Notice of Award

RESEARCH
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 09/18/2020

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Grant Number: 1R01NS118466-01 REVISED
FAIN: R01NS118466

Principal Investigator(s):
Cristopher M Niell, PHD

Project Title: Neural coding and functional organization of the octopus visual system

Mr. Bennett, Glen
Associate Director, Pre-award
5219 University of Oregon
Eugene, OR 974035219

Award e-mailed to: orsa@uoregon.edu

Period Of Performance:
Budget Period: 08/01/2020 – 05/31/2023
Project Period: 08/01/2020 – 05/31/2023

Dear Business Official:

The National Institutes of Health hereby revises this award to reflect an increase in the amount of $709,168 (see “Award Calculation” in Section I and “Terms and Conditions” in Section III) to UNIVERSITY OF OREGON in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the “Terms and Conditions” is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as “Research reported in this publication was supported by the National Institute Of Neurological Disorders And Stroke of the National Institutes of Health under Award Number R01NS118466. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.” Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator’s Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

James Washington
Grants Management Officer
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Additional information follows

SECTION I – AWARD DATA – 1R01NS118466-01 REVISED

Award Calculation (U.S. Dollars)

Federal Direct Costs	$727,500
Federal F&A Costs	$336,252
Approved Budget	$1,063,752
Total Amount of Federal Funds Obligated (Federal Share)	$1,063,752
TOTAL FEDERAL AWARD AMOUNT	$1,063,752
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$709,168

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
1	$1,063,752	$1,063,752

Fiscal Information:

CFDA Name:	Extramural Research Programs in the Neurosciences and Neurological Disorders
CFDA Number:	93.853
EIN:	1464727800A1
Document Number:	RNS118466A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2020

IC	CAN	2020
NS	8472428	$1,063,752

NIH Administrative Data:
PCC: eRA Commons User Name **OC**: 41021 / **Released:** eRA Commons User Name 09/17/2020
Award Processed: 09/18/2020 12:06:37 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 1R01NS118466-01 REVISED

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 1R01NS118466-01 REVISED

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of “Research and Development” at 45 CFR Part§ 75.2**.** As such, auditees

should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is excluded from Streamlined Noncompeting Award Procedures (SNAP).

MULTI-YEAR FUNDED AWARD: This is a multi-year funded award. A progress report is due annually on or before the anniversary of the budget/project period start date of the award, in accord with the instructions posted at: http://grants.nih.gov/grants/policy/myf.htm.

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01NS118466. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

This award represents the final year of the competitive segment for this grant. See the NIH Grants Policy Statement Section 8.6 Closeout for complete closeout requirements at: http://grants.nih.gov/grants/policy/policy.htm#gps.

A final expenditure Federal Financial Report (FFR) (SF 425) must be submitted through the eRA Commons (Commons) within 120 days of the period of performance end date; see the NIH Grants Policy Statement Section 8.6.1 Financial Reports, http://grants.nih.gov/grants/policy/policy.htm#gps, for additional information on this submission requirement. The final FFR must indicate the exact balance of unobligated funds and may not reflect any unliquidated obligations. There must be no discrepancies between the final FFR expenditure data and the Payment Management System's (PMS) quarterly cash transaction data. A final quarterly federal cash transaction report is not required for awards in PMS B subaccounts (i.e., awards to foreign entities and to Federal agencies). NIH will close the awards using the last recorded cash drawdown level in PMS for awards that do not require a final FFR on expenditures or quarterly federal cash transaction reporting. It is important to note that for financial closeout, if a grantee fails to submit a required final expenditure FFR, NIH will close the grant using the last recorded cash drawdown level. If the grantee submits a final expenditure FFR but does not reconcile any discrepancies between expenditures reported on the final expenditure FFR and the last cash report to PMS, NIH will close the award at the lower amount. This could be considered a debt or result in disallowed costs.

A Final Invention Statement and Certification form (HHS 568), (not applicable to training, construction, conference or cancer education grants) must be submitted within 120 days of the expiration date. The HHS 568 form may be downloaded at: http://grants.nih.gov/grants/forms.htm. This paragraph does not apply to Training grants, Fellowships, and certain other programs—i.e., activity codes C06, D42, D43, D71, DP7, G07, G08, G11, K12, K16, K30, P09, P40, P41, P51, R13, R25, R28, R30, R90, RL5, RL9, S10, S14, S15, U13, U14, U41, U42, U45, UC6, UC7, UR2, X01, X02.

Unless an application for competitive renewal is submitted, a Final Research Performance Progress Report (Final RPPR) must also be submitted within 120 days of the period of performance end date. If a competitive renewal application is submitted prior to that date, then an Interim RPPR must be submitted by that date as well. Instructions for preparing an Interim or Final RPPR are at: https://grants.nih.gov/grants/rppr/rppr_instruction_guide.pdf. Any other specific requirements set forth in the terms and conditions of the award must also be addressed in the Interim or Final RPPR. *Note that data reported within Section I of the Interim and Final RPPR forms will be made public and should be written for a lay person audience*.

NIH strongly encourages electronic submission of the final invention statement through the Closeout feature in the Commons, but will accept an email or hard copy submission as indicated below.

Email: The final invention statement may be e-mailed as PDF attachments to: NIHCloseoutCenter@mail.nih.gov.

Hard copy: Paper submissions of the final invention statement may be faxed to the NIH Division of Central Grants Processing, Grants Closeout Center, at 301-480-2304, or mailed to:

National Institutes of Health
Office of Extramural Research
Division of Central Grants Processing
Grants Closeout Center
6705 Rockledge Drive
Suite 5016, MSC 7986
Bethesda, MD 20892-7986 (for regular or U.S. Postal Service Express mail)
Bethesda, MD 20817 (for other courier/express deliveries only)

NOTE: If this is the final year of a competitive segment due to the transfer of the grant to another institution, then a Final RPPR is not required. However, a final expenditure FFR is required and should be submitted electronically as noted above. If not already submitted, the Final Invention Statement is required and should be sent directly to the assigned Grants Management Specialist.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – NS Special Terms and Conditions – 1R01NS118466-01 REVISED

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

REVISED AWARD:

This award has been converted to a multi-year funded award, with three years of funding provided in the current fiscal year. The fourth and fifth years of support will be funded contingent upon an acceptable administrative progress review and receipt of the information below.

Due to the expiration of funds in keeping with Public Law 101-510, any future no-cost extensions will be limited to May 31, 2023 to provide the awardee with sufficient time to complete the close out process. Public Law 101-510 limits the availability of funds to five fiscal years after the original obligation. Funds awarded expire on May 31, 2023 and will not be available for draw-down in the Payment Management System (PMS). Any funds drawn down after May 31, 2023 will need to be returned.

Effective December 22, 2010 (NOT-OD-11-010), NIH requires that all multi-year funded awards submit an annual progress report. The annual progress report is due each year on or before *April 1st* . Instructions on how to submit the report through the eRA Commons are posted at http://grants.nih.gov/grants/policy/myf.htm

In Years 2 and 4, in addition to submitting a progress report, the team is required to present their progress by teleconference with the BRAIN Program directors. Also, a representative from each project is required to attend the annual BRAIN Investigators meeting. Regarding resource and data sharing, the team is required to adhere to the policy outlined at NOT-MH-19-010 (https://grants.nih.gov/grants/guide/notice-files/NOT-MH-19-010.html).

ADMINISTRATIVE CONTINUATION APPLICATION:

The Principal Investigator will submit an Administrative Continuation Application in order to request support for the final year of this project. A signed PHS 2590 face page, which will serve as the application package, is due 2 months prior to the anticipated start of the 4th year of support and should be sent by email from the Authorized Organizational Representative (AOR) to the Program Official and Grants Management Specialist identified below or in the eRA Commons. **Note that the administrative review cannot be completed without the receipt of the RPPR documenting the 3rd year of progress.** In order to prevent a lapse in funding, we strongly encourage you to submit the information above as well as the RPPR documenting the 3rd year of progress **60 days prior to start of the 4th budget period**. We are unable to release additional funds until administrative review has been completed.

NINDS staff will review these documents administratively. If approved, a Notice of Award will be issued extending the project period for two additional years. If not approved for continued funding, a one-year no-cost extension will be permitted upon request.

THE PREVIOUS TERMS AND CONDITIONS STATED BELOW REMAIN IN EFFECT.

This award includes funds for twelve months of support. The competing budget period is awarded for less than 12 months. Future year budget periods will start on June *1st* Allowable preaward costs may be charged to this award, in accordance with the conditions outlined in the NIH Grants Policy Statement (revised October 2013) and with institutional requirements for prior approval. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/nihgps_2013/index.htm.

In order to meet Institute program objectives within Fiscal Year 2020 budget constraints, the recommended levels for this grant have been reduced. Future year recommended levels of support have also been reduced.

Per the NINDS funding strategy:
http://www.ninds.nih.gov/funding/ninds_funding_strategy.htm

Inflationary increases for future year commitments are not allowable. See NIH Guide Notice: NOT-OD-13-064- http://grants.nih.gov/grants/guide/notice-files/NOT-OD-13-064.html

In accordance with the Notice: NOT-OD-20-070, published on February 7, 2020 in the NIH Guide for Grants and Contracts, total direct costs (salary, fringe benefits and tuition remission) for graduate students are provided at a level not to exceed the NIH maximum allowable amount (zero level of the Ruth L. Kirschstein National Research Service Award stipend in effect at the

time of the competing award). Support recommended for future years has been adjusted accordingly, if applicable.

The full guide Notice describing the level of compensation allowed for a graduate student can be found at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-070.html

In future years, awards under the Streamlined Non-Competing Award Process (SNAP) must submit a non-competing application via the eRA Commons by the 15th of the month preceding the month in which the budget period ends. The non-competing application can be submitted using the Research Performance Progress Report (RPPR) format via the RPPR link in eRA Commons.

The use of the eRA Research Performance Progress Report (RPPR) Module for submitting Type 5 Progress Reports is required for all awards with start dates on or after October 17, 2014. See Guide Notice: NOT-OD-15-014 http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-014.html

The funds in this award shall not be used to pay the salary of an individual at a rate in excess of Executive Level II ($197,300) per year effective January 5, 2020 See NIH Guide Notice: NOT-OD-20-065 https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-065.html

To register to use the Commons go to https://commons.era.nih.gov/commons/. Questions regarding the Commons should be addressed to Commons Support at 1-866-504-9552 or commons@od.nih.gov.

Other documents applicable to this grant should be faxed to (301) 451-5635 or mailed to:

Grants Management Branch
National Institutes of Neurological Disorders and Stroke
6001 Executive Boulevard, Suite 3290, MSC 9537
Rockville, MD 20852 (Express Mail)
Bethesda, MD 20892-9537 (Regular Mail)

For additional information, you may access the NIH home page at http://www.nih.gov/ ;;;; and the NINDS Home Page at http://www.ninds.nih.gov

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Brenda Kibler
Email: kiblerb@ninds.nih.gov **Phone**: 301-496-7441 **Fax**: 301-451-5635

Program Official: Karen Kate David
Email: karen.david@nih.gov **Phone**: 301-496-9964

SPREADSHEET SUMMARY
GRANT NUMBER: 1R01NS118466-01 REVISED

INSTITUTION: UNIVERSITY OF OREGON

Budget	Year 1
TOTAL FEDERAL DC	$727,500
TOTAL FEDERAL F&A	$336,252
TOTAL COST	$1,063,752

PI: **Niell, Cristopher M**	Title: Neural coding and functional organization of the octopus visual system	
Received: 11/06/2019	FOA: NS18-030 Clinical Trial:Not Allowed	Council: 05/2020
Competition ID: FORMS-E	FOA Title: BRAIN Initiative: Targeted BRAIN Circuits Projects- TargetedBCP (R01 Clinical Trial Not Allowed)	
1 R01 NS118466-01	Dual: AA,AG,AT,DA,DC,EB,EY,HD,MH	Accession Number: 4372895
IPF: 6297005	Organization: UNIVERSITY OF OREGON	
Former Number:	Department: Institute of Neuroscience	
IRG/SRG: ZRG1 IFCN-T (55)R	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 250,000 Year 2: 250,000 Year 3: 250,000 Year 4: 250,000 Year 5: 250,000	Animals: N Humans: N Clinical Trial: N Current HS Code: Evaluative Info HESC: N HFT: N	New Investigator: N Early Stage Investigator: N
Senior/Key Personnel:	*Organization:*	*Role Category:*
Cristopher Niell Ph.D	University of Oregon	PD/PI
Redacted by agreement	University of Oregon	Other (Specify)-Other Significant Contributor

OMB Number: 4040-0001
Expiration Date: 10/31/2019

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	State Application Identifier

1. TYPE OF SUBMISSION*

❍ Pre-application ● Application ❍ Changed/Corrected Application

4.a. Federal Identifier

b. Agency Routing Number

2. DATE SUBMITTED | **Application Identifier**

c. Previous Grants.gov Tracking Number

5. APPLICANT INFORMATION

Organizational DUNS*: 0792896260000

Legal Name*: University of Oregon
Department: Institute of Neuroscience
Division: V. P. Research and Innovation
Street1*: 5219 University of Oregon
Street2:
City*: Eugene
County: Lane
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 97403-5219

Person to be contacted on matters involving this application
Prefix: Mr. First Name*: Glen Middle Name: Last Name*: Bennett Suffix:
Position/Title: Associate Director, Pre-award
Street1*: 5219 University of Oregon
Street2:
City*: Eugene
County: Lane
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 97403-5219
Phone Number*: 541-346-5131 Fax Number: 541-346-5138 Email: sponsoredprojects@uoregon.edu

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 1464727800A1

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

● New ❍ Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).
❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Neural coding and functional organization of the octopus visual system

12. PROPOSED PROJECT
Start Date* 06/01/2020
Ending Date* 05/31/2025

13. CONGRESSIONAL DISTRICTS OF APPLICANT
OR-004

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: First Name*: Cristopher Middle Name: M Last Name*: Niell Suffix: Ph.D

Position/Title: Associate Professor of Biology
Organization Name*: University of Oregon
Department: Institute of Neuroscience
Division: V. P. Research and Innovation
Street1*: 1254 University of Oregon
Street2:
City*: Eugene
County: Lane
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 97403-1254
Phone Number*: 541-346-8598 Fax Number: 541-346-4548 Email*: cniell@uoregon.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$1,827,755.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$1,827,755.00
d. Estimated Program Income*	$0.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: First Name*: David Middle Name: O. Last Name*: Conover Suffix: Ph.D

Position/Title*: Vice President for Research and Innovation
Organization Name*: University of Oregon
Department: Sponsored Projects Services
Division: V .P. Research and Innovation
Street1*: 5219 University of Oregon
Street2:
City*: Eugene
County: Lane
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 97403-5219
Phone Number*: 541-346-5131 Fax Number: 541-346-5138 Email*: sponsoredprojects@uoregon.edu

Signature of Authorized Representative*
Glen Bennett

Date Signed*
11/06/2019

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:

424 R&R and PHS-398 Specific
Table Of Contents

OMB Number: 4040-0010
Expiration Date: 10/31/2019

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	University of Oregon/Institute of Neuroscience
Duns Number:	0792896260000
Street1*:	1254 University of Oregon
Street2:	
City*:	Eugene
County:	Lane
State*:	OR: Oregon
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	97403-1254
Project/Performance Site Congressional District*:	OR-004

Additional Location(s) File Name:

Funding Opportunity Number: RFA-NS-18-030. Received Date: 2019-11-06T17:15:16.000-05:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ❍ **Yes** ● **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ❍ Yes ❍ No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 _ 7 _ 8

If NO, is the IRB review Pending? ❍ **Yes** ❍ **No**

IRB Approval Date:

Human Subject Assurance Number

2. Are Vertebrate Animals Used?* ❍ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ❍ Yes ❍ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ❍ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ❍ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ❍ Yes ❍ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ❍ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ❍ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	Abstract.pdf
8. Project Narrative*	Narrative.pdf
9. Bibliography & References Cited	References.pdf
10.Facilities & Other Resources	Facilities.pdf
11.Equipment	Equipment.pdf

ABSTRACT

Cephalopods have large and complex brains, and in particular a highly capable visual system. However, their brains evolved independently from vertebrates, and very little is known about how neural circuits in the cephalopod brain process visual information. In fact, there has never been a direct recording of receptive fields in the central visual system of cephalopods. This study will measure neural activity and visual coding in the optic lobe of *Octopus bimaculoides*, an emerging model organism for cephalopod research. The first aim will employ two-photon calcium imaging in the optic lobe of juvenile octopuses, combined with controlled visual stimuli, to measure receptive field properties in large ensembles of individual neurons. The second aim will combine this functional imaging with anatomical connectivity, identified via retrograde tracing, to determine how visual information is routed through the visual system and into higher brain regions associated with specific behaviors. The third aim will incorporate these experimental results into computational analysis of the visual features being encoded, and into network models of visual processing. Together, these aims will provide direct insight into the neural coding and functional organization of this unique visual system.

This work will be the first to describe neural computations in the central visual system of cephalopods. Examination of a system that is evolutionarily distinct, yet functionally parallel to the vertebrate system, has the potential to illuminate novel ways by which visual processing can be carried out. Likewise, observation of convergence of functional organization in cephalopods, relative to vertebrates and other invertebrates, such as Drosophila, would help identify key features necessary for the function of complex visual systems.

NARRATIVE

This project will provide the first measurements of visual response properties and functional organization in the octopus visual system. This has the potential to reveal aspects of visual processing that are shared across diverse species, which would suggest fundamental computations that are broadly required for vision.

RESEARCH FACILITIES

Laboratory

The PI's laboratory is located in the Redacted by agreement on the University of Oregon campus. The laboratory space consists of Redacted by agreement including a central bench space for molecular biology and electronics work, as well as multiple smaller rig rooms appropriate for in vivo microscopy and electrophysiology.

Animal

Animals are housed in the Animal Care Services vivarium, located directly beneath the PI's lab in the Redacted by agreement The facility is AALAC accredited and has full veterinary staff. PI Niell has one dedicated room for octopus housing.

Computers

The PI and each lab member have their own high-end desktop computer for data analysis, with Matlab and at least 64 GB of RAM, as well as work processing and other software. The Institute of Neuroscience has a Computer Technical Support group for assistance, with to full-time staff.

High performance computing

UO has recently invested in a high-performance computational cluster available for the research community. The flagship cluster contains 96 general purpose computational nodes providing 2,688 physical cores, 8 large memory machines with 1-2TB of RAM for high memory applications, and 24 compute nodes with dual Tesla K80 accelerators.

Other facilities

Shared core facilities available to support the experimental aims include histology, electron microscopy, media preparation, and a bioinformatics core, all with full-time staff. There are also both electronics and machine shop services, which are invaluable for the custom instrumentation we develop.

Research Environment

The Institute of Neuroscience, housed in the connected LISB and Huestis buildings, creates a dynamic multidisciplinary research environment to support this research. In particular, the same connected floor in LISB and Huestis also houses four other systems neuroscience labs, as well as faculty from Cognitive Neuroscience studying visual processing and attention in humans, including an in-house dedicated fMRI center. The Institute of Neuroscience has a long history of basic research in a range of species, and in particular, pioneered the development of zebrafish as a model system. Research across the Institute currently spans from neural development to sensory and motor systems, in species including worm, fly, zebrafish, stickleback fish, owls, mice, and humans. This provides a unique and highly interactive environment to study the neural circuits underlying visual processing in novel species.

MAJOR EQUIPMENT

All major equipment required for this project is currently available in the Niell lab.

Functional imaging microscopes: We currently have two separate two-photon microscopes, one from Sutter Instruments, and one recently acquired from Neurolabware with large (~1 mm^2) field of view. Both are driven by a Spectra-Physics Mai-Ti eHP ultrafast laser, and equipped with Nikon 16x/0.8NA objectives. We also have two separate widefield imaging scopes, one home-built single detector microscope, and one dual-detector microscope from Scimedia Inc. capable of two-color imaging. Both of these include feedback-controlled LED illumination and green reflectance channel for hemodynamic correction. All of these microscopes are equipped for behavioral tasks, and capable of pupil/locomotion tracking and optogenetics.

Stereotaxic surgical stations: We have three stereotaxic surgery stations, including one optimized for octopus experiments that is equipped with a fluorescence stereoscope and Micro4 pressure injection system (WPI Inc.) for performing calcium indicator and retrograde tracer injections.

Aquaria: We have a custom-built [Redacted by agreement] closed circulating aquarium system for housing octopuses in the vivarium. The system is in a temperature-controlled room with an automatic 12/12 hour light cycle. It was built with heavy aeration and filtration equipment, sufficient to compensate for the extreme metabolic rates of cephalopods and maintain healthy water quality. Independent housings within this larger system allow for the separation of animals while maintaining their access to a constant flow of the larger water volume.

Extracellular recording: Although we do not propose electrophysiology in this project, two extracellular recording systems from Tucker-Davis Technologies are available in the lab, comprised of a PZ2-64 pre-amplifier feeding into a RZ2-4 high-performance DSP processor. Each system is capable of recording up to 128 channels. Recordings are performed with Neuronexus silicon probes, using a custom design developed by the Niell lab in collaboration with Neuronexustech (a2x32-5mm-25-200-177).

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: First Name*: Cristopher Middle Name M Last Name*: Niell Suffix: Ph.D

Position/Title*: Associate Professor of Biology
Organization Name*: University of Oregon
Department: Institute of Neuroscience
Division: V. P. Research and Innovation
Street1*: 1254 University of Oregon
Street2:
City*: Eugene
County: Lane
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 97403-1254

Phone Number*: 541-346-8598 Fax Number: 541-346-4548

E-Mail*: cniell@uoregon.edu

Credential, e.g., agency login: eRA Commons User Name

Project Role*: PD/PI Other Project Role Category:

Degree Type: PHD, BS Degree Year: 2004, 1995

Attach Biographical Sketch*: File Name: Biosketch_Niell.pdf

Attach Current & Pending Support: File Name:

Tracking Number: GRANT12968534
Funding Opportunity Number: RFA-NS-18-030 . Received Date: 2019-11-06T17:15:16.000-05:00

Redacted by agreement

OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Cristopher M. Niell

eRA COMMONS USER NAME (credential, e.g., agency login): eRA Commons User Name

POSITION TITLE: Associate Professor of Biology

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
Stanford University, Stanford, CA	B.S.	1995	Physics
Stanford University, Stanford, CA	Ph.D	1998-2004	Neurosciences
University of California, San Francisco CA	Postdoc	2005-2011	Dept. of Physiology

A. Personal Statement

I have spent most of my research career studying the development and function of neural circuits. As a graduate student in Dr. Stephen Smith's lab at Stanford University, I used two-photon imaging in the zebrafish optic tectum to study both functional receptive field properties and the developmental processes of growth and synapse formation. I then began work on the mouse visual cortex, in the lab of Dr. Michael Stryker at UC San Francisco, utilizing the mouse as genetic model system to investigate aspects of cortical organization and development. In my lab at University of Oregon, we are focused on understanding large-scale cortical processing from the level of individual neurons up to brain-wide pathways, particularly in the context of visual processing and behavior. Throughout my career, I have applied a range of technical approaches, including optics, electrophysiology, behavior, and theoretical modeling, to the study of the visual system across two different species. This background makes me ideally prepared to undertake the study of a novel visual system, the octopus, in this proposal

Niell CM and Smith SJ. (2005) Functional imaging reveals rapid development of visual response properties in zebrafish tectum. *Neuron*. 45(6):941-951.

Niell, CM and Stryker MP. (2008) Highly selective receptive fields in mouse visual cortex. *Journal of Neuroscience.* 28(30):7520-7536.

Lee AM, Hoy JL, Bonci A, Wilbrecht L, Stryker MP, and **Niell CM**. (2014) Identification of a brainstem circuit regulating visual cortical state in parallel with locomotion. *Neuron*. 83(2): 455-466.

Wekselblatt JM, Flister ED, Piscopo DP, and **Niell CM.** (2016) Large-scale imaging of cortical dynamics during sensory perception and behavior. (2016) *Journal of Neurophysiology* 115(6): 2852-66.

Unpublished

B. Positions and Honors

RESEARCH POSITIONS

1994 – 1995	Honors thesis, Physics Department, Stanford University, (Dr. Steven Chu)
1998 – 2004	Ph.D., Neuroscience Graduate Program, Stanford University (Dr. Stephen Smith)
2005 – 2011	Postdoctoral Fellow, Department of Physiology, UC San Francisco (Dr. Michael Stryker)
2011 – 2017	Assistant Professor, Dept of Biology and Institute of Neuroscience, University of Oregon
2017 –	Associate Professor, Dept of Biology and Institute of Neuroscience, University of Oregon

HONORS AND AWARDS

1994	Carrington Award for achievement in undergraduate physics
1994	Phi Beta Kappa inductee
1997	Stanford Graduate Fellowship
1998	Howard Hughes Predoctoral Fellowship
2005	NIH Ruth Kirschstein NRSA postdoctoral fellowship
2006	Helen Hay Whitney Foundation postdoctoral fellowship
2012	Sloan Research Fellowship
2012	Searle Scholar Award
2012	NIH Director's New Innovator Award recipient
2013	University of Oregon Early Career Award recipient
2016	Office of Naval Research Young Investigator Award
2017	Medical Research Foundation of Oregon New Investigator Award

OTHER EXPERIENCE AND PROFESSIONAL MEMBERSHIPS

1998 - present	Member, Society for Neuroscience
2000	Student, Genetics and Neural Development of Zebrafish (MBL)
2003	Student, Advanced Course in Computational Neuroscience (IBRO/FENS)
2009	Co-chair, Society for Neuroscience minisymposium – Visual processing in the mouse
2013	Lecturer, CSHL summer course on Vision

C. Contributions to Science

1. Imaging function and development of neural circuits in zebrafish visual system

During my PhD, I developed in vivo imaging approaches to study both the structural and function development of neural circuits in the zebrafish optic tectum. These studies provided important insights into how neural circuits get wired up during development in the context of a functional visual system.

Niell CM, Smith SJ. (2004) Live optical imaging of nervous system development. *Annual Review of Physiology.* 66:771-798. (review)

Niell* CM, Meyer* MP, Smith SJ. (2004) In vivo imaging of synapse formation on a growing dendritic arbor. *Nature Neuroscience.* 7(3):254-260.

Niell CM and Smith SJ. (2005) Functional imaging reveals rapid development of visual response properties in zebrafish tectum. *Neuron*. 45(6):941-951.

Niell CM. (2006) Theoretical analysis of a synaptotropic dendrite growth mechanism. *Journal of Theoretical Biology.* 24(1):39-48.

2. Neural coding in the mouse visual system

Traditionally, studies of visual processing were performed in higher visual species such as cat and primate. In order to take advantage of genetic methods available in mice, we characterized functional response properties

in thalamus and cortex, and showed that these are similar to previously studies species. This laid the foundation for studies from many labs that are now using the mouse as a model system for studying vision. We have subsequently studied the receptive field properties in subcortical structures, thalamus and superior colliculus, as well as implementing an ethological behavioral task, prey capture.

Niell, CM and Stryker MP. (2008) Highly selective receptive fields in mouse visual cortex. *Journal of Neuroscience.* 28(30):7520-7536.

Piscopo DM, El-Danaf, R, Huberman AD, and **Niell CM.** (2013) Diverse visual features encoded in mouse lateral geniculate nucleus. *Journal of Neuroscience*. 33(11): 4642-56.

Niell, CM. (2015) Cell types, circuits, and receptive fields in mouse visual cortex. *Annual Review of Neuroscience*. 38:413-31. (review)

Unpublished

3. Modulation of visual processing by behavioral state

In order to understand how sensory processing depends on ongoing behavior, we investigated the effects of locomotion on visual processing. This revealed a striking increase in visual responses in cortex during movement, which we then demonstrated is initiated by a brainstem circuit. Recently we developed an in vivo imaging method to characterize cortex-wide dynamics during visual behavioral tasks, as well as establishing an ethological visual behavior task based on prey capture.

Niell CM and Stryker MP. (2010) Modulation of visual responses by behavioral state in the mouse visual cortex. *Neuron*. 65(4):472-9.

Lee AM, Hoy JL, Bonci A, Wilbrecht L, Stryker MP, and **Niell CM**. (2014) Identification of a brainstem circuit regulating visual cortical state in parallel with locomotion. *Neuron*. 83(2): 455-466.

Wekselblatt JM, Flister ED, Piscopo DP, and **Niell CM.** (2016) Large-scale imaging of cortical dynamics during sensory perception and behavior. (2016) *Journal of Neurophysiology* 115(6): 2852-66.

Hoy JL, Yavorska I, Wehr M, and **Niell CM**. (2016) Vision drives accurate approach behavior during prey capture in laboratory mice. *Current Biology* 26(22): 3046-3052.

4. Development of neural circuits in mouse visual cortex

Combining genetic manipulations of developmental genes with functional readout of receptive fields in mice has enabled us to test long-standing hypotheses about the mechanisms of neural development. During my post-doc with Michael Stryker, we showed that chemical gradients and neural activity work together to create retinotopic maps. In my lab at University of Oregon, we characterized the sequential refinement of receptive fields and network activity in mice from infancy through adulthood, and implemented gene profiling methods to identify candidate genes involved in layer-specific synapse formation.

Cang* JC, **Niell* CM**, Liu X, Pfeiffenberger C, Feldheim DA and Stryker MP. (2008) Selective disruption of one Cartesian axis of cortical maps and receptive fields by deficiency in Ephrin-As and structured activity *Neuron*. 57(4):511-23.

Hoy, JL, and **Niell CM**. (2015) Layer-specific refinement of visual cortex function after eye-opening in the awake mouse. *Journal of Neuroscience* 35(8):3370-83.

Tomorsky J, DeBlander L, Kentros CG, Doe CQ, **Niell CM**. (2017) TU-tagging: a method for identifying layer-enriched neuronal genes in developing visual cortex. *eNeuro* 0181-17.2017.

Tschetter WW, Govindaiah G, Etherington IM, Guido W, and **Niell CM**. (2018) Refinement of spatial receptive fields in the developing mouse LGN is coordinated with excitatory and inhibitory remodeling. *Journal of Neuroscience.* 38(19):4531-42.

A complete list of publications is available at https://www.ncbi.nlm.nih.gov/pubmed/?term=niell+cm

D. Additional Information: Research Support and/or Scholastic Performance

ACTIVE SUPPORT

Private Source (PI: Niell, Co-PI Hochner) 05/01/19 – 04/31/22
Imaging sensory processing and memory storage in the octopus brain
This collaborative project will seek to determine how visual information is stored as long-term memory in the octopus brain

NIH 1R34NS111669-01 (PI: Niell) 04/01/19 – 03/31/21
Visual coding in freely moving behavior
This project will develop technology to measure visual input in freely moving mice and relate this to neural signals in the visual cortex

NIH 1R21EY029888-01 (PI: Niell) 01/01/19-12/31/21
Impact of environmental experience on visual processing and behavior
This project will use determine how environmental experience impacts a broad range of measures of visual processing in mouse.

Office of Naval Research N00014-15-1-2148 (PI: Posner, Co-PI: Niell) 05/01/15 - 09/30/20
Towards a neural model of human skill learning
This project will pair studies in mice and humans to determine the brain regions and local circuit mechanisms underlying skill acquisition.

COMPLETED SUPPORT WITHIN LAST THREE YEARS

NIH R01 Grant 1R01EY023337-01 (PI: Niell) 05/01/13 - 03/31/18
Neural pathways and behavioral state in the mouse visual system
This project addresses the control of information flow in multiple visual pathways during changes in behavioral state, using electrophysiology and optogenetics in the awake mouse.

NIH-DHHS New Innovator Award 1DP2EY023190 (Niell, PI) 09/30/12 - 07/31/17
Connecting developmental mechanisms to visual function and perception.
This project addresses the assembly of functional circuits in the visual system using molecular genetics, psychophysics, and in vivo imaging.

Office of Naval Research N00014-16-1-3154 (PI: Niell) 09/01/16 - 08/31/19
Large-scale neural circuits underlying skilled task performance
This project will use imaging and behavioral methods in mice to determine how cortical circuits regulate learning and task engagement.

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Withheld pursuant to exemption

Redacted by agreement

of the Freedom of Information and Privacy Act

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

Expiration Date: 03/31/2020

1. Vertebrate Animals Section

Are vertebrate animals euthanized? ○ Yes ● No

If "Yes" to euthanasia

Is the method consistent with American Veterinary Medical Association (AVMA) guidelines?

○ Yes ○ No

If "No" to AVMA guidelines, describe method and provide scientific justification

2. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period *Anticipated Amount ($) *Source(s)

Tracking Number: GRANT12968534

Funding Opportunity Number: RFA-NS-18-030 . Received Date: 2019-11-06T17:15:16.000-05:00

PHS 398 Cover Page Supplement

3. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ○ Yes ● No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, check the box indicating that one from the registry will be used:

❑ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s) (Example: 0004):

4. Inventions and Patents Section (Renewal applications)

*Inventions and Patents: ○ Yes ● No

If the answer is "Yes" then please answer the following:

*Previously Reported: ○ Yes ○ No

5. Change of Investigator/Change of Institution Section

❑ Change of Project Director/Principal Investigator

Name of former Project Director/Principal Investigator

Prefix:

*First Name:

Middle Name:

*Last Name:

Suffix:

❑ Change of Grantee Institution

*Name of former institution:

PHS 398 Modular Budget

OMB Number: 0925-0001
Expiration Date: 03/31/2020

Budget Period: 1

Start Date: 06/01/2020 End Date: 05/31/2021

A. Direct Costs

	Funds Requested ($)
Direct Cost less Consortium Indirect (F&A)*	250,000.00
Consortium Indirect (F&A)	
Total Direct Costs*	250,000.00

B. Indirect (F&A) Costs

	Indirect (F&A) Type	Indirect (F&A) Rate (%)	Indirect (F&A) Base ($)	Funds Requested ($)
1.	Modified Total Direct Costs	47.50	243,265.00	115,551.00
2.				
3.				
4.				

Cognizant Agency (Agency Name, POC Name and Phone Number): DHHS (Dept. Health & Human Services) Cora Coleman
Telephone: (415) 437-7820

Indirect (F&A) Rate Agreement Date: 06/27/2019

Total Indirect (F&A) Costs: 115,551.00

C. Total Direct and Indirect (F&A) Costs (A + B)

Funds Requested ($): 365,551.00

Funding Opportunity Number: RFA-NS-18-030. Received Date: 2019-11-06T17:15:16.000-05:00

PHS 398 Modular Budget

Budget Period: 2			
Start Date: 06/01/2021 End Date: 05/31/2022			
A. Direct Costs			Funds Requested ($)
		Direct Cost less Consortium Indirect (F&A)*	250,000.00
		Consortium Indirect (F&A)	
		Total Direct Costs*	250,000.00

B. Indirect (F&A) Costs

	Indirect (F&A) Type	Indirect (F&A) Rate (%)	Indirect (F&A) Base ($)	Funds Requested ($)
1.	Modified Total Direct Costs	47.50	243,265.00	115,551.00
2.				
3.				
4.				

Cognizant Agency (Agency Name, POC Name and Phone Number): DHHS (Dept. Health & Human Services) Cora Coleman Telephone: (415) 437-7820

Indirect (F&A) Rate Agreement Date: 06/27/2019

Total Indirect (F&A) Costs: 115,551.00

C. Total Direct and Indirect (F&A) Costs (A + B)	Funds Requested ($)	365,551.00

Funding Opportunity Number: RFA-NS-18-030. Received Date: 2019-11-06T17:15:16.000-05:00

PHS 398 Modular Budget

Budget Period: 3

Start Date: 06/01/2022 End Date: 05/31/2023

A. Direct Costs

	Funds Requested ($)
Direct Cost less Consortium Indirect (F&A)*	250,000.00
Consortium Indirect (F&A)	
Total Direct Costs*	250,000.00

B. Indirect (F&A) Costs

	Indirect (F&A) Type	Indirect (F&A) Rate (%)	Indirect (F&A) Base ($)	Funds Requested ($)
1.	Modified Total Direct Costs	47.50	243,265.00	115,551.00
2.				
3.				
4.				

Cognizant Agency (Agency Name, POC Name and Phone Number): DHHS (Dept. Health & Human Services) Cora Coleman Telephone: (415) 437-7820

Indirect (F&A) Rate Agreement Date: 06/27/2019

Total Indirect (F&A) Costs: 115,551.00

C. Total Direct and Indirect (F&A) Costs (A + B)

Funds Requested ($): 365,551.00

Funding Opportunity Number: RFA-NS-18-030. Received Date: 2019-11-06T17:15:16.000-05:00

PHS 398 Modular Budget

Budget Period: 4			
Start Date: 06/01/2023 End Date: 05/31/2024			
A. Direct Costs			Funds Requested ($)
		Direct Cost less Consortium Indirect (F&A)*	250,000.00
		Consortium Indirect (F&A)	
		Total Direct Costs*	250,000.00

B. Indirect (F&A) Costs

	Indirect (F&A) Type	Indirect (F&A) Rate (%)	Indirect (F&A) Base ($)	Funds Requested ($)
1.	Modified Total Direct Costs	47.50	243,265.00	115,551.00
2.				
3.				
4.				

Cognizant Agency (Agency Name, POC Name and Phone Number): DHHS (Dept. Health & Human Services) Cora Coleman Telephone: (415) 437-7820

Indirect (F&A) Rate Agreement Date: 06/27/2019

Total Indirect (F&A) Costs: 115,551.00

C. Total Direct and Indirect (F&A) Costs (A + B)	Funds Requested ($)	365,551.00

Funding Opportunity Number: RFA-NS-18-030. Received Date: 2019-11-06T17:15:16.000-05:00

PHS 398 Modular Budget

Budget Period: 5			
Start Date: 06/01/2024 End Date: 05/31/2025			
A. Direct Costs			Funds Requested ($)
		Direct Cost less Consortium Indirect (F&A)*	250,000.00
		Consortium Indirect (F&A)	
		Total Direct Costs*	250,000.00

B. Indirect (F&A) Costs

	Indirect (F&A) Type	Indirect (F&A) Rate (%)	Indirect (F&A) Base ($)	Funds Requested ($)
1.	Modified Total Direct Costs	47.50	243,265.00	115,551.00
2.				
3.				
4.				

Cognizant Agency (Agency Name, POC Name and Phone Number): DHHS (Dept. Health & Human Services) Cora Coleman Telephone: (415) 437-7820

Indirect (F&A) Rate Agreement Date: 06/27/2019

Total Indirect (F&A) Costs: 115,551.00

C. Total Direct and Indirect (F&A) Costs (A + B)	Funds Requested ($)	365,551.00

Funding Opportunity Number: RFA-NS-18-030. Received Date: 2019-11-06T17:15:16.000-05:00

PHS 398 Modular Budget

Cumulative Budget Information

1. Total Costs, Entire Project Period

Section A, Total Direct Cost less Consortium Indirect (F&A) for Entire Project Period ($)	1,250,000.00
Section A, Total Consortium Indirect (F&A) for Entire Project Period ($)	0.00
Section A, Total Direct Costs for Entire Project Period ($)	1,250,000.00
Section B, Total Indirect (F&A) Costs for Entire Project Period ($)	577,755.00
Section C, Total Direct and Indirect (F&A) Costs (A+B) for Entire Project Period ($)	1,827,755.00

2. Budget Justifications

Personnel Justification	Personnel_Justification.pdf
Consortium Justification	
Additional Narrative Justification	

Tracking Number: GRANT12968534

Funding Opportunity Number: RFA-NS-18-030. Received Date: 2019-11-06T17:15:16.000-05:00

Key Personnel

Cristopher Niell, PhD. EFFORT Role : Principal Investigator

Dr. Niell is an Associate Professor in the Department of Biology at University of Oregon. He has extensive experience in studying the visual system, in zebrafish and mouse, and established the experimental approaches proposed here. Dr. Niell will supervise the project, including designing experiments, analyzing data, writing manuscripts, and preparing progress reports. He will ensure appropriate management and administration of the project, as well as compliance with institutional animal care protocols.

Redacted by agreement Role : Other significant contributor

Redacted by agreement is an Assistant Professor in the Departments of Biology and Mathematics at University of Oregon. He is an expert on mechanistic neural models of visual processing, and developed the modeling approach proposed here. He will collaborate with PI Niell on determining the computational principles derived from experimental findings (Aim 3), providing expertise on appropriate modeling and analysis methods.

Redacted by agreement EFFORT Role : Post-doctoral fellow

Redacted by agreement is a Post-Doctoral Fellow in the Niell lab. She has extensive experience in studying the octopus nervous system, during PhD work at Stanford's Hopkins Marine Station and as part of the octopus genome project. She generated the preliminary data on calcium imaging presented here, and will perform the experiments proposed in Aims 1 and 2. She will meet regularly with PI Niell to discuss research progress and data analysis, and to ensure appropriate scientific progress.

Redacted by agreement EFFORT Role : Graduate student

Redacted by agreement is a graduate student in the Neuroscience PhD program, currently co-advised by Dr. Niell and Redacted by agreement He has experience in neural modeling from undergraduate work as a physics major at UW with Drs. Redacted by agreement He will perform the data analysis for Aims 1 and 2, as well as the computational modeling proposed in Aim 3. He will meet regularly with Dr. Niell to discuss research progress and data analysis, and to ensure appropriate scientific progress.

Redacted by agreement EFFORT Role : Research technician

Redacted by agreement is a research technician working in the Niell lab. He will devote half-time effort to providing support for animal care, as well as assisting in the calcium imaging and tracing experiments.

PHS 398 Research Plan

OMB Number: 0925-0001
Expiration Date: 03/31/2020

Introduction	
1. Introduction to Application (for Resubmission and Revision applications)	
Research Plan Section	
2. Specific Aims	Aims.pdf
3. Research Strategy*	Approach.pdf
4. Progress Report Publication List	
Other Research Plan Section	
5. Vertebrate Animals	
6. Select Agent Research	
7. Multiple PD/PI Leadership Plan	
8. Consortium/Contractual Arrangements	
9. Letters of Support	SupportLetter Redacted by agreement .pdf
10. Resource Sharing Plan(s)	Data_Sharing_Plan.pdf
11. Authentication of Key Biological and/or Chemical Resources	Authentication.pdf
Appendix	
12. Appendix	

Tracking Number: GRANT12968534
Funding Opportunity Number: RFA-NS-18-030. Received Date: 2019-11-06T17:15:16.000-05:00

Neural coding and functional organization of the octopus visual system

Vision is a critical sensory modality that is not only pervasive in the animal kingdom, but has arisen independently in different species through distinct evolutionary processes. Most studies of visual processing focus on the visual system of vertebrates, including the transformation of center-surround receptive fields in the retina to orientation selective cells in the visual cortex, and on to higher order areas that code for more complex features, such as motion and faces. Similar work has been carried out in flies, including Drosophila, tracing the flow of information from the retina to deeper visual processing areas that encode motion and color.

Cephalopods represent a third, unexplored example of a highly capable visual system. They have eyes that are similar to those of vertebrates, but brains that are more similar to those of other invertebrates yet rival some mammals in size and complexity. Cephalopods are highly dependent on vision, and use it to detect predators and prey, navigate their environment, and find mates. Cephalopods also use visual information to drive unique behaviors, including rapid body pattern camouflage in response to their environment. Remarkably, their elaborate visual system evolved completely independently from that of other highly visual species, so that both the eye and the underlying neural circuitry are evolutionarily distinct. Studying octopus vision therefore provides a unique opportunity to explore a completely novel image processing system.

How is visual information represented, processed, and distributed in the independently evolved visual system of the octopus? Did convergent evolution of eye structure result in convergent evolution of brain function? Or did cephalopods evolve completely different, and perhaps unexpected, solutions to analyzing the visual scene with neural circuitry? By addressing these questions, we expect to gain broader insight into general principles of visual function.

In our three Aims, we will first use calcium imaging to determine how visual information is encoded and transformed in the octopus brain (Aim 1), and then combine this with retrograde tracing to determine how visual information is distributed into downstream brain areas that drive the animals' repertoire of visually guided behaviors (Aim 2). Finally, we will use computational approaches to measure visual information coding, and develop a model of the functional organization of the octopus visual system (Aim 3).

Aim 1: Determine the visual features encoded by neurons in the octopus optic lobe
There have been no direct recordings of visual response properties of neurons in the cephalopod brain, so it is completely unknown how this independently evolved system processes visual information. Will the receptive fields resemble those of well-studied systems such as the simple/complex cells of mammalian cortex or motion detectors of the fly medulla, or will they have completely novel response properties? In this aim, we will use calcium imaging to measure neural responses to a large battery of visual stimuli to determine how information is represented and transformed by neurons at different points along the optic lobe circuitry.

Aim 2: Determine the information distributed to distinct output pathways of the octopus optic lobe
Cephalopods have a diverse set of visual behaviors, which are mediated by specific brain regions that receive projections from the optic lobe. However, it is unknown what visual information is transmitted to each of these regions to drive different behaviors, such as prey capture or camouflage. In this aim, we will use retrograde tracing to identify optic lobe neurons projecting to other specific central brain areas, and then perform calcium imaging to measure the visual response properties of neurons within each projection pathway.

Aim 3: Determine the computational functions performed by the octopus visual system
Studies of visual processing in other species have benefited from formal models that encapsulate measurements of receptive field properties. Here, we will take two approaches to provide a quantitative description of the computations performed in the octopus optic lobe. First, we will use decoding methods to determine the visual information that is represented in the activity of populations of neurons within layers and pathways of the optic lobe. Second, we will use a method recently developed by our collaborator, Dr. Yashar Ahmadian, to fit the parameters of a neural network model to the measurements in the first two Aims. This will allow us to deduce unique and conserved computational motifs, as well as make predictions about novel response types in the octopus visual system.

Significance

Our understanding of how brains generate perception and drive behavior can benefit greatly from exploring the different solutions that evolution has developed to solve these challenges in different species. Cephalopods possess the largest and most complex brains outside of vertebrates [1, 2], yet it is largely unknown how their brains process visual information. In fact, there has been no direct measurement of receptive field properties in the central visual system of any cephalopod. Here we propose to perform systematic measurements of visual response properties and functional organization in the octopus visual system. This proposal will thereby fill a significant gap in our knowledge of the computational principles mediating visual processing across the animal kingdom (Fig 1). In addition, by identifying mechanisms that are either shared with other species, or unique to the octopus, we will gain new insight into fundamental aspects of visual function. Finally, by determining the visual pathways that distribute information to different brain regions in the octopus, we will provide a foundation for studying the neural basis of the unique repertoire of natural behaviors in this under-studied model system.

Background

The cephalopods, which include octopuses, squids, and cuttlefish, diverged from other molluscs, their relatives the clams and snails, over 500 million years ago. They evolved a unique set of complex anatomical features, including dexterous arms and large central brains [4]. One particular area of interest is their independently evolved, highly sophisticated visual system. Like vertebrates, cephalopods possess camera-like eyes, with lenses that focus an image onto a retina densely packed with photoreceptors. Roughly two thirds of their central nervous system is dedicated to visual processing areas, namely the optic lobes that lay behind the animals' eyes [5] (Fig 2A). These lobes receive direct input from photoreceptors, perform processing that presumably extracts important visual features, and relay this information to numerous higher order areas of the central brain. The optic lobes of cephalopods not only mediate visual processing, but also play a direct role in the initial stages of a rich repertoire of complex, visually guided behaviors, including control of chromatophore patterning and spatial and observational learning [7]. However, there has been no direct measurement of the visual response properties of neurons in the brain of any cephalopod. It is therefore unknown what information this powerful visual system extracts from the visual scene, how it encodes these features, or what signals it conveys to higher brain areas.

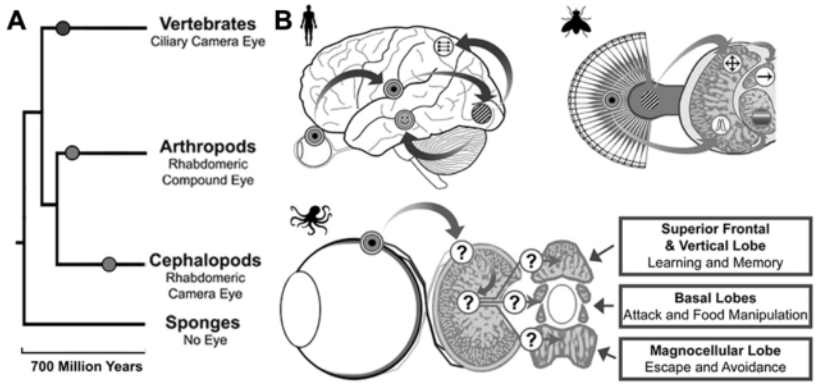

Figure 1: Relationship of cephalopod visual system to other species
A) Tree showing independent evolution of eyes, each with unique organization, for three distantly related groups of animals. Colored points on tree show estimated emergence of eyes along each branch [3]. **B)** Conceptual schematic of the visual systems of human, fly and octopus. Whereas the information represented in the visual processing pathways of humans and flies is relatively well characterized, little is known about visual processing and response properties in cephalopods beyond the level of the photoreceptors [6].

Organization of the Cephalopod Visual System

Anatomy

Cephalopod visual processing begins in their retina, which contains only photoreceptors and a population of horizontal cells that connect them. Photoreceptors project their axons directly into the central brain, in contrast to vertebrates, whose retinas contain significant additional circuitry.

Axons from the photoreceptors arrive in the optic lobe, where it is thought that most of the visual processing in the cephalopod brain occurs. Classic histological studies using Golgi stains [5] have provided a detailed description of the anatomical organization and morphological cell types of the optic

lobe (Fig 2B, C). Lining the perimeter is a layer of cell bodies, termed the outer granular layer (OG), containing amacrine cells which synapse onto photoreceptor axon terminals in the adjacent layer of processes, the plexiform layer (PL). OG cells are situated to potentially regulate incoming signals across multiple photoreceptors, similarly to horizontal cells in the vertebrate retina. The next cell body layer is the inner granular layer (IG), which is thought to contain the second order cells in the visual pathway, serving to integrate and process information from the photoreceptors, like bipolar cells in vertebrates. While these outer layers resemble, morphologically, the cell types and layers found in the vertebrate retina [5], their specific computational functions remain undetermined. Finally, in the interior of the optic lobe is the medulla (med), a region of cell body "islands" surrounded by neuropil. It is hypothesized that these contain the third order cells of the visual pathway, serving to integrate higher order features for dissemination to other central brain regions [5]. However, there are no recordings from any of the cell types to confirm this hypothesis functionally.

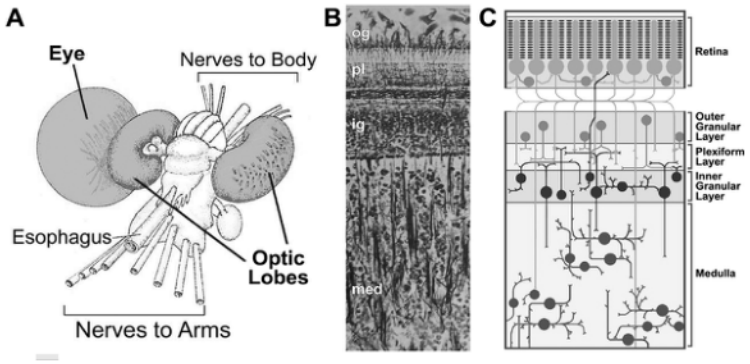

Figure 2: Organization of the octopus optic lobe

A) Schematic of octopus brain organization, showing location of eyes and optic lobe. **B)** Cross-section of the optic lobe showing laminar organization from Young (1971). **C)** Schematic of cell types and projections within the layered circuitry of the optic lobe (modified from Pungor, 2014).

The optic lobe sends projections to a number of brain regions that have been shown to be involved in specific behaviors (Fig 1B), including prey capture, predator avoidance, learning/memory, navigation, and camouflage [6]. Anatomical studies have charted the output connections of the optic lobe, which projects to a majority of the lobes in the central brain of the octopus (for a review, see [6]). Among these are the vertical lobe, known to play an important role in learning and memory, the magnocellular lobe, which is responsible for escape behavior, and the basal lobe, which plays a role in governing attack behaviors. The basal lobes then project to the chromatophore lobes, which drive the animals' stunning camouflaging abilities [5, 8]. However, there is no functional evidence for the kind of visual information that is distributed to each of these various higher-level pathways, to enable these diverse behaviors.

Functional properties

Early recordings from photoreceptors in the cephalopod eye provided a preliminary description of visual processing at the input stage, demonstrating localized receptive fields with lateral inhibition [9, 10], as well as polarization sensitivity [11, 12]. Interestingly, the optic nerves also contain efferent axons of optic lobe neurons projecting back to the retina, and recordings from these have shown that they can contribute a sustained series of bursts following a return to darkness [9, 13]. Additionally, early studies using bulk recordings of evoked potentials in the brain characterized responses to light flashes [14]. However, there have been no direct recordings from individual identified neurons in the optic lobe, so it is unknown how visual information is encoded in the central visual system.

Background summary

Despite the enticing complexity and tremendous capability of the cephalopod visual system, relatively little work has explored visual coding and neural computations in these animals. As described above, anatomical studies have delineated the morphology and structural connectivity of neurons in the retina and optic lobe, and identified connections from the optic lobe to other areas of the brain. Likewise, traditional electrophysiology has characterized the first step of visual processing, through recordings of photoreceptors and optic nerve activity. This proposal will perform the first direct measurement of visual response properties of neurons within visual pathways of the octopus brain. We will thereby begin to reveal what information the octopus extracts from the visual scene, how it processes this information, and what signals it conveys to higher brain areas that mediate complex behaviors, such as learning and memory and camouflage.

Our *central hypothesis* throughout this project is that the octopus visual system will use both similar neural mechanisms (resulting from convergent evolution) as well as novel neural mechanisms relative to other species, to execute visual processing. Identifying convergent mechanisms, where neurons are performing similar functions despite overt differences in brain structure, will give insight into fundamental computations that may be universally necessary for vision. These would also be remarkable from a biological perspective, demonstrating how nature can arrive at similar computations utilizing different neural architectures. On the other hand, any novel forms of processing will reveal alternative solutions to solving the problem of vision, or specializations due to the octopus's unique capabilities, which will expand our understanding of how brains can function.

Innovation

Conceptual

A major innovation in this project is proposing to study a highly complex visual system that has remained largely unexplored by modern neuroscience. The octopus brain is roughly the size of a mouse's brain, and two-thirds of it is devoted to visual processing [5]. It therefore represents the largest and most complex visual system outside of vertebrates, yet we have no idea how its neural circuits encode and process visual information. By applying modern experimental and computational approaches to study the octopus visual system, our project will fill this major gap in our understanding of how brains can implement vision.

Technical

Historically, a major limitation in studying the cephalopod brain has been the challenge in recording neural activity, as conventional extracellular electrode methods have proven difficult for reasons including small cell size, the presence of connective tissue in the brain that impairs electrical isolation, and the difficulty in stabilizing electrodes relative to brain tissue in a soft bodied organism. Here we will overcome these challenges by using in vivo calcium imaging, which allows for the direct visualization of activity in large populations of neurons simultaneously (e.g. [15-17]). As we demonstrate below in preliminary data, this approach has allowed the first measurement of visual responses in the octopus visual system.

The Niell lab has expertise in both the conceptual and technical aspects of characterizing visual processing across species, and is therefore ideally suited to take on this project. PI Niell performed the first quantification of visual processing in the larval zebrafish optic tectum as a graduate student [15], implementing similar two-photon calcium imaging and data analysis methods as proposed here for the octopus optic lobe (Fig 3).

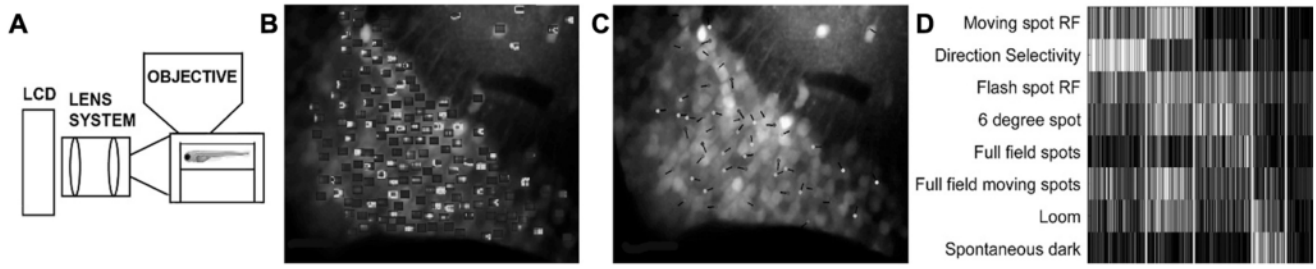

Figure 3: Calcium imaging of visual responses in zebrafish optic tectum

A) Diagram of imaging and stimulus presentation setup. **B)** Receptive fields of individual neurons in a zebrafish, overlaid on their spatial location within the tectum. **C)** Direction selectivity of neurons overlaid onto cells with significant direction preference. Dark bars show preferred direction. **D)** Clustering analysis, delineating functional classes of neurons with distinct response profiles. All from Niell and Smith, 2005 [15].

As a post-doc, PI Niell performed pioneering studies on the function of the mouse visual system, including characterizing receptive field properties [18] and effects of behavioral state [19]. Recently, the Niell lab extended the use of two-photon calcium imaging, as well as other methods including extracellular recording and widefield imaging, to investigate visual processing in the thalamus and cortex of mice [16, 20, 21]. The Niell lab has also generated transgenic mouse lines expressing both calcium and voltage sensors, and has used these to study large-scale cortical dynamics [16, 22].

In this project we will apply this broad range of expertise derived from studying the visual system of two different species, in order to understand neural coding and functional organization the octopus.

Approach

Overview of animal use

The octopus is an ideal model system to study visual processing in a complex brain distinct from vertebrates. They have camera-like eyes that create a high-resolution image on the retina, they have large brains that rival the size and complexity of some mammals yet are organized completely differently, and they have a wide range of visually-driven behaviors [2, 5, 7].

Our experiments will be carried out in *Octopus bimaculoides*, an emerging model organism for comparative biology. There is a growing amount of research focused on the octopus's nervous system and cognitive ability [23], and the recent publication of the *O. bimaculoides* genome [24] opened the door for the use of genetic tools to study this species in particular, setting the stage for this animal to become a primary experimental model for modern systems neuroscience. While genetic access in cephalopods is not currently possible, developing this is a major focus for several research groups. However, the work proposed here does not require genetic methods, as we will gain information about cell types based on laminar identity and projection patterns, and we use an organic calcium indicator dye rather than genetically encoded sensors. Importantly, our findings in this project will provide the fundamental knowledge of basic visual processing needed to dissect neural circuits in depth as genetic tools become available.

O. bimaculoides is found in abundance off the coast of Southern California. Clutches of eggs are available from Redacted by agreement and juvenile octopuses are now being distributed by the Redacted by agreement PI Niell has a custom-built aquarium system for housing octopuses in the University of Oregon animal facility, and we regularly receive and raise animals, with roughly 10-20 available for experiments at a given time. Imaging will be performed on juveniles between 1-3 months of age, at a size optimal for experimental feasibility and optical access, as their optic lobes are 1-2mm in diameter. Animal husbandry and protocols in the Niell lab are carried out in accordance with published guidelines for the care and welfare of cephalopods in the laboratory [25, 26]. Because these animals are wild-caught, we will study both males and females.

It is important to note that although we will be studying juvenile octopuses, which are not yet full size or sexually mature, most of their behavioral repertoire is fully developed at this age. In particular, they successfully carry out visual behaviors, including navigating their environment, capturing prey for food, avoiding predators, and effectively camouflaging their bodies, from the moment they hatch from their eggs. Nevertheless, to ensure that the visual system is largely similar to that of mature adults [27], we will use animals that are at least one month old.

Aim 1 – Determine the visual features encoded by neurons in the octopus optic lobe

Motivation

Hubel and Wiesel's discovery of orientation selectivity in primary visual cortex was transformative, as it revealed that the mammalian brain does not only represent visual information in a pixel-based center surround organization, but extracts specific visual features, such as edges, that are useful for downstream computations. Does the cephalopod visual system, with a vertebrate-like eye and invertebrate brain, extract visual features similarly to the mammalian cortex or the medulla of the fly? Or does it use a completely different means of encoding visual scenes, potentially due to the challenges posed by the underwater visual environment, the unique needs of the animal's behavioral repertoire, or simply due to a different evolutionary trajectory?

In our first aim, we will answer this question by using calcium imaging to measure the response properties of cells in the octopus optic lobe with a battery of visual stimuli. Using similar approaches as previously applied to zebrafish and mice by PI Niell [15, 20], we will characterize the visual features that drive neurons, and classify neurons into categories of response types (Fig 3D). These results will provide the first measurement of how the visual scene is encoded by a cephalopod central visual system, and how information is transformed across stages of processing.

Experimental approach

In order to determine how the octopus visual system encodes and processes visual information, we will use two-photon calcium imaging to record visually evoked responses in the optic lobe. Calcium imaging provides a powerful tool for analyzing neural activity in large populations of neurons, particularly in brain regions that are not conducive to extracellular recordings. It also allows for assessment of large-scale spatial organization of the tuning properties of recorded neurons, as well as measurement of dynamic temporal patterns of activity across populations. We will apply similar calcium imaging and visual stimulation techniques to those developed by PI Niell [15] for the zebrafish optic tectum (Fig 3). In this paradigm, a synthetic calcium indicator dye is injected into the brain, and the animal is immobilized underneath the objective of a 2-photon microscope in a custom imaging chamber, with a screen for presentation of visual stimuli (Fig 3A, 4A). Our previous work in zebrafish showed that this approach was successful in measuring receptive fields and other response properties in large numbers of neurons, allowing us to determine both their spatial organization (Fig 3B, C) and functional classes (Fig 3D).

Our experimental approach for the octopus entails first deeply anesthetizing the animal, and then performing dissection to expose the brain and remove musculature that can contribute to motion artifacts. The intact central brain and eyes are then affixed to the base of an imaging chamber (Fig 4A), and calcium indicator dye is injected directly into the optic lobe. We use the recently developed dye Cal520 [28], which we have found provides better loading and larger fluorescence signals than our previous experiments with the commonly used Oregon Green BAPTA-1. The dye will be loaded in AM-ester form, dissolved in a Pluronic/DMSO solution and diluted in physiological saline. This approach has been used broadly in mammalian cortex and zebrafish brain [29, 30], including in previous experiments by PI Niell [15]. A similar loading method has been recently described in squid [31], although the study did not measure single neuron activity.

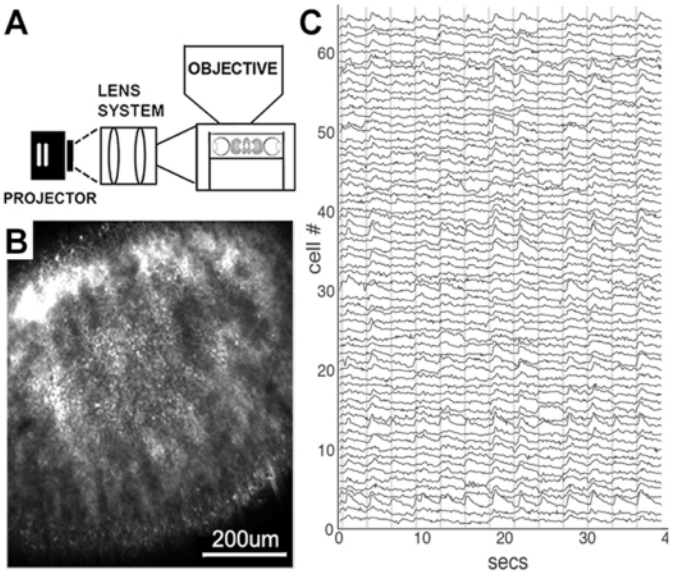

Figure 4: Calcium imaging in the octopus optic lobe
A) Schematic of imaging system. **B)** Two-photon image of the optic lobe labeled with synthetic calcium indicator Cal-520. **C)** Activity in 64 neurons (out of >800 simultaneously recorded) during visual stimulation (onsets at gray bars). Niell lab, unpublished data.

Calcium imaging will be performed using a two-photon microscope (Neurolabware, Inc.), which provides optical access for recording neural responses across the optic lobe with minimal photodamage. The field of view of this microscope is ~1mm^2, which allows us to observe a large population of cells across the optic lobe simultaneously (Fig 4B). Custom generated visual stimuli, rendered using the Psychtoolbox package for Matlab [32], will be displayed using a pico LCD projector (AAXA Technologies) onto a white diffusion filter mounted onto the side of the chamber containing the preparation, as in our previous zebrafish study [15] (Figs 3A, 4A). This configuration allows us to present high-resolution stimuli across most of the visual field of one eye.

Our preliminary data show that this approach is effective in allowing us to measure visual responses in hundreds of neurons simultaneously in the octopus brain. Figure 4B shows a mean fluorescence image in an optic lobe loaded with calcium indicator, demonstrating our ability to load indicator dye and image neurons across large areas within the octopus visual system. Figure 4C shows traces of the fluorescence response of 64 neurons to drifting gratings, demonstrating that activity is time-locked to the stimulus, with selective responses across different neurons.

In preliminary experiments, we have used this approach to map visual responses using sparse noise (flashing spots) stimuli. Figure 5A shows example receptive fields of neurons in the inner granular layer, based on reverse correlation, which demonstrate spatially localized On and Off responses. Furthermore, mapping the location of each cell's receptive field center onto the location within the lobe revealed a retinotopic organization, with neurons across the lobe responding to adjacent locations in visual space in an orderly progression (Fig 5B).

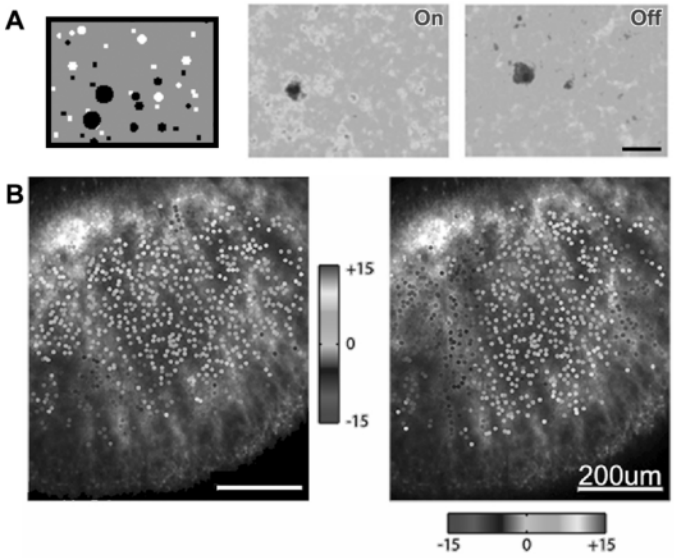

Figure 5: Spatial receptive fields and retinotopic organization in the optic lobe
A) Mapping receptive fields using sparse noise stimuli. Example of stimulus (left) and an On (middle) and Off (right) spatial receptive field computed by reverse correlation between the visual stimulus and calcium response. Scalebar 20 degrees of visual field. **B)** Topographic organization of visually evoked responses. Each dot represents an individual neuron (745 total), color-coded based on its receptive field location in elevation (left) and azimuth (right), mapped with sparse noise. Niell lab, unpublished data.

In addition, the timecourse and magnitude of response to spots of different sizes in the sparse noise allowed us to measure spatial integration, in terms of size selectivity (Fig 6). This revealed an intriguing difference in the computations for light and dark stimuli. The mean response to On (light) spots showed strong size *suppression*, which is consistent with mechanisms of lateral inhibition as commonly seen in the retina in other species. However, the response to Off (dark) spots showed moderate spatial *summation* over the same size range. Neurons also showed a slight suppression to a full-field Off flash, followed by a rebound On response. There are several hypothetical mechanisms that could explain these findings. However, this preliminary data already suggests that On and Off pathways are processed differently in the early stages of the optic lobe.

These results represent the first direct recordings of single cell neural activity in the octopus central visual system. Importantly, this confirms that we can measure stimulus-specific responses. Furthermore, it reveals that first-order neurons in the optic lobe have spatially localized On and Off receptive fields, and demonstrates a fundamental form of functional organization, the retinotopic map. This data also demonstrated the ability to measure spatial integration and revealed differences in On and Off pathways.

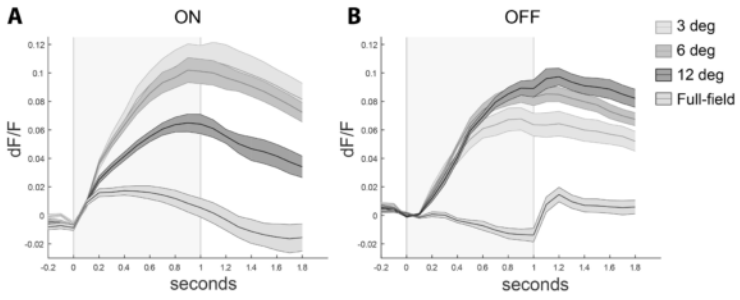

Figure 6: Size selectivity in On and Off pathways.
Mean timecourse of response across recorded neurons, for On spots (**A**) and Off spots (**B**) of different sizes (3-12 degree diameter) centered on the measured receptive field location, as well as a full-field flash. Stimulus duration demonstrated by grey bar. N=6 imaging planes in 3 animals. Niell lab, unpublished data.

Visual stimuli and data analysis

Following our previous studies characterizing visual areas in mouse and zebrafish [15, 18, 20], we will present a broad battery of visual stimuli (Fig 7) to probe for specific types of visual processing that we expect may be present in the octopus visual system, as well as to identify potentially unexpected forms of visual processing or feature detection.

First, we will present standard geometric stimuli that are known to drive responses in the retina and central brain regions of vertebrates and invertebrates, including sinusoidal gratings, flashing spots, and moving spots (Fig 7A). These stimuli are ideal for measuring basic properties of the

visual response, such as spatial and temporal frequency preference, orientation selectivity, and motion selectivity. Measuring responses to these stimuli will provide a baseline understanding of how neurons in the optic lobe respond to standard stimuli relative to neurons in the visual systems of other species.

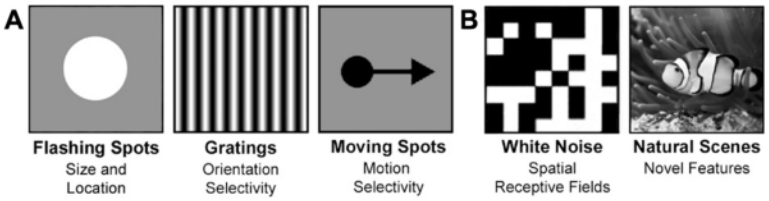

Figure 7: Examples of visual stimuli to probe responses

A) Examples of geometric stimuli that will be presented to probe for basic tuning properties such as size, orientation and motion selectivity. **B)** White noise and natural scenes will be used to extract more complex receptive fields and response properties.

In addition, we will use white noise and natural underwater scene stimuli to probe for spatial receptive fields and visual response properties in an unbiased manner (Fig 7B). Analysis of response to white noise is more mathematically tractable, while natural scenes may drive stronger neural responses due to the image statistics. By measuring responses to these stimuli, we can apply computational methods such as reverse correlation [33] or generalized linear models [34] to quantify the visual features that drive a neuron's response. In addition, differences in the responses to white noise and natural scenes may reveal how the octopus visual system is optimized for its underwater visual environment. These approaches may reveal selectivity that is not based on assumptions from other species.

Finally, based on hypotheses generated by the results of computational analysis in Aim 3, we can circle back and design new stimuli to be tested to probe for further visual response properties. This will take advantage of our close integration of experimental and computational approaches in one project.

Data analysis will largely follow standard approaches, used in the Niell lab and others, to compute stimulus selectivity, tuning curves, and receptive fields from measures of neural activity [16, 18, 20]. In addition, we will perform clustering of neurons based on their response properties, in order to define functional response types. This clustering is not intended to definitively identify the underlying cell types, rather it provides an approach to preserve the heterogeneity of responses, rather than averaging out over the population. In our previous studies, this approach identified distinct response profiles in zebrafish that are established early in development (Fig 3 and [15]), and also revealed diverse responses in the mouse LGN beyond classical center-surround [20]. In Aim 3, we will expand this single-neuron analysis to use decoding methods to determine the information represented across populations of neurons.

Finally, we will map the responses of neurons back onto their location within the optic lobe, which provides an initial assignment of cell type and processing stage based on the layered organization of the optic lobe. This will allow us to determine how visual features are extracted and transformed through the circuitry of the visual system. We can also identify forms of spatial organization, such as retinotopy or other clustering. For instance, applying this approach in mouse LGN revealed a clustering of direction-selective neurons in the dorsolateral shell [20], which was subsequently shown to be part of a circuit linking direction selectivity from the retina to cortex [35].

Expected outcomes

These experiments will provide the first measurement of neural responses in the octopus central visual system, and will determine the features that neurons in the octopus visual system extract from the visual scene. These data are essential to understanding how this unique brain organization processes sensory information, and are likely to provide novel insight into the basic neural principles of vision. In particular, based on our preliminary data we already expect that certain types of organization are likely to be preserved, such as retinotopy (Fig 5), while others are likely to be more divergent, such as the differential spatial integration in On and Off pathways (Fig 6).

We also expect that response properties will differ by position within the optic lobe, particularly laminar identity, representing the transformation of visual information through the circuit (Fig 2C). Importantly, although we do not have the ability to genetically identify cell types in cephalopods, laminar identity and location can provide a significant amount of cell type information, given the extensive anatomical studies of the optic lobe [5]. In addition, we will further expand our ability to define cell types anatomically in Aim

2, where we identify neurons based on their projection pattern to downstream brain regions.

Potential limitations and contingency plans

We do not anticipate significant technical limitations, since we have already overcome the major obstacle in the field – recording neural activity within the octopus brain during sensory stimulation. Our preliminary data (Figs 4, 5, 6) show our ability to measure response properties of neurons across the optic lobe, including spatial receptive fields and size selectivity, and have demonstrated a fundamental form of brain organization, the retinotopic map. Furthermore, the data analysis methods we will use have been well-established by PI Niell [15, 16, 20].

One significant improvement to our approach would be the use of genetically encoded indicators, such as GCaMP6 [36]. Using a genetically encoded calcium indicator would remove the invasive step of dye injection immediately prior to recording, and allow imaging in more intact preparations over extended periods of time. However, this would require gene delivery methods, which have not yet been demonstrated in cephalopods. We are currently working to implement electroporation of plasmid constructs in the octopus, and if successful we will complete the project using this alternate approach.

A potential caveat in interpreting this data is that calcium signals may differ across cellular compartments, such as soma versus dendrites and axons, a concern because the somas of many invertebrate neurons are not excitable. However, calcium imaging has been used successfully in other invertebrates, such as worm and fly [37], and our pilot data show robust calcium responses in cell bodies in the optic lobe. Alternate imaging methods, such as sparse labeling to observe processes, or voltage imaging to observe membrane dynamics, could provide a further understanding of how signals are integrated across the neuron.

Perhaps the most fundamental conceptual challenge in this aim is the ability to identify novel response properties that we are currently unable to predict. While this is a fundamental challenge in visual physiology, we will address it by using a broad range of stimuli paired with computational analyses. Nevertheless, even these methods are limited, as highly derived non-linear response properties such as face cells would not be detected without presenting actual faces. However, a promising new approach would be to implement recent deep learning methods to estimate visual stimuli that drive neural responses, which would allow us to explore nonlinear representations [38-40].

Future work could probe several aspects of octopus vision beyond the scope of this proposal. For example, cephalopods can detect the polarization of light, which can provide important visual cues, particularly in the underwater environment [12, 41]. Examining the neural basis of this ability would require a more sophisticated stimulus presentation system to deliver images that are also spatially modulated in polarization, which we are currently developing. In addition, although octopus photoreceptors only express one type of photopigment, rendering them ostensibly colorblind, there have been suggestions that they can perceive color [42]. With the use of color stimuli, we could determine whether and how this sensitivity is represented in the brain. Finally, to perform camouflage the animals must match their chromatophore patterns to statistics of the visual scene, and we could design specific stimuli such as varied textures that might probe this mechanism more directly than the standard visual stimuli presented here.

Aim 2 – Determine the information distributed to distinct output pathways of the optic lobe

Motivation

The visual system must extract specific information and route it to appropriate downstream regions – for example, the primate magnocellular and parvocellular pathways respond to different types of stimuli, and subsequently project to dorsal or ventral streams, each of which drive different aspects of behavior and cognition [43]. Previous anatomical studies in octopus characterized projections of the optic lobe into a variety of central brain regions [5, 6, 8], each of which mediate unique sets of behaviors such as escape, attack, and learning and memory (Fig 1B). However, it is unknown what specific visual information is distributed to these higher order processing centers. We therefore aim to determine the unique visual response properties of neurons projecting to specific downstream targets that drive distinct behaviors.

To achieve this, we will combine calcium imaging in the optic lobe with retrograde labeling from other

brain regions, to measure the visual responses in neurons that project to specific targets, similar to methods used to probe visual pathways in cortex (e.g. [44]). This will provide the first measurement of the functional organization of visual pathways in the cephalopod brain. In addition, it will provide insight into the distinct types of processing that are required for different visual capabilities, and provide the basis for future studies investigating the neural basis of visual behaviors in the cephalopod.

Experimental approach and analysis

To identify neurons projecting via known anatomical pathways, we will perform retrograde tracing from target regions of the optic lobe. Briefly, Lumafluor Retrobeads will be injected into one of three downstream target regions: the superior frontal lobe, the magnocellular lobe, or the basal lobe. Injections will be performed 24-48hr before recording, during which time the animal will be allowed to recover while the beads are retrogradely transported to the optic lobe. Preliminary work in the Niell lab tracing projections *into* the optic lobe has demonstrated this to be an effective in vivo method to label neurons projecting to a given brain region (Fig 8). Calcium imaging will then be performed as described above, with visual stimuli optimized to characterize distinct response types, based on the findings of Aim 1.

We will use a static image taken in the fluorescence channel of the retrograde tracer to demarcate individual projection neurons within the optic lobe. We will then correlate the visual response properties of these neurons with their target brain region. Analysis of visual responses of these cells will be performed as described in Aim 1, including cluster analysis to define functional response groups. We will then perform statistical tests to determine which aspects of the neuronal response properties are predicted by their downstream projection target, thereby defining the functional output pathways from the optic lobe. In addition, in Aim 3, we will expand this analysis to use population decoding approaches to determine the differences in information coding across populations projecting to different brain regions.

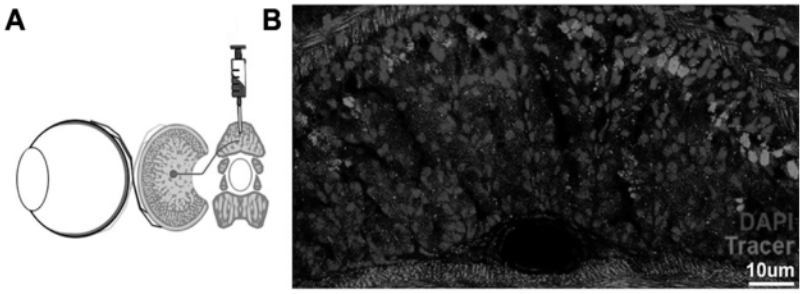

Figure 8: Tracing projections between brain regions

A) Schematic of tract tracing protocol. Retrograde tracers injected into areas of the central brain will show connections of optic lobe cells to other areas. **B)** Retrograde labeling of cells in the basal lobe. Beads were injected into the right optic lobe, which lies to the right of this image, in a juvenile octopus. Niell lab, unpublished.

Expected outcomes

We hypothesize that, as in other species, visual information will be selectively distributed into pathways associated with specific functions. This hypothesis is supported by anatomical studies showing distinct projection pathways from the optic lobe to higher brain areas. However, due both to the unique organization of the octopus central brain and our lack of understanding of its visual response properties, we do not have strong expectations about how information will be segregated across these projections. Based on behavioral demands, though, it is possible that projections to the vertical lobe will carry high spatial acuity information to accurately encode images for learning and memory, whereas projections to the magnocellular lobe may encode size and motion information to identify predators and drive escape responses. It will be particularly interesting to determine the information in the basal lobe projection, which starts the pathway to the chromatophore lobes that modulate skin pigmentation for camouflage and other signaling. We expect that this may involve global statistics about the visual scene such as texture and brightness, that are matched to drive this unique behavior and therefore may represent novel forms of visual feature encoding.

Potential limitations and contingency plans

Our preliminary data show that we can perform retrograde tracing to identify cell bodies of neurons projecting to a given region, so we do not expect fundamental technical challenges. However, retrograde tracing does not generally label all of the cells in any given tissue, so we will probably not characterize

the complete population of neural connections to the optic lobe. However, this limitation is not unique to this study but is inherent in tracing experiments generally, and will still allow us to differentiate properties of neurons that project to different locations.

In future studies, we can follow up these findings by performing measurements of neural activity and visual responses within the downstream regions, applying similar calcium imaging techniques as described above to other lobes in the octopus central brain complex. While such an endeavor is beyond the scope of this project, it will be an important subsequent direction to pursue in linking visual processing to specific behaviors.

While projection pattern and laminar identity are important aspects of cell type identity, fully understanding the organization of the visual pathways of the optic lobe would benefit from determining the morphology of recorded neurons as well. This could be achieved through the laborious process of filling cells after recording. More promising is the potential to use genetically encoded fluorophores to sparsely label targeted populations of cells for visualization of their morphologies, which could be achieved with electroporation methods.

Aim 3 – Determine the computational functions performed by the octopus visual system

Motivation

The end result of the above experimental studies will be an understanding of both the neural coding and functional pathways of the octopus visual system. As a final step, we will implement our findings into a computational framework, with our collaborator Dr. Yashar Ahmadian, a theoretical neuroscientist studying network models of visual function. This will allow us to provide a concise and mechanistic representation of our findings, as well as to use the network models to generate new hypotheses to test experimentally.

Based on our experimental results, we will take two approaches towards this goal. The first is to use the findings from neural recordings to infer the computational role of different neural populations and pathways, by determining what types of visual information can be easily read out (i.e. by a linear decoder) from their activity. In the second approach, we will use the data from neural activity to constrain a novel neural network model that implements the computational capabilities of the octopus visual system. These two approaches will provide a quantitative framework for *what* computations are performed in the octopus visual system, and *how* the computations are implemented, respectively.

Determine the information encoding of neural populations and pathways

Our results from Aims 1 and 2 will provide a quantitative description of receptive fields and tuning properties of neurons in the optic lobe, and how these vary based on connectivity to downstream brain regions. In some cases, knowledge of this feature extraction can be used to directly deduce computational roles of specific response types in image processing. For instance, the finding that V1 simple cell receptive fields resemble Gabor filters suggested that they can serve as edge detectors. However, a more recent approach is to use population decoding methods, in which a linear decoder is trained to “read out” specific stimulus properties from the neural activity [45]. The success of the decoder implies that the population is explicitly coding that type of information. This method has, for example, shown how cortical areas along the ventral stream pathway evolve from representing low-level features, to object identity and continuous object-coordinates [46].

We will use the decoding approach to determine how octopus visual response properties enable specific types of image processing, particularly in relation to known behavioral capabilities and pathways. First, we will use the responses of neurons to the stimuli we have presented, including simple geometric patterns and complex scenes, and train a linear decoder of population activity to recapitulate various features of the image. These features will range from low-level aspects such as edges, orientation, and local motion, to more complex features such as surface texture, object identity and location. We will intentionally limit the decoder complexity by choosing a linear decoder, so that it will reveal which features are represented nearly explicitly, and thus can be easily read out from recorded neural activity. Performing this analysis at different levels in the optic lobe, and in different projection pathways, will reveal the computations being performed in each stage of processing.

We will also couple this type of decoding analysis with our findings from anatomical connectivity, to determine how the type of information processed by specific populations depends on their projection target in downstream brain regions. For example, determining the type of information encoded in the responses of neurons projecting to camouflage pathways would provide an important basis for understanding this unique behavior.

Implement network models that encapsulate octopus visual coding

In this approach, we will use our knowledge of the neural responses in the octopus visual system to directly implement a mechanistic neural network model. This approach has proven powerful in modeling other neural systems, from the vertebrate visual to motor control systems, serving to both gain understanding of the function of the underlying network, and to create artificial networks to achieve similar goals. Our approach to generating this model will take advantage of recent advances in constraining network models from data based on machine learning techniques. This approach was recently successful in recapitulating both known network and processing capabilities of the retina [47]. In the study, the individual connection weights of a convolutional neural network were trained so that the responses of its output neurons to a set of stimuli matched one-to-one the responses of individual recorded retinal ganglion cells. A related method to achieve this goal was developed recently by the Ahmadian lab, based on generative adversarial networks (GAN), in which the parameters characterizing the statistical structure of connectivity (or single-cell properties) are directly inferred by matching the distribution of functional response properties between the modeled neurons and recorded cells [48]. We will constrain network models using this approach and determine their ability to match experimental predictions. In essence, we will be learning the statistical structure of the octopus neural network based on our neural data.

To implement the GAN-based approach, we will start with a generic multi-layer network model with horizontal recurrent connections within each layer as well as feedforward connections between layers (Fig 9). Next we will present the network with the same stimulus set presented to the animal, and will train the individual synaptic weights in this model, or parameters controlling their statistics, using stochastic gradient descent. Notably, we do not train the network to achieve a specific task, such as classifying images, but to match the output of neurons to specific neural activity we have recorded (either individually, or in their distribution). Importantly, this approach obviates the need for detailed connectivity data, and is based on the detailed response properties of neurons probed by the stimulus set in Aim 1.

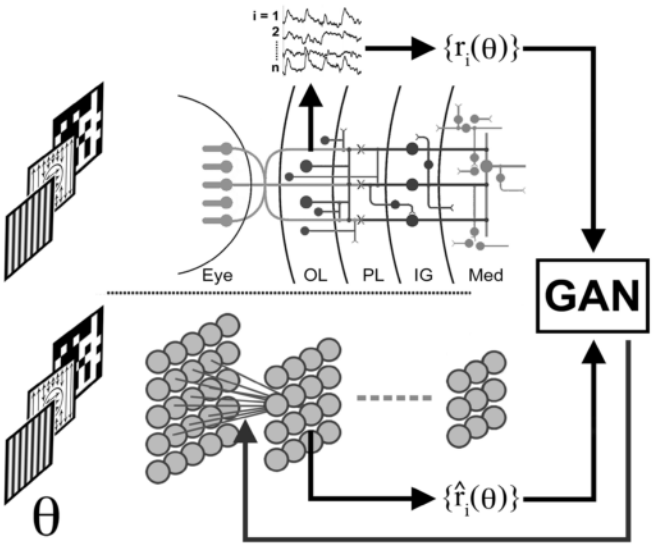

Figure 9: Using a GAN-based approach to constrain a network model. In this approach, we present the network (bottom) with the same stimuli presented to the animal (top), characterized by parameters θ. Using the responses we extract tuning curves $r_i(\theta)$ for different cells, in both the real neurons and the modeled neurons. By fitting the statistics of modeled neuron tuning curves to the empirically measured statistics, the GAN framework infers the connectivity of the model.

In addition to reproducing the octopus visual system in a network model that can be applied to image processing, these models will provide deeper insight into the computational principles of the octopus visual system. As mechanistic models, the trained networks can then be simulated in conditions beyond those used in their training. For example, we can predict the responses of a given area to stimuli after certain components have been removed, to test their role in the computations, thus providing predictions for subsequent experiments. In addition, the GAN-based approach, which yields a model specified by a few structural parameters, has the further advantage that analytical methods can be applied in order to determine the role of unique aspects of network structure in visual function.

Expected outcomes

Through the two above approaches, we will gain insight into the computational implications of our experimental findings by providing a mathematical description of the information computed in different populations and pathways of the octopus visual system, and build a mechanistic network model that encapsulates the computational mechanisms given experimental constraints. Together, these will provide an understanding that goes beyond a summary of experimental data, revealing what computations are performed and how they are achieved mechanistically. Importantly, we will also use these findings to refine our experimental approaches. In particular, the results of both decoding and network modeling can lead to new hypotheses about the computations being performed in the optic lobe, that could be directly tested by generating appropriate visual stimuli for calcium imaging.

Potential limitations and contingency plans

We do not anticipate technical challenges in the implementation of these modeling approaches, since the computational methods are already in use in the Redacted by agreement ab. There are, however, limitations to the interpretation of the findings from these methods.

For the decoding approach, the use of a linear decoder is ideal for revealing information that is explicitly represented across a population. However, if the optic lobe does not explicitly represent a feature, we would need to search downstream within other brain regions to find this representation. For the network model approach, we will start with a simple generic model, that ignores biological cell types and feedback. The model can nevertheless learn *functional* cell types, and we can assess whether our model nonetheless captures the natural computational capabilities of the octopus system by comparing the output of the network to our actual neural data, and future models that can incorporate more realistic physiology as it becomes known. We have also omitted feedback pathways in our model, in order to start with a more constrained model focusing mainly on the role of feedforward processing. More generally, we also recognize that the details of the model and potential outcomes are somewhat speculative at this point, because so little is known about neural activity in the octopus visual system. This is a challenge inherent in undertaking the study of a novel neural system. However, based on the close collaboration between Niell and Redacted by agreement we can continuously refine the implementation of these objectives based on our experimental findings, for example if we find striking novel types of feature selectivity in Aim 1, or novel connectivity motifs in Aim 2.

Future Directions

Successful completion of this project will provide fundamental information about how visual information is encoded in the octopus brain, how it is transformed across stages of processing within the optic lobe, and how it is distributed to downstream brain areas involved in specific behaviors. In addition to providing the first understanding of how the octopus visual system works, this will open up a wide range of future directions to investigate how neural circuits mediate perception and behavior. In particular, it will be interesting to determine the synaptic circuit mechanisms that mediate any unique aspects of visual coding we find in the octopus. This could be done using patch recording, which is challenging in small invertebrate neurons but has now become standard in species such as Drosophila. Building towards behavior, similar calcium imaging approaches could be applied in the downstream target areas, such as the chromatophore lobes that mediate camouflage. Additionally, octopuses and cephalopods have several unusual aspects of visual function, such as the ability to discriminate stimuli based on the polarization angle of light, and the ability to match their camouflage to the color of the environment despite having only one type of photoreceptor. Using similar methods to those described here, we could determine the neural coding that mediates these aspects of vision.

Finally, the eventual goal of this work will be to apply the full range of circuit dissection techniques that are used in other model species, from flies to mice, which depend on genetic manipulations. Linking neural function to behavior in the octopus, particularly with the prospect of awake behaving subjects, will benefit greatly from tools such as genetically encoded sensors, optogenetics, and cell type specificity. The work in this project will provide a critical framework to apply these tools to the visual system of cephalopods as they become available.

PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

Are Human Subjects Involved	❍ Yes ● No
Is the Project Exempt from Federal regulations?	❍ Yes ❍ No
Exemption Number	❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8
Does the proposed research involve human specimens and/or data	❍ Yes ● No
Other Requested information	

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UNIVERSITY OF OREGON

October 30, 2019

To whom it may concern,

I am pleased to be able to collaborate with Dr. Cristopher Niell on his project for a BRAIN Initiative R01, entitled "Functional organization of the octopus visual system". This is a fascinating endeavor, to explore the mysterious brain of the octopus, and I look forward to participating in the computational aspects of this project.

I am an Assistant Professor at University of Oregon, in the Institute of Neuroscience. I received my PhD in theoretical physics, and then began working in theoretical neuroscience, first with Dr. Liam Paninski and then with Dr. Ken Miller. My lab at UO is focused on developing mechanistic and computational models of cortical dynamics, and using these to understand how specific visual computations can be achieved. Recently, my lab has also had several projects applying these models to questions in machine vision and natural scenes, as well as developing methods to infer neural architectures from measurements of neural activity.

The prospect of applying these approaches to a totally novel brain architecture is very exciting. I have enjoyed my recent discussions with Cris about this project, learning about the octopus visual system and brainstorming ideas to apply their data to computational models. I expect that our extensive modeling and theoretical expertise will help contribute significantly to the project. In particular, I will assist them in implementation and interpretation of the GAN approach we published to deduce neural architecture from recorded neural activity. It will be a unique scientific endeavor to create the first neural network models based on the octopus visual system.

I already have several collaborative projects with the Niell lab based on their studies of the mouse visual system, including a co-mentored graduate student on this project. Although my lab will be moving to Cambridge in 2020, I do not expect that this will impede my ability to continue these interactions and to participate in the computational components of this project. In particular, I will maintain close ties with University of Oregon, but also, as a theorist I am quite used to collaborating across institutions.

In summary, I am happy to contribute my expertise towards this project and I look forward to seeing the results.

Sincerely,

Redacted by agreement

Institute of Neuroscience
1254 University of Oregon, Eugene OR 97403-1254
541-346-7636 | LABORATORY 541-346-7637 | FAX 541-346-4548 www.neuro.uoregon.edu

Data Management Plan

This project will generate large-scale datasets from calcium imaging of visual responses in the optic lobe. As these represent the first recordings from the visual system of a cephalopod, they are likely to be useful for a range of analyses by other groups. Code that will be developed for data analysis will also potentially be of interest to the wider neuroscience community. Therefore, our data management plan is designed to facilitate dissemination of collected data and developed code to the community, in addition to supporting the project directly.

Following acquisition, data will be stored on a local data server in the Niell lab for pre-processing and analysis. We have a dedicated 8-core data workstation where day-to-day analysis can be performed, whereas large data analysis runs (pooling across multiple experiments) can be loaded onto the new UO High Performance Computing core. The local data server will have mirrored backup installed in UO's data center in Allen Hall. The university is currently installing a 10GE network for research labs, so that the Niell lab, the High Performance Computing center, and the data center will all be connected by a high-speed network suitable for transferring large datasets.

We will make data on the local server available for public download, following registration for access by request. All data presented in papers will be made available upon publication, at the latest. Datasets that are not part of a publication, but are sufficiently complete to be useful to the scientific community, will be curated and made available as well. In addition to the data, we will make all code we develop freely available as a stable branch of our local GitHub repository, along with documentation for use.

Authentication of key biological resources

The only reagent requiring verification in this project are the calcium indicator and retrograde tracer beads. Both reagents can directly verified by efficacy in experimental protocols.

Just In Time Report

Report submitted on : 06/12/2020 10:52 AM

IRB Confirmation:	No IRB Certification was required
Human Subjects Assurance Number:	No Human Subjects Assurance was required
IACUC Confirmation:	No IACUC Certification was required

UNIVERSITY OF OREGON | Sponsored Projects Services

June 12, 2020

Brenda A. Kibler
Grants Management Specialist
NINDS/DER/GMB
6001 Executive Blvd., Room 3268
Bethesda, MD 20892-9531

Dear Ms. Kibler,

Below please find the response to your Just in Time request dated June 11, 2020. Please let me know if you need any more information or clarification on any of the items.

- **Updated Facilities and Administrative Cost is needed at this time for University of Oregon.**

  Please find this document attached. It can also be found here: https://research.uoregon.edu/sites/research2-stage.uoregon.edu/files/2019-12/F_A_Rate_Agreement.pdf

- **For Graduate Students listed on this project, please state the name of the Graduate Student and state if there is any other support for the Graduate Student listed, please include the Grant Number, Budget Period Start Date, Project Period End date, number of months, and state if there is any overlap should this project be funded.**

  Please find this document attached.

- **Please state if there are any Foreign Components on this project; if so, please submit the Name of the Institution, Institutional address, email, and voice mail.**

  None.

Please feel free to contact me if any additional information is needed and thank you for considering the University of Oregon.

Sincerely,

Ashley Boehme
Sponsored Projects Administrator
Sponsored Projects Services, University of Oregon

Sponsored Projects Services
5219 University of Oregon, Eugene OR 97403-5219
T (541) 346-5131 | **F** (541) 346-5138 | **sps.uoregon.edu**
sponsoredprojects@uoregon.edu

COLLEGES AND UNIVERSITIES RATE AGREEMENT

EIN:

ORGANIZATION:

University of Oregon-Eugene, OR
1266 University of Oregon
203 Johnson Hall
Eugene, OR 97403-1266

DATE:04/24/2020

FILING REF.: The preceding agreement was dated 12/16/2019

The rates approved in this agreement are for use on grants, contracts and other agreements with the Federal Government, subject to the conditions in Section III.

SECTION I: INDIRECT COST RATES

RATE TYPES: FIXED FINAL PROV. (PROVISIONAL) PRED. (PREDETERMINED)

EFFECTIVE PERIOD

TYPE	FROM	TO	RATE(%)	LOCATION	APPLICABLE TO
PRED.	07/01/2019	06/30/2021	47.50	On-Campus	Organized Research
PRED.	07/01/2019	06/30/2021	26.00	Off-Campus	Organized Research
PRED.	07/01/2019	06/30/2021	46.00	On-Campus	Instruction
PRED.	07/01/2019	06/30/2021	26.00	Off-Campus	Instruction
PRED.	07/01/2019	06/30/2021	30.70	On-Campus	Other Sponsored Activities
PRED.	07/01/2019	06/30/2021	26.00	Off-Campus	Other Sponsored Activities
PROV.	07/01/2021	Until Amended		(A)	

*BASE

Modified total direct costs, consisting of all salaries and wages, fringe benefits, materials, supplies, services, travel and subgrants and subcontracts up to the first $25,000 of each subgrant or subcontract (regardless of the period covered by the subgrant or subcontract). Modified total direct costs shall exclude equipment, capital expenditures, charges for patient care, student tuition remission, rental costs of off-site facilities, scholarships, and fellowships as well as the portion of each subgrant and subcontract in excess of $25,000.

(A) Use same rates and conditions as those cited for fiscal year ending June 30, 2021.

SECTION I: FRINGE BENEFIT RATES**

TYPE	FROM	TO	RATE(%)	LOCATION	APPLICABLE TO
FIXED	7/1/2020	6/30/2021	79.00	All	Faculty/Staff A
FIXED	7/1/2020	6/30/2021	52.50	All	Faculty/Staff B
FIXED	7/1/2020	6/30/2021	31.00	All	Faculty/Staff C
FIXED	7/1/2020	6/30/2021	119.30	All	Classified Services
FIXED	7/1/2020	6/30/2021	102.30	All	Classified Skilled/Clerical
FIXED	7/1/2020	6/30/2021	87.10	All	Classified Technical
FIXED	7/1/2020	6/30/2021	34.90	All	Temps
FIXED	7/1/2020	6/30/2021	3.00	All	Students
PROV.	7/1/2021	6/30/2023		(B)	

** DESCRIPTION OF FRINGE BENEFITS RATE BASE:

Salaries and wages excluding vacation, holiday, sick leave pay and other paid absences.

(B) Use same rates and conditions as those cited for fiscal year ending June 30, 2021.

SECTION II: SPECIAL REMARKS

TREATMENT OF FRINGE BENEFITS:

The fringe benefits are charged using the rate(s) listed in the Fringe Benefits Section of this Agreement. The fringe benefits included in the rate(s) are listed below.

TREATMENT OF PAID ABSENCES

The costs of vacation, holiday, sick leave pay and other paid absences are included in the organization's fringe benefit rate and are not included in the direct cost of salaries and wages. Claims for direct salaries and wages must exclude those amounts paid or accrued to employees for periods when they are on vacation, holiday, sick leave or are otherwise absent from work.

DEFINITION OF OFF-CAMPUS
An off-campus rate is applicable to those projects conducted in facilities not owned or operated by the University, which include charges for facility rental as a direct expenditure and for which more than 50% of the project salaries and wages are for effort conducted in the rental facility.

DEFINITION OF EQUIPMENT
Equipment means tangible personal property (including information technology systems) having a useful life of more than one year and a per-unit acquisition cost which equals or exceeds $5,000.

The following fringe benefits are included in the fringe benefit rates: HEALTH INSURANCE, OTHER, PAYROLL TAX, RETIREMENT, UNEMPLOYMENT, WORKER's COMPENSATION-SAIF, and LEAVE.

NEXT PROPOSAL DUE DATE
An indirect cost and fringe benefits proposal based on actual costs for fiscal year ending 06/30/20, will be due no later than 12/31/20.

SECTION III: GENERAL

A. LIMITATIONS:

The rates in this Agreement are subject to any statutory or administrative limitations and apply to a given grant, contract or other agreement only to the extent that funds are available. Acceptance of the rates is subject to the following conditions: (1) Only costs incurred by the organization were included in its facilities and administrative cost pools as finally accepted: such costs are legal obligations of the organization and are allowable under the governing cost principles; (2) The same costs that have been treated as facilities and administrative costs are not claimed as direct costs; (3) Similar types of costs have been accorded consistent accounting treatment; and (4) The information provided by the organization which was used to establish the rates is not later found to be materially incomplete or inaccurate by the Federal Government. In such situations the rate(s) would be subject to renegotiation at the discretion of the Federal Government.

B. ACCOUNTING CHANGES:

This Agreement is based on the accounting system purported by the organization to be in effect during the Agreement period. Changes to the method of accounting for costs which affect the amount of reimbursement resulting from the use of this Agreement require prior approval of the authorized representative of the cognizant agency. Such changes include, but are not limited to, changes in the charging of a particular type of cost from facilities and administrative to direct. Failure to obtain approval may result in cost disallowances.

C. FIXED RATES:

If a fixed rate is in this Agreement, it is based on an estimate of the costs for the period covered by the rate. When the actual costs for this period are determined, an adjustment will be made to a rate of a future year(s) to compensate for the difference between the costs used to establish the fixed rate and actual costs.

D. USE BY OTHER FEDERAL AGENCIES:

The rates in this Agreement were approved in accordance with the authority in Title 2 of the Code of Federal Regulations, Part 200 (2 CFR 200), and should be applied to grants, contracts and other agreements covered by 2 CFR 200, subject to any limitations in A above. The organization may provide copies of the Agreement to other Federal Agencies to give them early notification of the Agreement.

E. OTHER:

If any Federal contract, grant or other agreement is reimbursing facilities and administrative costs by a means other than the approved rate(s) in this Agreement, the organization should (1) credit such costs to the affected programs, and (2) apply the approved rate(s) to the appropriate base to identify the proper amount of facilities and administrative costs allocable to these programs.

BY THE INSTITUTION:

University of Oregon-Eugene, OR

(INSTITUTION)

(SIGNATURE)

Jamie Moffitt + Adm.

(NAME)

VP for Finance + CFO

(TITLE)

5/13/20

(DATE)

ON BEHALF OF THE FEDERAL GOVERNMENT:

DEPARTMENT OF HEALTH AND HUMAN SERVICES

(AGENCY)

(SIGNATURE)

Arif Karim

(NAME)

Director, Cost Allocation Services

(TITLE)

4/24/2020

(DATE) 7122

HHS REPRESENTATIVE: Jeanette Lu

Telephone: (415) 437-7820

OTHER SUPPORT

Redacted by agreement

Current Research Support

R34 NS111669 (Niell) 04/01/20 – 03/31/21 EFFORT
NIH/NINDS

Overlap

None. If funded, Redacted by agreement full time research effort will be focused on the R01.

Just In Time Report

Report submitted on : 04/21/2020 11:39 AM

IRB Confirmation:	No IRB Certification was required
Human Subjects Assurance Number:	No Human Subjects Assurance was required
IACUC Confirmation:	No IACUC Certification was required

For New and Renewal Applications – DO NOT SUBMIT UNLESS REQUESTED

PHS 398 OTHER SUPPORT

NIELL, C.

ACTIVE

R21 EY029888 (Niell) 01/01/19 – 12/31/20 EFFORT
NIH/NEI $125,000
Impact of environmental experience on visual processing and behavior

This project will determine how environmental experience impacts a broad range of measures of visual processing in mouse.

R34 NS111669 (Niell) 04/01/19 – 03/31/21 EFFORT
NIH/NINDS $218,250
Visual coding in freely moving behavior

This project will develop technology to measure visual input in freely moving mice and relate this to neural signals in the visual cortex.

Private Source (Niell) 05/01/19 - 04/30/22 EFFORT
Private Source $125,000
Imaging sensory processing and memory storage in the octopus brain

This collaborative project, with co-PI Redacted by agreement aims to determine how visual information is stored as long-term memory in the octopus.

N00014-15-1-2148 (Posner) 05/01/15 – 09/30/20 EFFORT
Office of Naval Research No cost extension
Towards a Neural Model of Human Skill Learning

This project will pair studies in mice and humans to determine the brain regions and local circuit mechanisms underlying skill acquisition.

Renee James Seed Grant (Niell) 07/01/19– 06/30/20 EFFORT
University of Oregon $40,000
Cracking the code of the octopus visual system

The major research goal of this project is to establish transcriptionally defined cell types within the octopus visual system using single-cell RNA-seq.

PENDING

Pending Support

Pending Support

OVERLAP

None. Effort for active grants will be either reduced within NIH policy or charged to the academic year in order to resolve any over commitment.