aug-2024 Cal: 0 Acad: 0 Sumr: 0.01

University of Rochester / NIH NIAID

Tissue Regulation of T Cell Function

The major goals of this project are to serve a core facility providing and developing methods to image as many cells as possible with hyperspectral microscopy.

Role: CO

1R21AG066001-01 REVISED (Nishimura, N) 01-Jan-2020 to 31-Dec-2021 Cal: 0 Acad: 0.45 Sumr: 0

National Institutes of Health

Neural activity underlying rapid behavioral recovery after blood flow improvement in Alzheimer mouse models

The major goals of this project are to measure neural activity and micro-seizures in cortex in somatosensory after treating capillary stalls.

Role: CO

Pending

(Spring, B) 01-Apr-2021 to 31-Mar-2023 Cal: 0.00 Acad: 0.18 Sumr: 0.00

Northeastern University / National Institutes of Health

Disease-Homing Light Delivery by Engineering Bioluminescent Immune Cells for Whole Body Precision Photomedicine

The Schaffer–Nishimura Lab will create genetic constructs to drive the expression of bioluminescent proteins in targeted classes of inflammatory cells and will work with members of Prof. Spring's laboratory to explore both the light production capability of these cells as well as their efficacy in activating photosensitizing agents for therapeutic purposes.

Role: PI on subaward

(Schaffer, C) 01-Apr-2021 to 31-Mar-2026 Cal: 0 Acad: 1.35 Sumr: 0

National Institutes of Health

Stalled capillary flow: a novel mechanism for hypoperfusion in Alzheimer disease

This award. The major goals of this project are to elucidate the cellular causes and molecular drivers of capillary stalling in AD mouse models and explore the consequences of reducing capillary stalling for disease progression.

Role: PI

(Butcher, J) 01-Jul-2021 to 30-Jun-2025 Cal: 0 Acad: 0.50 Sumr: 0

National Institutes of Health

Mechanbiology of Cardiac Outflow Tract Morphogenesis

The Schaffer laboratory will support the use of targeted femtosecond laser ablation for creating defects in cardiac outflow tracts in embryonic chicks to model heart developmental abnormalities.

Role: CO

(Macknik, S) 01-Jul-2021 to 30-Jun-2026 Cal: 0.00 Acad: 1.00 Sumr: 0.00

SUNY Downstate / National Institutes of Health

An Advanced Ultra-Widefield Mesoscope to Examine Computational Neurobiological Circuit Model of Skill Learning in the Cortex

The Schaffer/Nishimura lab will help with both the design of viruses and the construction of hyperspectral imaging instruments to support these studies in non-human primates.

Role: CO

(Nishimura, N) 01-Jun-2021 to 31-May-2023 Cal: 0.00 Acad: 0.25 Sumr: 0.25

National Institutes of Health

Simultaneous, cell-resolved, bioluminescent recording from microcircuits (current project)

This project aims to use transsynaptic virus delivery to drive expression of bioluminescent calcium indicators in neurons up- or down-stream from a target cell, enabling analysis of correlated firing in connected microcircuits.

Role: CO

(Nishimura, N) 01-Jul-2021 to 30-Jun-2026 Cal: 0.00 Acad: 1.00 Sumr: 0.00

National Institutes of Health

Rescue of hypoxia in heart failure mouse models through treating stalled capillaries

This project explores the hypothesis that arrested leukocytes in cardiac capillaries contribute to hypoxia and reduced cardiac performance in heart failure though experiments in mouse models.

Role: CO

(Maxfield, F) 09/01/2021 to 08/31/2026 Cal: 0 Acad: 0.45 Sumr: 0

Weill Cornell Medicine / National Institutes of Health

Microglial lysosomes and inflammation in Alzheimer’s disease

The major goals of this project are to explore the role of altered lysosome and degradative function in microglia in neuroegenerative disease

Role: Cornell sub-contract PI