OMB Number: 4040-0001
Expiration Date: 11/30/2025

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
DC023126

b. Agency Routing Number

2. DATE SUBMITTED

Application Identifier
75091-A1

c. Previous Grants.gov Tracking Number

5. APPLICANT INFORMATION **UEI*:** FXKMA43NTV21

Legal Name*: BAYLOR COLLEGE OF MEDICINE
Department: Neurosurgery
Division:
Street1*: BAYLOR COLLEGE OF MEDICINE
Street2: 1 BAYLOR PLAZA
City*: HOUSTON
County: Harris
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 770303411

Person to be contacted on matters involving this application
Prefix: First Name*: Leanne Middle Name: Scott Last Name*: Franch Suffix: Ph.D
Position/Title: Executive Director, Sponsored Programs
Street1*: One Baylor Plaza, BCM 310
Street2:
City*: Houston
County: Harris
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 77030-3411
Phone Number*: 7137981297 Fax Number: Email: spo@bcm.edu

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 1741613878A1

7. TYPE OF APPLICANT* O: Private 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 of language semantics and speaker identity during speech comprehension

12. PROPOSED PROJECT
Start Date* Ending Date*
12/01/2025 11/30/2028

13. CONGRESSIONAL DISTRICTS OF APPLICANT
TX-009

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: First Name*: Melissa Middle Name: C Last Name*: Franch Suffix: Ph.D

Position/Title: Postdoctoral Researcher
Organization Name*: BAYLOR COLLEGE OF MEDICINE
Department: Neurosurgery
Division:
Street1*: One Baylor Plaza
Street2:
City*: Houston
County: Harris
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 77030-3411
Phone Number*: 9199029217 Fax Number: Email*: melissa.franch@bcm.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$229,932.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$229,932.00
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*: Darin Middle Name: Last Name*: Garrett Suffix:

Position/Title*: Associate, Sponsored Programs
Organization Name*: Baylor College of Medicine
Department: Office of Research
Division:
Street1*: One Baylor Plaza
Street2: MS: BCM310
City*: Houston
County: Harris
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 77030-3411
Phone Number*: 7137981297 Fax Number: Email*: spo@bcm.edu

Signature of Authorized Representative*
Darin Garrett

Date Signed*
04/04/2025

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:Cover_Letter_F32_resubmit.pdf

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

OMB Number: 4040-0010
Expiration Date: 12/31/2026

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:	Baylor College of Medicine
UEI:	FXKMA43NTV21
Street1*:	One Baylor Plaza
Street2:	
City*:	Houston
County:	Harris
State*:	TX: Texas
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	77030-3411
Project/Performance Site Congressional District*:	TX-009

Additional Location(s) File Name:

OMB Number: 4040-0010
Expiration Date: 11/30/2025

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: 09-16-2024

Human Subject Assurance Number 00000286

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*	Project_Abstract.pdf
8. Project Narrative*	Project_Narrative_F32.pdf
9. Bibliography & References Cited	references_resubmit.pdf
10. Facilities & Other Resources	Franch_facilitiesAndResources.pdf
11. Equipment	Equipment_F32.pdf

Project Abstract

Effective communication requires understanding both the meaning of spoken words (semantics) and the identity of the speaker. This integration of semantics and speaker identity is vital for social interactions, yet the neural mechanisms supporting this process are not fully understood. This project investigates how the anterior cingulate cortex (ACC), a region involved with both language and social cognition, contributes to the integration of semantic content and speaker identity during natural conversations and speech comprehension. We propose that the ACC encodes semantics and speaker identity using distinct but related neural population subspaces, allowing efficient generalization across different speakers while maintaining specificity. To test this hypothesis, we will record single-neuron activity in the ACC of patients with epilepsy during both passive listening to podcast stories and active participation in natural conversations. Our specific aims are to delineate how ACC neurons respond to different semantic categories and speakers (Aim 1) and to determine how neural populations align these semantic representations across different speakers using neural subspace analysis (Aim 2). Our findings will have important implications for basic science research and understanding of communication disorders. This study will provide new insights into the neural coding of language and social information, improving the development of assistive communication technologies and neural prosthetics aimed at individuals with language impairments, such as those with autism or aphasia. Collectively, this proposal aims to elucidate single neuron dynamics in real-life communication and will provide me with the skills needed to continue social communication and language neuroscience research as a principal investigator.

Project Narrative

This research aims to uncover how the brain integrates the meaning of words with the identity of the speaker during speech comprehension. The research leverages the unique opportunity to record from single neurons in humans during natural conversations. Understanding this integration process in the anterior cingulate cortex will provide crucial insights into how communication functions and how it may be impaired in conditions like autism and aphasia, ultimately informing the development of assistive technologies and therapies for individuals with communication deficits.

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Facilities and other resources

Institution: Baylor College of Medicine (BCM) is part of the Texas Medical Center (TMC) in Houston, Texas, a 700-acre complex home to 19 academic institutions. BCM has primary affiliations with six teaching hospitals, each with national and international reputations for medical excellence. Basic scientific research covering a range of topics related to human health and disease built the foundation of BCM's name in research, which has since expanded into many interdisciplinary research facilities. BCM's prominence in the field of research is well-reflected in the consistency of federal and private funding. Since 2006, BCM has ranked first in Texas medical schools in NIH funding, and top 20 in NIH funding among all U.S. medical schools in 2022. Specifically for the Department of Neuroscience, BCM ranked second in the Top 30 neuroscience departments receiving NIH funding in 2022, with annual total research funding nearly reaching $30 million. The Department of Neurosurgery ranks sixth in the country for NIH funding, bringing in nearly $10 million this year, and is projected to shift even higher with the recent addition of more well-funded research faculty.

Intellectual Environment: The collaborative nature of BCM yields an ideal environment to learn from surrounding colleagues and other resources. As a member of the Hayden lab, I will work alongside students and scientists in a multitude of programs at BCM both in the medical school as well as part of the Graduate School of Biomedical Sciences. Faculty I will work alongside in the neurosurgery department are part of the Neuroscience, Quantitative and Computational Biosciences (QCB), and Development, Disease Models & Therapeutics (DDMT) programs. Journal clubs, data presentations, lab meetings, Neurosurgery department-sponsored events, and other conferences and seminars provide consistent opportunities to build and enhance skills pertinent for personal and professional development.

Neurotechnology Development: This research has direct implications for developing speech neuroprosthetics. Our research team is a member of BrainGate, a pre-eminent cross-institutional research team focused on BCI. I will attend weekly BrainGate meetings. In addition, I will meet monthly with Dr. Nishal Shah, a member of the Rice Neuroengineering Initiative and the BCM Neurosurgery department to support the clinical application of our findings.

Physical Resources: The necessary equipment for completion of the proposed research is available through my Sponsor's lab and Baylor St. Luke's Medical Center Hospital (BSL), as described below. Additionally, both of my sponsors have sufficient funding to financially support any additional equipment such as computer storage devices. With 3.7 TB of storage, 128 GB of RAM, a 12 GB GPU, and a 3.1 GHz intel processor, my personal BCM computer is well equipped to manage large data files and run computational analysis. I also store data on our group's server.

Research Laboratory Space: Dr. Hayden and Dr. Sheth's research area is located on the first floor of the Neurosensory Building of Baylor College of Medicine in the Texas Medical Center. I have a designated private office (shared with 2 others) with a personal desk and desktop computer. My office is two doors down from Drs. Hayden and Sheth's private offices. The laboratory space includes a machine shop, private offices, and open area desk seating. In total, we have office space for 25 trainees and 7 faculty. Additional shared laboratory space is available in common areas within both the office suite, including one large conference room, a conference table, and break rooms. The Hayden lab has immediate access to all equipment relevant to the proposed work.

Clinical

Epilepsy Monitoring Unit (EMU): The EMU at Baylor St. Luke's Hospital is a 10-room inpatient ward that is designed for inpatient video-EEG monitoring and is staffed by a multidisciplinary team of specialists, including attending physicians, fellows, psychiatrists, EEG technicians, nurses, and information-technology technicians from the Healthcare Information Services (Hc-IS). The EMU contains 10 computers with monitors, one station per room, to visualize the real-time recording of EEG and video data. The data is automatically stored on a server in the EMU for secure storage and access. The EMU continuously monitors the daily progress and health of each patient server for secure storage and access. The EMU rotates personnel to monitor and care for each patient daily (24 hours per day) during the patient's stay (on average 2-3 weeks) in the EMU. A patient under pre-surgical evaluation is discharged from the EMU at the discretion of the treating physicians. Patients are discharged generally after 5 weeks with no seizures or if the patient has had at least 3-5 reliable seizures with ostensibly focal epileptic activity according to the EEG.

Epilepsy Surgical Service: The Epilepsy Surgical Service is a multidisciplinary clinical unit that provides state-of-the-art procedures including intracranial monitoring of treatment-resistant epilepsy, cutting-edge surgical treatments efforts like stereotactic laser ablation, laser interstitial thermal therapy, radiofrequency ablation, and canonical treatments such as open resection and de-afferentation procedures. The clinical framework for recruiting patients to the proposed study is implemented through this Epilepsy Surgical Service. Posts of this service include epilepsy-focused neurologists, epilepsy surgeons (Dr. Sameer Sheth), neuroradiologists, neurophysiologists, neuropsychologists, and other related staff.

Institutional Resources and Cores

Advance Technology Core for Advanced Magnetic Resonance Imaging (CAMRI): CAMRI is a ~9000 sq ft state-of-the-art Houston research community imaging facility supporting biomedical research projects working to advance understanding of physiology, anatomy, and function. The core is equipped with two 3T PrismaFit Siemens MRI Scanners with VE11e software. Scanners support ample product pulse sequences, enabling high-resolution structural, diffusion-weighted, and blood-oxygen level dependent functional magnetic resonance image (MRI) acquisition, as well as Arterial Spin Labeling and single and multi-voxel MR spectroscopy. In-house MR technologists provide Level 1 and Level 2 MRI safety courses for independent scanning. A full-time receptionist, patient reception area, testing rooms, and a large conference room enable efficient screening, training, and testing of patient subjects.

Equipment

As described below, the Hayden laboratory, the Baylor College of Medicine facilities, and the Epilepsy Monitoring Unit at Baylor St. Luke's Medical Center Hospital provide all necessary equipment for completion of the proposed research.

Electrophysiological Measurement

All electrophysiological data will be collected through FDA- and BCM IRB-approved devices including EMU clinical and research sEEG data acquisition systems (Nihon-Kohden and Blackrock Microsystems Neuroport Data Acquisition System). Patients will typically receive AdTech Medical and PMT Corp. probes in a Behnke-Fried configuration. Each probe includes 8-20 macro-sEEG electrodes, each with 16 contacts used for recording local field potentials (LFPs), as well as a smaller subset of microwires, each with 8 contacts, specifically designed for recording single-neuron activity. All sEEG electrodes (with 12 to 16 contacts each depending on depth and patient-specific measurements) will be connected to the recording system (two NeuroPort systems, Blackrock Neurotech). The NeuroPort is an FDA-approved (510(k) number K09095) system for recording and processing neural signals from up to 256 electrodes each, in addition to auxiliary analog signals and digital experimental events. Macroelectrode local field potential data is recorded at 2kHz and single neuron activity will be recorded at 30kHz during the proposed language experiments. Electrophysiological data is directly uploaded to a password protected 2-Petabyte RAID server securely managed by BCM Healthcare Information Services.

High-resolution Audio Recording

The patient's room has two high-quality microphones (Logitech, Blue Yeti) – one that is positioned near the patient's bed and another near the guest seating - to record unscripted conversations that patients naturally have with the doctors and visitors. During this fellowship, we will acquire lavalier microphones that visitors or researchers can wear during conversations to improve audio quality and transcription. The microphones in the patient's room and the audio from story podcast monologues are directly synchronized with the neural recording system via BNC cables, providing analog input to the system. All signals, neural and audio, are recorded at 30kHz.

Computers

Our neurosurgery research team has 3 computers in the EMU (hospital research room) that are dedicated to recording neural and audio data, running behavioral tasks, or recording video from surveillance cameras in the patient room. After experiments, data is automatically uploaded to a server that I can access from my local machine, which is a high-performance computer: 3 TB storage, 12 GB GPU, 128 GB of RAM, and 3.1 GHz Intel Xeon Processor. Each BCM student and employee has software licenses for Matlab and Adobe Illustrator.

Data storage

The Hayden lab and BCM neurosurgery research team has access to a secure server, *Elias*, that is currently 512 TB but can scale up to 4 PB. All data on this server is backed up to Amazon Glacier Cloud storage.

OMB Number: 4040-0001
Expiration Date: 11/30/2025

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: First Name*: Melissa Middle Name C Last Name*: Franch Suffix: Ph.D

Position/Title*: Postdoctoral Researcher
Organization Name*: BAYLOR COLLEGE OF MEDICINE
Department: Neurosurgery
Division:
Street1*: One Baylor Plaza
Street2:
City*: Houston
County: Harris
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 77030-3411

Phone Number*: 9199029217 Fax Number:

E-Mail*: melissa.franch@bcm.edu

Credential, e.g., agency login: mfranch

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

Degree Type: PhD,BS Degree Year: 2023,2012

Attach Biographical Sketch*: File Name: Biosketch_F32_MF_resubmit1_rev.pdf

Attach Current & Pending Support: File Name:

Tracking Number: Opportunity Number: . Received Date:

PROFILE - Senior/Key Person

Prefix: First Name*: Benjamin Middle Name Yost Last Name*: Hayden Suffix: Ph.D

Position/Title*: Professor
Organization Name*: Baylor College of Medicine
Department: Neurosurgery
Division:
Street1*: One Baylor Plaza
Street2:
City*: Houston
County: Harris
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 77030-3411

Phone Number*: 4257492341 Fax Number:

E-Mail*: Benjamin.Hayden@bcm.edu

Credential, e.g., agency login: hayden@neuro

Project Role*: Other (Specify) Other Project Role Category: Sponsor

Degree Type: PhD, BA Degree Year: 2005, 2000

Attach Biographical Sketch*: File Name: Hayden_Biosketch_3.2025.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Sameer Middle Name Anil Last Name*: Sheth Suffix: M.D.

Position/Title*: Professor
Organization Name*: Baylor College of Medicine
Department: Neurosurgery
Division:
Street1*: 7200 Cambridge St
Street2: 9th Floor
City*: Houston
County: Harris
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 77030-0000

Phone Number*: 7137985060 Fax Number:

E-Mail*: sameer.sheth@bcm.edu

Credential, e.g., agency login: SAMEER1

Project Role*: Other (Specify) Other Project Role Category: Co-Sponsor

Degree Type: MD, PhD, BA Degree Year: 2005, 2005, 1998

Attach Biographical Sketch*: File Name: NIH_Sheth_Biosketch.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: J Liberty Middle Name S Last Name*: Hamilton Suffix: Ph.D

Position/Title*: Assistant Professor
Organization Name*: University of Texas at Austin
Department: Speech, Language, and Hearing Sciences
Division:
Street1*: 2504A Whitis Ave. (A1100)
Street2:
City*: Austin
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 787020000

Phone Number*: 5124711929 Fax Number:

E-Mail*: liberty.hamilton@austin.utexas.edu

Credential, e.g., agency login: LHamilton11

Project Role*: Consultant Other Project Role Category:

Degree Type: PhD, BA Degree Year: 2013, 2006

Attach Biographical Sketch*: File Name: Hamilton-biosketch.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Ashutosh Middle Name Last Name*: Sabharwal Suffix:

Position/Title*: Professor
Organization Name*: Rice Univesity
Department: Electrical and Computer Engineering
Division:
Street1*: 6100 Main St
Street2: MS380
City*: Houston
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 770050000

Phone Number*: 713-348-5057 Fax Number:

E-Mail*: ashu@rice.edu

Credential, e.g., agency login: asabharwal

Project Role*: Consultant Other Project Role Category:

Degree Type: PhD, MS, BS Degree Year: 1999, 1995, 1993

Attach Biographical Sketch*: File Name: Ashu-Biosketch_NIH_March_2025_rev.pdf

Attach Current & Pending Support: File Name:

OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 01/31/2026)

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: Melissa Franch

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

POSITION TITLE: Postdoctoral Associate

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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
North Carolina State University; Raleigh, NC	BS	08/2008	05/2012	Biological Sciences
North Carolina State University; Raleigh, NC	BS	08/2008	05/2012	Science Education
The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences (GSBS); Houston, TX	PhD	08/2017	12/2023	Neuroscience
Baylor College of Medicine (BCM); Houston, TX	Postdoc	01/2024		Department of Neurosurgery

A. Personal Statement

With a deep passion for research and education, my ultimate goal is to become an academic researcher, where I can make meaningful contributions to both fields. Growing up with a brother who has profound autism sparked my early curiosity about neural interactions and how their alterations might contribute to atypical behaviors. This curiosity led me to pursue opportunities in both research and education throughout college and into my career, recognizing the importance of not only conducting rigorous research but also teaching it effectively. Collectively, these experiences motivate my service as a neuroscientist, educator, and caring member of my community.

I started my professional career as a high school Biology teacher and worked as a research associate at Pacific Northwest National Lab (PNNL) during the summer months, from which I gained the skills to think critically, plan experiments, and analyze research data while also communicating it to others. After three years, I left teaching and PNNL to pursue full-time research in a neuroscience lab so I could investigate questions specific to this field. As a research technician in the Kevin Franks lab at Duke University, I learned how electrophysiology and optogenetics is used to investigate odor encoding circuits in mouse piriform cortex. These skills prepared me for my graduate research in the Dragoi lab at UTHealth, where I pioneered wireless, chronic neural recordings in freely moving monkeys to study social cognition.

During graduate school, I shifted my focus to understanding how neural circuits encode visual stimuli and decisions during social learning, particularly in brain regions not traditionally considered part of the ‘social brain.’ To investigate how both visual and prefrontal regions contribute to cooperative learning, I developed a novel experimental paradigm that combined behavioral monitoring, wireless eye tracking, and neural recordings from visuo-frontal areas while two animals learned to cooperate for a food reward. Using machine learning models to analyze neural data, I found that both visual and executive brain regions improved their coding of socially relevant visual cues, such as partner viewing and reward, during learning. Furthermore, the prefrontal cortex exhibited enhanced neural coding of each animal’s decision to cooperate when social cues were present. This work provided the first evidence of the visual cortex's role in encoding socially relevant information, expanding our understanding of social cognition. My research was supported by a NIMH F31-Diversity Award and resulted in a first-author publication in *Nature* (Franch et al., 2024). My knowledge of applying statistical and computational methods to analyze interactions between evolving stimuli (such as visual fixations) and single-neuron activity will complement the study of language comprehension, specifically word processing, in my proposed research plan.

In the Franch lab, I aim to test theories for how neurons represent and integrate the information we convey through words and visual cues, such as body language and facial expressions, during social interactions. Given that language is the foundation of human communication, my postdoctoral research builds on my graduate work, which focused on visual cues, by investigating neural coding of word meaning and speaker identity during natural conversations and listening. Working with Dr. Hayden, Dr. Sheth (co-sponsor), and Drs. Hamilton and Sabharwal (consultants) provides a unique opportunity to apply my expertise in modeling and social cognition to study how human neurons integrate speaker identity and semantic information. The proposed research and training plan leverages the exceptional clinical environment at BCM, equipping me with the skills needed to become an independent researcher in social and language neuroscience, capable of investigating neural changes in both healthy and autistic individuals.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

01/2024 – present	Postdoctoral Associate, Baylor College of Medicine
01/2024 – present	Volunteer audio editor for Stories of Women in Neuroscience (Stories of WiN) podcast
08/2017 – 2023	Graduate Student, Dragoi lab, The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences, Houston, TX
08/2021 – 2022	Representative, Neuroscience Program Steering Committee
08/2020 – 2022	Representative, UTHealth Graduate Student Education Committee
08/2019 – 2020	Teaching Assistant, Neuroanatomy, The University of Texas School of Dentistry, Houston, TX
01/2020	Volunteer, Science Night, MD Anderson UTHealth GSBS
04/2019	Volunteer, Brain Night for Kids, UTHealth Neuroscience Research Center
07/2019	Volunteer, Summer Biomedical Academy, MD Anderson UTHealth GSBS
08/2018 – 2021	Representative, Neuroscience Student Council (GSBS Neuroscience Program)
07/2016 – 08/2017	Clinical Research Coordinator, Neurosurgery team, UTHealth, Houston, TX
06/2015 – 07/2016	Research Technician II, Neurobiology, Franks lab, Duke University, Durham, NC
06-08/2013, 06-08/2014	Post Bachelors Research Associate, Thrall lab, Pacific Northwest National Lab, Richland, WA
08/2012 – 06/2015	Teacher, Academic, Honors, and International Baccalaureate (IB) Biology, Millbrook High School, Raleigh, NC
06-12/2012	Teaching Assistant, Biochemistry (BCH 351), North Carolina State University, Raleigh, NC
08-11/2011	Teacher, English, Beijing Royal School, Changping District, Beijing, China
06-08/2010	Undergraduate Research Intern for the Department of Energy Pre-Service Teacher Internship, Thrall lab, Pacific Northwest National Laboratory, Richland, WA

Honors

2024	NIH BRAIN Initiative Scholar Spotlight at the 10th annual BRAIN Initiative conference
2023	Michael R. Blackburn Outstanding Dissertation Award from GSBS
2022	Investing in Student Futures Fellowship
2021	Ruth L. Kirschstein National Research Service Award (NRSA) Individual Predoctoral Fellowship to Promote Diversity in Health-Related Research (Parent F31-Diversity) – NIH/NIMH
2021	Dee S. and Patricia Osborne Endowed Scholarship in Neuroscience (lecture presentation)
2021	UTHealth McGovern Medical School Research Competition (lecture presentation)
2020	Terry J. Crow Ph.D. Scholarship in the Neurosciences (best candidacy exam performance)
2020 – 2022	Russell and Diana Hawkins Family Foundation Discovery Fellowship
2020 – 2021	UTHealth*Leads* – leadership fellowship program participant
2020	UTHealth Neuroscience Research Center's Brain Awareness Outreach Award
2019	Sam Taub and Beatrice Burton Endowed Fellowship in the Neurosciences
2019	Dee S. and Patricia Osborne Endowed Scholarship in Neuroscience (poster presentation)
2019	Society for Neuroscience "Hot Topic" Award for Innovative Research
2019	MD Anderson UTHealth GSBS Travel Award
2018	Dee S. and Patricia Osborne Endowed Scholarship in Neuroscience (lecture presentation)
2012	Magna Cum Laude (overall GPA 3.5-3.749) Graduate, North Carolina State University

2012 "Most Outstanding Senior in Science Education" Award, North Carolina State University
2011 – 2012 National Science Teachers Association NCSU chapter president
2010 – 2012 Burroughs Wellcome Scholarship for Science Education
2008 – 2012 Dean's List, North Carolina State University

C. Contributions to Science

1. Undergraduate Research: I completed a summer internship in the lab of Dr. Karla Thrall, where we focused on radiation research. To promote drug development for mitigating nuclear terrorism, I conducted a study to test the efficacy of a proprietary compound on its ability to restore hematopoietic stem cells and increase survival in lethally irradiated mice. After recording and analyzing changes in body weight, hematological parameters, and survival, I concluded that the mice in the group who received the treatment repeatedly post-irradiation survived significantly longer than other treatment groups and controls, who never received treatment. I presented my poster from this work at symposiums held on campus and at the DOE SERCh at Argonne National Lab. I also wrote a manuscript of the study titled "Proline Rich Polypeptides Enhance Survivability of Whole Body Radiation Exposure in Mice" that was submitted for publication to *Radiation Research*, however, publication is contingent on replication of the study.

a. **Franch, M**., Morris, J.E., Weller, R.E., and Thrall, K.D. Proline rich polypeptides enhance survivability of whole-body radiation exposure in mice. Department of Energy Science and Energy Research Challenge (SERCh). Poster presentation delivered on November 13, 2010 at Argonne National Lab, Chicago, IL.

2. Post-Bachelors Research: The ability to reliably determine both the identity and the intensity of a stimulus is necessary in order for an organism to accurately perceive and respond to it. While working as a research technician in the lab of Dr. Kevin Franks at Duke University, we investigated the neural circuits used in the encoding of odors in mice. Although not an author on the cited paper, I contributed to page 3, "strategy to eliminate recurrent excitation." I performed stereotaxic surgery on emx1-cre mice where I injected AAV-DIO-TeLC-GFP virus into three different locations of the piriform cortex. Injection of this virus causes expression of tetanus toxin light chain (TeLC) in principal cells of piriform cortex, blocking their neurotransmitter release and preventing recurrent circuitry without altering their excitability. After neural recordings, I spike-sorted the data and created raster plots in Matlab to visualize individual neuron responses to odors and calculated neural firing rates for specific odors over multiple trials. We were able to determine that recurrent cortical circuits in piriform cortex underlie accurate and concentration invariant coding of odors. My research in this lab was very rewarding as it contributed to the discovery of a novel coding strategy for odors, later published in *Science*.

a. Bolding, K. A., & Franks, K. M. (2018). Recurrent cortical circuits implement concentration-invariant odor coding. *Science (New York, N.Y.)*, *361*(6407).

3. Post-Bachelors Research: Traumatic brain injury commonly results in lifelong physical and mental disabilities. As a clinical research coordinator in the neurosurgery team at UTHealth, I investigated how traumatic brain injury (TBI) changes neuromodulators, proteins, and ultimately the circuitry of the human brain. The research goal is to develop reliable biomarkers of the effects of TBI to aid in recognition, assessment, and treatment of TBI associated neuronal injury. I identified, consented, and followed-up with patients at Memorial Hermann Hospital to collect biospecimen data, enrolling 78 patients during my brief employment. While this study has over 2000 patients enrolled and is still ongoing with pending results, I did help complete and publish a retrospective analysis of clinical factors that are associated with mortality in elderly (70 years or older) patients with traumatic subdural hematoma (SDH). Our multivariable logistic regression analysis showed that age, Glasgow Coma Scale score, and surgery type had a significant impact on mortality. This research can be used to inform medical professionals how to determine the optimal treatment for elderly patients presenting with traumatic SDH.

a. Monsivais, D., Choi, H. A., Kitagawa, R., **Franch, M.**, & Cai, C. (2018). A retrospective analysis of surgical outcomes for acute subdural hematoma in an elderly cohort. *Interdisciplinary Neurosurgery, 14*, 130-134.

4. Graduate Research: My graduate work investigated the neural circuits that underlie complex behaviors, such as decision-making and social interactions in non-human primates (rhesus macaque). I hypothesized that visual brain areas, such as the visual cortex, as well as executive regions in the prefrontal cortex were improving their processing of visual information to guide decisions during social learning. If confirmed, this would expand our knowledge of social cognition to include regions like the visual cortex, which was not previously considered as part of the 'social brain'. To test this hypothesis, I developed a novel experimental paradigm combining behavioral

monitoring, wireless eye tracking, and neural recordings from visuo-frontal areas to study how interacting rhesus monkeys learn cooperation for a food reward. I found that animals learned to cooperate by improving their action coordination and reaction times. Notably, animals became more likely to cooperate after viewing a social cue, such as the reward or partner monkey. Importantly, I discovered that the visual-frontal cortical network prioritizes this relevant sensory information to facilitate learning social interactions through improved spike timing coordination between regions and encoding of social cues within areas (Franch et al., 2024). Additionally, I contributed to a separate study, where we examined the neural correlates of complex decision-making in uncertain environments while a monkey foraged for food. We found that neural representations of task variables within the low-dimensional space of neural population activity predicts the choice to switch patches better than the animal's behavioral dynamics and as well as the entire neural population. This is an important confirmation of how targeted dimensionality reduction can reveal neural computations better than behavior or unprocessed neural activity (Shahidi et al., 2024). Overall, my graduate work provided a foundation in using electrophysiology and statistics of single neuron activity to launch my postdoctoral work using similar methods to study language during communication in humans.

a. **Franch, M.,** Yellapantula, S., Parajuli, A. *et al.* Visuo-frontal interactions during social learning in freely moving macaques. *Nature* 627, 174–181 (2024).

b. Shahidi, N., **Franch, M.,** Parajuli, A. *et al.* Population coding of strategic variables during foraging in freely moving macaques. *Nature Neuroscience* 27, 772–781 (2024).

c. Parajuli, A., **Franch, M**. and Dragoi, V. Sparseness facilitates image encoding across visuo-frontal networks in freely moving macaque. *Nature Communications,* 2024 (under review).

d. Milton, R. Slapik, M., Egranov, S. Parajuli, A., **Franch, M**., and Dragoi, V. Locomotor activity enhances visuo-frontal communication during natural viewing. *Science*, 2024 (submitted).

5. Postdoctoral Research. Given the fundamental role of language in communication and social behavior, I am eager to investigate how single neurons in the human brain process word meaning and align it with speaker identity during listening and natural conversations with others. This project is an important first step in preparing me to study multi-modal integration theories of words and visual cues that I want to test later in the Franch lab. I hypothesize that semantics and speaker identity are bound through distinct neural subspaces. The Hayden lab is a well-suited environment for me to test this theory as our laboratory has developed 1) a mathematical framework for subspace orthogonality, binding, and generalization and 2) a pipeline for collecting single neurons in humans as they perform language tasks. I have already begun collecting single neuron data from five hospitalized patients (with chronic epilepsy but healthy language function), as they watched and listened to people tell stories and naturally spoke with me and another researcher. I have learned new skills using transcription tools and natural language processing algorithms to transcribe words, extract embeddings, and align with neural activity. My preliminary results, as seen in the proposed research plan, suggest neurons in the ACC are encoding semantics and speaker identity. I presented these preliminary findings at four conferences and my postdoctoral work was recognized at the NIH BRAIN Initiative conference as a scholar spotlight. I have also completed my first postdoctoral study on semantic coding in the human hippocampus, available on BioRxiv.

a. **Franch, M.**, Mickiewicz, E. A., Belanger, J., Chericoni, A., Chavez, A. G., Katlowitz, K., ... & Hayden, B.Y. (2025). A vectorial code for semantics in human hippocampus. *bioRxiv*, 2025-02.

b. **Franch, M**., Mickiewicz, E., Belanger, J., and Hayden, B. Single cell and population coding regimes for language semantics in human cortex. Society for Neuroscience Conference. Poster presentation delivered on October 9, 2024 at the McCormick Conference Center in Chicago, IL.

c. **Franch, M**., Mickiewicz, E., Belanger, J., and Hayden, B. Single cell and population coding regimes for language semantics in human cortex. Gordon Research Conference – The Frontal Cortex. Poster presentation delivered on August 5, 2024 at the Holderness School in Holderness, NH.

d. **Franch, M.**, Mickiewicz, E., Belanger, J., and Hayden, B. Single neuron encoding of audio-visual speech comprehension. NIH BRAIN Initiative Annual Conference. Scholar Spotlight talk delivered on June 17, 2024 in Rockville, Maryland.

D. Scholastic Performance

YEAR	COURSE TITLE	YEAR	COURSE TITLE
North Carolina State University, 2008-2012, GPA 3.73			
2008	Biology	2010	Physics I
2008	Public Speaking	2010	Genetics and Genetics Lab
2008	Chemistry and Chemistry Lab	2010	Microbiology and Microbiology Lab
2008	Calculus I	2011	Physics II
2008	Students Advocate for Youth	2011	School and Society
2008	Orientation to Math and Science	2011	Endocrinology
2008	Weight Training	2011	Ecology
2009	Cellular and Molecular Biology	2011	Methods of Teaching Science I
2009	Quantitative Chemistry and Quantitative Chemistry Lab	2011	Teaching Exceptional Students
2009	Academic Research Writing	2011	Introductory Oceanography
2009	Calculus II	2011	Anatomy and Physiology
2009	Students Advocate for Youth	2011	Student Teaching in Science
2009	Organic Chemistry and Organic Chemistry Lab	2011	Methods of Teaching Science II
2009	Introduction to Teaching Math and Science	2011	Specific Problems in Teaching and Learning
2009	English Literature II	2011	Senior Seminar Math Science Education
2009	Europe 1300-1815	2012	External Learning Experience (study abroad)
2009	Geology and Geology Lab	2012	Biochemistry
2009	Indoor Group Cycling	2012	Introduction to the New Testament
2010	Educational Psychology	2012	Captive Animal Biology
2010	Rise of Modern Science	2012	Plant Life Biology
2010	Society of Family	2012	Developmental Psychology
2010	Cultural Anthropology	2012	Advanced Anatomy and Physiology
2010	Instructional Material Science		
2010	Organic Chemistry II and Organic Chemistry II Lab		

YEAR	COURSE TITLE	GRADE	YEAR	COURSE TITLE	GRADE
The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences, 2017-2023, GPA 4.0					
2017	Tutorial Research Experience	P	2019	Research in Biomedical Sciences	P
2017	Molecular Neurobiology	A	2020	Research in Biomedical Sciences	P
2017	Cellular Neurophysiology	A	2020	NIH Fellowship Proposal Development	P
2017	Ethical Dimensions in Biomedical Sciences	P	2020	Dissertation Research	P
2018	Tutorial Research Experience	P	2020	Dissertation Research	P
2018	Systems Neuroscience	A	2021	Dissertation Research	P
2018	Cognitive Neuroscience	A	2021	Dissertation Research	P
2018	Biostatistics for Life Scientists	A	2021	Dissertation Research	P
2018	Tutorial Research Experience	P	2022	Dissertation Research	P
2018	Research in Biomedical Sciences	P	2022	Dissertation Research	P
2018	Research in Biomedical Sciences	P	2022	Dissertation Research	P
2018	Scientific Writing	A	2023	Dissertation Research	P
2019	Research in Biomedical Sciences	P	2023	Dissertation Research	P
2019	Research in Biomedical Sciences	P	2023	Language and the Brain	P

Courses, unless otherwise noted, are graded on a 4.0 grading scale. Some courses are “Pass” or “Fail” and denoted with a P/F grade. A to F grading scale requires C or better to pass, and the highest grade possible is A.

OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 01/31/2026)

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: **Benjamin Yost Hayden, Ph.D.**

eRA COMMONS USER NAME (credential, e.g., agency login): **hayden@neuro**

POSITION TITLE: **Professor**

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
Rice University, Houston, TX	B.A.	05/2000	Chemistry and Linguistics
University of California, Berkeley, Berkeley, CA	Ph.D.	06/2005	Molecular & Cell Biology
Duke University	Post-doc	06/2011	Neurobiology

A. Personal Statement

My lab is interested in understanding the neural circuitry of cognition, especially reward, decision-making, and executive control, especially in naturalistic contexts. This work is done in the service of understanding and developing improved treatments for mental health diseases like anxiety and depression, as well as drug addiction. To this end, we use carefully designed laboratory tasks and corresponding analyses of behavior and simultaneously collected neural data (most commonly isolated single neurons). We are especially interested in complex naturalistic and interactive behavioral tasks, including ones that make use of foraging theoretic principles. We have been especially interested in the medial wall of the prefrontal cortex (especially ACC) and the orbitofrontal surface (especially OFC and vmPFC), and, more recently, the hippocampus. In the past, I worked primarily in rhesus macaques (*Macaca mulatta*), albeit with a long-standing interest in human neurophysiology through collaborations.

In March, 2023, I moved to the department of Neurosurgery at Baylor College of Medicine, where my focus is primarily on human intracranial electrophysiology. (I continue to participate in primate electrophysiology in collaboration with Dr. Jan Zimmermann, University of Minnesota, and with Dr. Jeffrey Yau, Baylor College of Medicine). In the Neurosurgery department, I work closely with Dr. Sameer Sheth, who directs the neurosurgery research program. Indeed, the neurosurgery research group at BCM is one of the most exciting and productive human neurophysiology research groups in the world – a truly exceptional environment for Dr. Melissa Franch to complete the proposed research. I have worked closely with human data and have published three empirical papers, two review papers, and two preprints (currently under review) in the field. I also am co-PI on one project that is exclusively devoted to human neurophysiology (MH129439).

Melissa's project will investigate ACC neural population coding and alignment of semantics and speaker identity during real-life conversations and listening. She will record single ACC neurons from our human patients with epilepsy while they listen to stories and speak with her, the doctors, and visitors. By elucidating the role of neural computations underlying communication, this research will further our understanding of speech comprehension and guide development of assistive technologies and neural prosthetics to address language deficits. I am committed to providing the best possible scientific environment and support for Melissa during this fellowship. Melissa will also receive training from a team of scientists we cultivated for her mentorship, including Dr. Sameer Sheth, neurosurgeon and scientist, Dr. Liberty Hamilton, professor and expert in speech and language neuroscience, and Dr. Ashutosh Sabharwal, leader in speech recognition and transcription technology, which will be instrumental for her immediate and future enterprise. My lab environment and personal dedication to trainee mentoring will foster Melissa's growth into a successful scientist during this award.

B. Positions, Scientific Appointments, and Honors

Positions

2023-present Professor of Neurosurgery, Baylor College of Medicine
2023-present Adjunct Professor of Electrical and Computer Engineering, Rice University
2021-2023 Professor of Neuroscience, University of Minnesota
2017-2021 Associate Professor of Neuroscience, University of Minnesota
2016-2017 Associate Professor of Brain and Cognitive Sciences, University of Rochester
2011-2016 Assistant Professor of Brain and Cognitive Sciences, University of Rochester
2005- 2011 Postdoctoral Researcher, Platt Lab, Dept. Neurobiology, Duke University
2005 Postdoctoral Researcher, Gallant Lab, Helen Wills Neuroscience Institute, UC Berkeley

Honors

2009 Outstanding Young Investigator Award, Society for Neuroeconomics
2010 Spotlight poster, COSYNE meeting
2011 Travel Award, American College of Neuropsychopharmacology Annual Meeting
2012 Sloan Foundation Fellowship
2013 NARSAD Young Investigator Award
2013 Elected as Associate Member, American College Neuropsychopharmacology
2014 Klingenstein-Simons Foundation Fellowship
2014 Templeton Fellowship
2015 Best paper, Psychonomic Society
2023 McNair Scholar, Baylor College of Medicine

Active Grants

- Posterior cingulate cortex and executive control of memory.

Role: Co-PI (With Brett Foster, University of Pennsylvania). NIH R01 MH129439 (2022-2027)

- Neural basis of behavior in freely moving macaques

Role: PI. NIH R01 MH125377 (2021-2026)

- Neuronal basis of persistence

Role: PI. NIH R01 DA038615 (2015-2026, renewed in 2020)

- Modeling circuit-specific psychiatric deep-brain stimulation and its cognitive effects in macaques

Role: Lead PI (with co-PI Alik Widge, Psychiatry). NIH R01 MH124687 (2020-2025)

Recent Invited Talks

11/23 Naturalistic Neuroeconomics. George Mason University.
05/23 Neuroscience of curiosity. Columbia Conference on Curiosity. New York, NY.
04/23 Neuroscience of naturalistic choice. SOBP Conference, San Diego, CA.
04/23 Neuroscience of naturalistic choice. Caltech.
12/22 Naturalistic Decision-making. Northwestern University.
10/22 Neuroscience in freely moving monkeys and humans. Harvard University.
03/22 Orbitofrontal cortex in the natural world. Oxford University.
03/22 New frontiers in orbitofrontal cortex research. Imperial College London.
03/22 A navigational role for prefrontal regions. University College London.
03/22 Big questions in animal tracking. Brain Behavior Quantification Symposium. NIH BRAIN Initiative panel.
02/22 Pose tracking in primates. Public talk at the Minnesota Zoo.
10/21 Monkey tracking. SymPOSEium, University of Minnesota.
10/21 ACC, addiction, control. Harvard University.
10/21 Posterior cingulate cortex and navigation. Society for Neuroscience Conference. Chicago, IL.
04/21 The population doctrine and cognitive neuroscience. Imperial College London.

Former trainees with tenure-track faculty positions:
• Becket Ebitz (Université de Montréal, Quebec, Canada), 2020
• Ruyuan Zhang (Jiao Tong University, Shanghai, China), 2020
• Seng Bum Yoo (Institute for Basic Science, Sung Kwon Kang University, Seoul, South Korea), 2021
• Rei Akaishi (RIKEN, Tokyo, Japan), 2020

Junior faculty mentorship:
• David Darrow (Neurosurgery, UMN, 2020-2023)
• Jocelyn Richard (Neuroscience, UMN, 2019-2023)
• Jan Zimmermann (Neuroscience, UMN, 2019-2023)
• Alexander Herman (Psychiatry, UMN, 2018-2023)
• Nicole Provenza (Neurosurgery, BCM, 2023-2024)

C. Contributions to Science

Neural mechanisms of reward-based choice

We are keenly interested in developing a basic understanding of the neural mechanisms that support economic choice. Our work supports the idea that value comparison depends on a mutual inhibition operation that occurs simultaneously in multiple reward regions, including the vmPFC (Strait et al., 2014), the ventral striatum (Strait et al., 2015) and dACC (Azab and Hayden, 2017). More broadly, our work argues against standard modular and localized functional models, but instead supports distributed and hierarchical ones (Hunt and Hayden, 2017). One exciting new direction lies in linking neural representations of offers with those of past outcomes, to begin to understand how learning drives choice processes (Wang and Hayden, 2017).

Jurewicz, K., Sleezer, B. J., Mehta, P. S., **Hayden, B. Y.**, & Ebitz, R. B. (2024). Irrational choices via a curvilinear representational geometry for value. Nature Communications. In press.
Johnston, W. J., Fine, J. M., Yoo, S. B. M., Ebitz, R. B., & **Hayden, B. Y.** (2024). Semi-orthogonal subspaces for value mediate a tradeoff between binding and generalization. Nature Neuroscience.
Fine, J. M., Maisson, D. J. N., Yoo, S. B. M., Cash-Padgett, T. V., Wang, M. Z., Zimmermann, J., & Hayden, B. Y. (2023). Abstract value encoding in neural populations but not single neurons. Journal of Neuroscience, 43(25), 4650-4663.
Yoo, S. B. M., & **Hayden, B. Y.** (2020). The Transition from Evaluation to Selection Involves Neural Subspace Reorganization in Core Reward Regions. Neuron, 105(4), 712-724.

Neurophysiology of cognition in humans

My lab's current central focus is on human methods, and on answering questions we can best answer in humans. The appeal of human research is that I can study research questions that are inaccessible – or difficult to assess – through model organisms. I have worked closely with leading scholars in these methods and have made important contributions to the following papers.

Franch, M., Mickiewicz, E. A., Belanger, J., Chericoni, A., Chavez, A. G., Katlowitz, K., ... & **Hayden, B.Y.** (2025). A vectorial code for semantics in human hippocampus. *bioRxiv*, 2025-02.
Chericoni, A., Fine, J. M., Chavez, A. G., Franch, M., Mickiewicz, E., Mathura, R., ... & **Hayden, B. Y.** (2025). Independent Continuous Tracking of Multiple Agents in the Human Hippocampus. *bioRxiv*, 2025-03.
Fine, J. M., Chericoni, A., Delgado, G., Franch, M., Mickiewicz, E., Chavez, A. G., ... & **Hayden, B. Y.** (2025). Complementary roles for hippocampus and anterior cingulate in composing continuous choice. *bioRxiv*, 2025-03.
Aponik-Gremillion, L., Chen, Y. Y., Bartoli, E., Koslov, S. R., Rey, H. G., Weiner, K. S., Yoshor, D., **Hayden, B. Y.**, Sheth, S. & Foster, B. L. (2022). Distinct population and single-neuron selectivity for executive and episodic processing in human dorsal posterior cingulate. Elife, 11, e80722.
Smith, E. H., Horga, G., Yates, M. J., Mikell, C. B., Banks, G. P., Pathak, Y. J.,…, **Hayden, B., Y.** & Sheth, S. A. (2019). Widespread temporal coding of cognitive control in the human prefrontal cortex. Nature neuroscience, 22(11), 1883-1891.

Widge, A. S., Heilbronner, S. R., & **Hayden, B. Y.** (2019). Prefrontal cortex and cognitive control: new insights from human electrophysiology. F1000Research, 8.

Provenza, N. R., Reddy, S., Allam, A. K., Rajesh, S. V., Diab, N., Reyes, G., ... & Sheth, S. A. (2024). Disruption of neural periodicity predicts clinical response after deep brain stimulation for obsessive-compulsive disorder. Nature Medicine, 1-11.

Neural basis of naturalistic decisions

Animals, including humans, are evolved to make decisions in the context of foraging. We believe in making use of the body of insights about the psychological basis of foraging, aggregated in the form of foraging theory, to drive our neuroscientific questions. This involves a theoretical reorientation – towards accept-reject decisions, towards consideration of long-term strategic considerations. It also involves using classic foraging problems as direct inspiration for tasks – we have used both the patch-leaving problem and the diet selection. It also involves consideration of the need to trade off immediate reward for the delayed benefits derived from information – a major driver in curiosity. This work has led us to propose major changes in the way we think about economic choice, value, and learning.

Voloh, Benjamin, David J-N. Maisson, Roberto Lopez Cervera, Indirah Conover, Mrunal Zambre, **Benjamin Hayden**, and Jan Zimmermann. Hierarchical action encoding in prefrontal cortex of freely moving macaques. Cell reports 42, no. 9 (2023).

Maisson, D. J. N., Cervera, R. L., Voloh, B., Conover, I., Zambre, M., Zimmermann, J., & **Hayden, B. Y.** (2023). Widespread coding of navigational variables in prefrontal cortex. Current Biology, 33(16), 3478-3488.

Yoo, S. B. M., Tu, J. C., Piantadosi, S. T., & Hayden, B. Y. (2020). The neural basis of predictive pursuit. Nature neuroscience, 23(2), 252-259.

Hayden, B. Y., Park, H. S. and Zimmermann, J. (2021). Automated pose estimation in primates. American Journal of Primatology

Neuroanatomy of reward and decision-making

Several brain regions are implicated in economic choice but their relative contributions are debated. My lab is interested in understanding how they relate to each other. A major focus of the lab is on understanding how different regions can interact to make decisions related to choice without qualitatively different functions. We have a special interest in trying to understand how anatomy relates to function – how closely do anatomical regions relate to functional boundaries? In general, our work provides support for functional distinctions, but raises questions about how closely those distinctions relate to borders as inferred through traditional anatomical parcellations.

Maisson, D. J. N., Cash-Padgett, T. V., Wang, M. Z., Hayden, B. Y., Heilbronner, S. R., & Zimmermann, J. (2021). Choice-relevant information transformation along a ventrodorsal axis in the medial prefrontal cortex. Nature communications, 12(1), 4830.

Wang, M. Z., Hayden, B. Y., & Heilbronner, S. R. (2022). A structural and functional subdivision in central orbitofrontal cortex. Nature communications, 13(1), 3623.

Fine, J. M., & Hayden, B. Y. (2022). The whole prefrontal cortex is premotor cortex. Philosophical Transactions of the Royal Society B, 377(1844), 20200524.

Hayden, B. Y. (2022). The dangers of cortical brain maps. Journal of Cognitive Neuroscience

OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 01/31/2026)

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: Sheth, Sameer Anil

eRA COMMONS USER NAME (credential, e.g., agency login): SAMEER1

POSITION TITLE: Professor of Neurosurgery, Baylor College of Medicine, Houston, TX

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
Harvard University, Cambridge, MA	B.A.	06/1998	Physics & Astronomy
University of California, Los Angeles, LA, CA	Ph.D.	12/2003	Neuroscience
UCLA School of Medicine, Los Angeles, CA	M.D.	06/2005	Medicine
Massachusetts General Hospital	Internship	06/2006	General Surgery
Massachusetts General Hospital	Postdoc	02/2011	Neurophysiology
Massachusetts General Hospital	Residency	06/2012	Neurosurgery

A. Personal Statement

I am a Board-Certified neurosurgeon with a clinical practice focused on stereotactic and functional neurosurgery, including the treatment of psychiatric disorders, epilepsy, and movement disorders. I am also a neuroscientist and run the Functional and Cognitive Neurophysiology Laboratory at Baylor. My research activities focus on two topics, which I view as flip sides of the same coin. One leverages the unique opportunities available from neurosurgical procedures to study human neurophysiology. By recording from individual or populations of neurons during these procedures, we can learn about complex cognitive functions such as controlled decision-making and emotional regulation with unparalleled precision. The second focus is on improving our understanding and treatment of severe, refractory psychiatric disorders. I believe that a deeper appreciation of the physiological underpinnings of mood and anxiety disorders will lead to more effective treatments using surgical neuromodulation. These two aspects of my research work hand-in-hand to apply cognitive neuroscientific rigor to the management of psychiatric disorders.

Melissa's proposed work aligns well with current research in our neurosurgery research team and maximizes a unique opportunity to record from single neurons in intractable epilepsy patients undergoing neural monitoring. Our neural and speech recording equipment and control room is permanently stationed right next to the patient room, making it easy and enjoyable for both the patient and researcher to participate in research. I am dedicated to providing Melissa with the best possible scientific environment and support during this fellowship. I will work with her to oversee this clinical trial, as I have done for many others, and I will also expose her to new opportunities here in the Texas Medical Center that she can engage in for future work. I have no doubt that Melissa will become an expert in human intracranial recordings and language neuroscience, establishing herself as an independent scientist during this award.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022 – Present Professor, Department of Neurosurgery and, via Joint Appointment, Department of Neuroscience and Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, TX

2022 – Present	Director, Gordon and Mary Cain Pediatric Neurology Research Foundation Laboratories, Texas Children's Hospital, Baylor College of Medicine
2021 – Present	Appointed Member, NIH Neuroethics Working Group (NEWG)
2020 – Present	Appointed Member, NIH NINDS Advisory Council (NANDS)
2020 – Present	Appointed Member, NIH BRAIN Initiative Multi-Council Working Group (MCWG)
2019 – Present	Adjunct Associate Professor, Department of Electrical and Computer Engineering, Rice University, Houston, TX
2019 – Present	Associate Professor via Secondary Appointment, Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, TX
2019 – Present	Associate Professor via Joint Appointment, Department of Neuroscience, Baylor College of Medicine, Houston, TX
2018 – Present	Founder and Director, Functional and Cognitive Neurophysiology Lab, Baylor College of Medicine, Houston, TX
2018 – Present	Director, Psychiatric Neurosurgery, Department of Neurosurgery, Baylor College of Medicine, Houston, TX
2018 – Present	Vice-Chair, Clinical and Translational Research, Department of Neurosurgery, Baylor College of Medicine, Houston, TX
2018 – Present	Associate Professor, Department of Neurosurgery, Baylor College of Medicine, Houston, TX
2013-2018	Assistant Professor, Department of Neurosurgery, Columbia University, New York, NY
2012	Instructor, Department of Neurosurgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Other Experience and Professional Membership

2022	Invited by NIH BRAIN Director to serve on Program Committee for the 8th Annual NIH BRAIN Initiative Meeting
2021 – Present	Elected Member, American Academy of Neurological Surgery
2019	Chair, Scientific Program Committee, 2020 ASSFN Biennial Meeting
2018 – Present	Elected Member, Society of University Neurosurgeons
2018 – Present	Professional Advisory Board, Epilepsy Foundation of Texas, Houston, TX
2018 – Present	Associate Editor in Neuroscience and Editorial Review Board Member, *Neurosurgery* journal
2016 – Present	Scientific Program Committee, Annual Meetings for WSSFN 2017, NANS 2018, ASSFN 2018, CNS 2018, AANS 2019, WSSFN 2019, CNS 2019, AANS 2020, CNS 2020, NANS 2021, AANS 2021, CNS 2021, AANS 2022
2015 – Present	Executive Council, American Society for Stereotactic and Functional Neurosurgery (ASSFN)
2015 – Present	Co-chair, ASSFN Psychiatric Neurosurgery Committee
2014 – Present	Editorial Review Board, Self Assessment in Neurological Surgery (SANS) committee, Congress of Neurological Surgeons
2014-2018	Advisory Committee, Columbia Translational Neuroscience Initiative (CTNI), New York, NY
2014-2017	Unit Director, 8 Hudson North (Neurosurgery/Neurology floor), NY Presbyterian Hospital, New York, NY
2013-2018	Director, Psychiatric Neurosurgery Service, Columbia University, New York, NY
2013-2018	Founder and Director, Functional and Cognitive Neurophysiology Lab, Columbia Univ., NY

Honors

2024	John Jane Lecturer, University of Virginia Department of Neurosurgery, Charlottesville, VA
2024	Visiting Professor, Mayo Clinic Jacksonville Department of Neurosurgery, Jacksonville, FL
2024	Visiting Professor, Massachusetts General Hospital Department of Neurosurgery, Boston, MA
2024	Visiting Professor, Vanderbilt University Department of Neurosurgery, Nashville, TN
2024	Visiting Professor, University of Pennsylvania MindCORE, Philadelphia, PA
2024	Visiting Professor, Stanford University Department of Neurosurgery, Palo Alto, CA
2023	Visiting Professor, 35th Annual Pan Philadelphia Neurosurgery Conference, Philadelphia, PA
2023	Plenary Lecture, NIH BRAIN Investigators Annual Meeting
2023	Plenary Lecture, Society of Biological Psychiatry Annual Meeting
2023	Visiting Professor, Montreal Neurological Institute, Department of Neurology, Montreal, Canada
2022	Visiting Professor, SUNY Upstate, Department of Neurosurgery, Syracuse, NY
2021	Cullen Foundation Endowed Chair

2021 Visiting Professor (Virtual), Cornell University Department of Psychiatry, New York, NY
2021 Visiting Professor (Virtual), University of Pennsylvania Department of Neurosurgery, Philadelphia, PA
2021 Visiting Professor (Virtual), Northwestern University Department of Neurosurgery, Chicago, IL
2021 Visiting Professor (Virtual), UCSF Department of Neurosurgery, San Francisco, CA
2020 Visiting Professor (Virtual), UCLA Department of Neurosurgery, Los Angeles, CA
2020 Visiting Professor (Virtual), Cleveland Clinic Department of Neuroscience, Cleveland, OH
2020 Visiting Professor (Virtual), University of Minnesota Center for Neuroeningeering, Minneapolis, MN
2019 CNS Vanguard Leadership Course
2019 Visiting Professor, Barrow Neurological Institute, Phoenix, AZ
2018 Caroline Wiess Law Endowment for Academic Excellence Award, Baylor College of Medicine
2018 McNair Scholar, Baylor College of Medicine
2018 Visiting Professor, University of São Paulo Department of Psychiatry, São Paulo, Brazil
2017 Keynote Lecture, International IEEE EMBS Conference on Neural Engineering, Shanghai, China.
2017 Gildenberg Lecture, Baylor College of Medicine, Houston, TX, Department of Neurosurgery
2017 Visiting Professor, Massachusetts General Hospital Department of Neurosurgery, Boston, MA
2016 Keynote Speaker, Stonybrook University Medical Scientist Training Program (MSTP) Research Day
2013 American Academy of Neurological Surgery Award, 2nd place
2012 Philip L. Gildenberg Resident Award, 2012 AANS annual meeting
2012 Plenary Session platform presentation, 2012 AANS annual meeting (“Cingulotomy for severe, treatment-refractory obsessive-compulsive disorder: a prospective long-term follow-up of 63 patients”)
2012 Plenary Session platform presentation, 2012 AANS annual meeting (“Reward Prediction Encoded by Single-Neuron Responses in the Human Nucleus Accumbens”)
2012 Harvard Medical School Resident Teaching Award
2011 Integra Foundation Award, 2011 AANS annual meeting
2011 Plenary Session platform presentation, 2011 AANS annual meeting (“Transsphenoidal surgery for Cushing's disease after non-diagnostic inferior petrosal sinus sampling”)
2010 Schmidek Fellowship to visit Professor Tipu Aziz in Oxford University Dept. of Neurosurgery
2010 CNS travel award for Neurological Society of India (NSI)-CNS meeting in Jaipur, India
2010 Best Paper, Neurology Category, 2010 Neurological Society of India (NSI)-CNS joint meeting
2010 Best Clinical Research Award for Residents/Fellows, 2010 ASSFN annual meeting
2010 Second Place, Stereotactic/Functional Award, 2010 AANS annual meeting
2009 Sherry Apple Resident Travel Scholarship, 2009 CNS annual meeting
2007 Stereotactic and Functional Neurosurgery Resident Award, 2007 CNS annual meeting
2002 Organization for Human Brain Mapping conference travel fellowship
2001 ARCS (Achievement Rewards for College Scientists) Foundation Scholarship
2001 UCLA Affiliates/Fishbaugh Scholarship
1998 Cumulative Group I Standing, Dean’s List every semester
1997 Harvard College Scholarship
1996 John Harvard Scholarship

C. Contributions to Science

1. I am interested in applying human neurophysiology towards an improved understanding of psychiatric disorders. Disorders such as OCD, depression, addiction, schizophrenia, chronic pain, and many others share dysfunction in the cortical/subcortical circuits discussed in the previous section. As we learn more about cognitive/emotional circuitry in the normal state, we can develop rationally designed neuromodulatory treatments for patients with refractory psychiatric disorders. I am PI of DBS for Depression grant UH3 NS103549 and Co-I of adaptive DBS for OCD grant UH3 NS100549.
   a. Provenza NR, Reddy S, Allam A, Rajesh SV, Diab N, Reyes G, Caston RM, Katlowitz KA, Gandhi AD, Bechtold R, Dang HQ, Najera RA, Giridharan N, Kabotyanski K, Momin F, Hasen M, Banks GP, Mickey BJ, Kious BM, Shofty B, Hayden BY, Herron JA, Storch AE, Patel AB, Goodman WK, **Sheth SA**. Disruption of neural periodicity predicts clinical response after deep brain stimulation for obsessive-compulsive disorder. *Nature Medicine.* (2024). PMID: 38997607
   b. Xiao J, Adkinson JA, Myers J, Allawala AB, Mathura RK, Pirtle V, Najera R, Provenza NR, Bartoli E, Watrous AJ, Oswalt D, Gadot R, Anand A, Shofty B, Mathew SJ, Goodman WK, Pouratian N, Pitkow X,

Bijanki KR, Hayden B, **Sheth SA**. Beta activity in human anterior cingulate cortex mediates reward biases. *Nature Communications.* 15(1):5528. (2024). PMID: 39009561

c. Xiao J, Provenza NR, Asfouri J, Myers J, Mathura RK, Metzger B, Adkinson JA, Allawala AB, Pirtle V, Oswalt D, Shofty B, Robinson ME, Mathew SJ, Goodman WK, Pouratian N, Schrater PR, Patel AB, Tolias AS, Bijanki KR, Pitkow X, **Sheth SA**. "Decoding depression severity from intracranial neural activity." *Biological Psychiatry*. 94(6):445-453. (2022). PMID: 36736418

d. Provenza NR, **Sheth SA**, et al. "Long-Term Ecological Assessment of Intracranial Electrophysiology Synchronized to Behavioral Markers in Obsessive-Compulsive Disorder." *Nature Medicine.* 27(2):2154-2164. (2021). PMID: 34887577, PMCID PMC8800455

2. I believe that we are poised to see a dramatic increase in targeted interventions for refractory neuropsychiatric disorders, fueled by advances in physiology and neuroimaging, as described above. My lab has sought to guide future efforts to improve neuromodulatory treatments for a number of such disorders, including depression, OCD, autism-spectrum disorders, and epilepsy.
   a. Malekmohammadi M, Mustakos R, **Sheth SA**, Pouratian N, McIntyre C, Bijanki K, Tsolaki EC, Chiu K, Robinson M, Adkinson J, Oswalt D, Carcieri S. "Automated Optimization of Deep Brain Stimulation Parameters for Modulating Neuroimaging-Based Targets." *Journal of Neural Engineering.* 19(4). (2022). PMID: 35790135
   b. Gadot R, Najera RA, Hirani S, Anand A, Storch EA, Goodman WK, Shofty B, **Sheth SA**. "Efficacy of Deep Brain Stimulation for Treatment-Resistant Obsessive-Compulsive Disorder: Systematic Review and Meta-Analysis." *J Neurol Neurosurg Psych* (2022). PMID: 36127157
   c. **Sheth SA** et al. "Deep brain stimulation for depression informed by intracranial recordings." *Biological Psychiatry*. S0006-3223(21)01747-9. (2021). PMID: 35063186.
   d. Bijanki KR, Pathak YJ, Najera RA, Storch EA, Goodman WK, Blair Simpson H, **Sheth SA**. "Defining Functional Brain Networks Underlying Obsessive-Compulsive Disorder (OCD) Using Treatment-Induced Neuroimaging Changes: A Systematic Review of the Literature." *Journal of Neurology, Neurosurgery & Psychiatry*. 92(7):776-786. (2021). PMID: 33906936

3. My lab uses intracranial electrophysiology recordings from patients undergoing neurosurgical procedures to study human cognitive neurophysiology. My focus is the study of controlled decision-making processes using single-neuron and LFP recordings in human prefrontal cortex (PFC). I am PI on BRAIN U01 NS121472, which uses these recordings to study abstract navigation.
   a. Allawala A, Bijanki KB, Oswalt D, Mathura RK, Adkinson J, Pirtle V, Metzger B, Shofty B, Robinson M, Anand A, Najera RA, Gadot R, Harrison MT, Mathew SJ, Goodman WK, Pouratian N, **Sheth SA**, Borton DA. "Prefrontal Network Engagement by Deep Brain Stimulation in Limbic Hubs." *Frontiers in Human Neuroscience.* 17:1291215. (2024). PMID: 38283094, PMCID: PMC10813208
   b. Myers JC, Smith EH, Leszczynski M, O'Sullivan J, Yates M, McKhann GM II, Mesgarani N, Schroeder C, Schevon C, **Sheth SA**. "The Spatial Reach of Neuronal Coherence and Spike-field Coupling across the Human Neocortex." *Journal of Neuroscience.* 42(32):6285-62954. (2022). PMID: 35790403
   c. Das A, Myers M, Mathura R, Shofty B, Metzger B, Bijanki KR, Wu C, Jacobs J, **Sheth SA**. "Spontaneous Neuronal Oscillations in the Human Insula are Hierarchically Organized Traveling Waves." *eLife* (2022). PMID: 35616527, PMCID: PMC9200407
   d. **Sheth SA**, Mian MK, Patel SR, Asaad WF, Williams ZM, Dougherty DD, Bush G, Eskandar EN. "Human Dorsal Anterior Cingulate Cortex Neurons Mediate Ongoing Behavioral Adaptation." *Nature.* 488(7410):218-221. (2012). PMID: 22722841, PMCID PMC3416924

4. As a clinician-scientist who studies intracranial recordings in humans using opportunities provided by neurosurgical procedures, I am very invested in neuroethical issues that surround this approach. I am an invited member of the NIH NeuroEthics Working Group (NEWG) and the NIH BRAIN Research Opportunities in Humans (ROH) neuroethics working group and Co-PI on an NIH BRAIN neuroethics grant focused on stakeholder concerns related to data sharing (R01 MH126937).
   a. Rahimzadeh V, Maxson Jones K, Anderlik Majumder M, Kahana MJ, Rutishauser U, Zheng J, Paulk AC, Cash SS, Williams ZM, Beauchamp MS, Collinger JL, Pouratian N, McGuire ML, **Sheth SA**. "Benefits of Sharing Neurophysiology Data from the BRAIN Initiative Research Opportunities in Humans Consortium." *Neuron*. 111(23):3710-3715. (2023). PMID: 37944519

b. Visser-Vandewalle V, … **Sheth SA**, Coyne T, Kuhn J, Mallet L, Nuttin B, Hariz M, Okun MS. “Deep brain stimulation for obsessive compulsive disorder: a crisis of access.” *Nature Medicine.* 28(8):1529-1532. (2022). PMID: 35840727
c. Feinsinger A, Pouratian N, Hamasa E, Ralph A, Andersen R, Beauchamp M, Chang EF, Crone NE, Jennifer CL, Fried I, Mamelak A, Richardson M, Rutishauser U, **Sheth SA**, Suthana N, Tandon N, Yoshor D, NIH Research Opportunities in Humans Consortium. “Ethical commitments, principles, and practices guiding intracranial neuroscientific research in humans.” *Neuron*. 110(2):188-194. (2022). PMID: 35051364
d. Davis RA, Giordano J, Hufford DB, **Sheth SA**, Warnke P, Widge AS, Richardson RM, Rosenow JM, Rossi PJ, Storch EA, Winston H, Zboyan J, Dougherty DD, Foote KD, Goodman WK, McLaughlin NCR, Ojemann S, Rasmussen S, Abosch A, Okun MS. “Restriction of Access to Deep Brain Stimulation for Refractory OCD: Failure to Apply the Federal Parity Act.” *Frontiers in Psychiatry*. 12:706181. (2021). PMID: 34456762, PMCID PMC8387630

5. Neuromodulation strategies targeting memory enhancement have obvious implications for patients with memory disorders. In collaboration with several groups, we have used opportunities from intracranial recordings in epilepsy patients to study the neurophysiological basis of memory formation and test hypotheses regarding modulating it with direct intracranial stimulation.
   a. Metzger BA, Kalva P, Mocchi MM, Cui B, Adkinson JA, Wang Z, Mathura RK, Kanja K, Gavvala J, Krishnan V, Lin L, Maheshwari A, Shofty B, Magnotti JF, Willie JT, **Sheth SA**, Bijanki KR. “Intracranial Stimulation and EEG Feature Analysis Reveal Affective Salience Network Specialization.” *Brain*. 146(10):4366-4377. (2023). PMID: 37293814, PMCID: PMC10545499
   b. Michalak AJ, Greenblatt A, Wu S, Tobochnik S, Dave H, Raghupathi R, Esengul YT, Guerra A, Tao JX, Issa NP, Cosgrove GR, Lega B, Warnke P, Chen I, Lucas T, **Sheth SA**, Banks GP, Kwon C-S, Feldstein N, Youngerman B, McKhann G, Davis KA, Schevon CA. “Seizure Onset Patterns Predict Outcome After Stereo-Electroencephalography-Guided Laser Amygdalohippocampotomy.” *Epilepsia*. 64(6):1568-1581. (2023). PMID: 37013668, PMCID: PMC10247471
   c. Kragel JE, Ezzyat Y, …, **Sheth SA**, Zaghloul KA, Stein JM, Kahana MJ. “Distinct Cortical Systems Reinstate the Content and Context of Episodic Memories.” *Nature Communications*. 12(1):4444. (2021). PMID: 34290240
   d. Goyal A, Miller J, …, **Sheth SA**, McKhann GM, Smith EH, Schevon C, Jacobs J. “Functionally Distinct High and Low Theta Oscillations in the Human Hippocampus.” *Nature Communications.* 11(1):2469. (2020). PMID: 32424312

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1fwkSjp9AZzki/bibliography/51765740/public/?sort=date&direction=descending

OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 01/31/2026)

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: J. Liberty S. Hamilton

eRA COMMONS USER NAME (credential, e.g., agency login): LHAMILTON11

POSITION TITLE: Associate Professor

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
Scripps College, Claremont, CA	B.A.	05/2006	Neuroscience
University of California, Berkeley	Ph.D.	12/2013	Neuroscience
University of California, San Francisco	Postdoc	07/2017	Neuroscience / Neurosurgery

A. Personal Statement

The goal of my research is to understand the representation of speech in the human brain across the lifespan, with an emphasis on how acoustic information is transformed into meaningful linguistic content using naturalistic speech stimuli. My work involves a combination of scalp EEG and intracranial EEG and computational modeling to understand speech processing in the brain. My research has uncovered how spectrotemporal and phonetic features are processed during natural speech perception and production (Kurteff et al. *J Neuro.* 2024; Hamilton et al. *Cell*, 2021; Desai et al. *J Neuro,* 2021; Hamilton et al. *Current Biology*, 2018; Tang, Hamilton, and Chang *Science* 2017; Cheung & Hamilton et al., *eLife* 2016). One major discovery used a combination of supervised and unsupervised methods to uncover structure in responses to natural speech. We found that the auditory cortex and broader auditory-responsive networks can be subdivided into two regions with distinct temporal response profiles that work in parallel to process fast and slow changes in the speech signal (Hamilton et al. 2018). In another study, we showed that phonetic feature representations are processed independently from intonational pitch, which is a prosodic cue used to determine meaning (Tang et al. 2017). My work also showed that speech information is processed by a parallel pathway in the posterior superior temporal gyrus that may bypass the primary auditory cortex (Hamilton et al. 2021). This parallel pathway overlaps with the anterior-posterior distinction seen in our prior work for speech onsets (Hamilton et al. 2018). In tandem with investigating brain representations of acoustic and linguistic features, we also work on methods for decoding acoustic or linguistic features from brain activity, as could be used in a speech brain computer interface (Sakthi et al. 2021, Hamilton et al. 2018).

In my lab at UT Austin in the Department of Speech, Language, and Hearing Sciences and Department of Neurology, we investigate speech processing in children who are undergoing surgery for epilepsy. I have established an intracranial electrophysiology (ECoG) research group in collaboration with Dell Children's Medical Center in Austin, TX, and Texas Children's Hospital/Baylor College of Medicine in Houston, TX. In this work, funded by NIH (1R01DC018579, PI: Hamilton) and the Department of Defense (TS230003, PI: Hamilton), we examine speech representations in the human cortex, employing computational models to investigate dynamic interactions between simultaneously recorded brain areas and investigating how auditory response properties change during development. In addition, I also have had several foundation-funded projects (through the Texas Speech Language Hearing Foundation and a research contract through Meta/Facebook) to understand continuous natural speech processing using scalp EEG. Some of this work validates the use of naturalistic stimuli for uncovering phoneme tuning using EEG (Desai et al. *J Neuro*, 2021, Desai et al. *Frontiers in Human Neuroscience* 2022, and Kurteff et al. *J Cog. Neuro* 2023). Recently, one of my

students was awarded a small grant to understand auditory attention using EEG and gaming from the Texas Speech Language Hearing Foundation.

I am committed to mentoring trainees including postdoctoral fellows, graduate students, undergraduates, and postbaccalaureate students interested in scientific careers. I began my independent position in 2017, and since then have been the primary research mentor for 3 postdoctoral fellows, 4 PhD students, one MD student, 5 doctorate of audiology (AuD) students, and 3 master's students. I am currently the direct mentor for 2 PhD students, one AuD student, and three postbaccalaureate researchers. I work with each student to develop an individual development plan (IDP) that caters to their individual goals and includes training in grant-writing, scientific communication (written and oral). Each student is required to submit a fellowship or grant application with feedback from me and with support from others at UT Austin, which has resulted in 1 AuD student being awarded a Diversity Supplement on my NIH R01, 1 PhD student being awarded a $40,000 dissertation fellowship, and 4 students (3 PhD, 1 AuD) collectively being awarded over $6,500 in funding from the Texas Speech Language Hearing Foundation. My trainees receive direct supervision and training in weekly meetings with me in addition to project meetings with other members of the laboratory. This training includes statistical analysis methods, experimental design and data collection for human neurophysiology (both invasive and noninvasive EEG), working with patients and ethical considerations therein, and more. I also incorporate training in code and data sharing for enhancing the reproducibility of our scientific endeavors. My trainees have applied for and attended external courses including the Genetics & Neurobiology of Language course at Cold Spring Harbor Laboratories and Neurohackademy.

As part of Dr. Franch's mentoring team, I am excited to provide my expertise in speech and language representations and analysis of intracranial recordings, which is of importance to the work proposed here. While much of my earlier work has related to low level acoustic and phonetic properties of the speech signal, we have recently started to branch out into semantic models and using large language models for understanding low to high-level features in human neural activity. I am already collaborating with Dr. Ben Hayden on new work related to the current project, and have active grants with Dr. Howard Weiner (Neurosurgeon at Texas Children's Hospital/Baylor College of Medicine) and Dr. Anne Anderson (epileptologist at Texas Children's Hospital/Baylor College of Medicine). I am happy to provide direct training in concepts such as automated transcriptions and analysis of conversation data (including use of forced aligners, Praat, and other methods). I will also provide support for analysis of neural recordings – given my prior work in human intracranial recordings as well as multi-unit/single-unit recordings in mice and rats during my PhD, I have appropriate expertise in this area.

Ongoing and recent projects I would like to highlight include:

R01 DC018579 Hamilton (PI) 12/01/20–11/30/25
Electrophysiological Approaches to Understanding Functional Organization of Speech in the Brain
Total costs: $2,756,787.00

TS230003 Hamilton (PI) 07/01/24–06/31/27
Brain Representations of Speech in Children with Tuberous Sclerosis Complex
Total Costs: $630,735.59 to UT Austin (second award to partnering PI Dr. Howard Weiner, BCM)

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2024	Ad hoc reviewer, UK Research and Innovation grants
2023-	Associate Professor with Tenure, Department of Speech, Language, and Hearing Sciences and Department of Neurology, The University of Texas at Austin
2023	Ad hoc reviewer, Swiss National Science Foundation
2021-	Ad-hoc member, LCOM study section (NIH NIDCD) and NIH Fellowships Panel
2021-	Adjunct Assistant Professor, Department of Neurosurgery, Baylor College of Medicine
2021	CIVIS Postdoctoral Fellowships reviewer (European Union Mechanism)
2021	Ad-hoc reviewer, Wellcome Trust
2020-	Review Panel, National Science Foundation (Fellowships and Large Grants)
2019-	Member, Texas Speech-Language-Hearing

2017-2023	Assistant Professor, Department of Speech, Language, and Hearing Sciences and Department of Neurology, The University of Texas at Austin
2017-2020	Program Committee Member, Advances and Perspectives on Auditory Neuroscience
2016	Technical Committee Member, *Workshop on Speech Engineering and the Computational Neuroscience of Speech (SECNS),* a satellite conference of INTERSPEECH 2016. San Francisco,
2014-2017	Postdoctoral fellow, Department of Neurological Surgery/Center for Integrative Neuroscience, University of California, San Francisco
2010-2011	Graduate Student Instructor, Department of Molecular and Cellular Biology, University of California, Berkeley
2010	Member, Association for Research in Otolaryngology
2009	Member, Society for Neuroscience
2006-2008	Staff Research Associate, Department of Neurology, University of California, Los Angeles

Academic and Professional Honors

2024	APAN Junior Faculty Award (Advances and Perspectives in Auditory Neuroscience)
2024	Shine Award for Excellence in Research Mentorship – Dell Medical School, The University of Texas at Austin
2024	Nominee, Regents' Outstanding Teaching Award (ROTA) – The University of Texas System (finalist, not awarded)
2022	Ellen A. Wartella Distinguished Research Award, Moody College of Communication, The University of Texas at Austin
2022	Kavli Fellow. Selected by the National Academy of Sciences as a Kavli Fellow for the 5th Israeli-American Kavli Frontiers of Science Symposium - October 2022.
2021	Nominee, 2022 TAMEST O'Donnell Awards. Selected by UT Austin Dell Medical School as a nominee for the TAMEST O'Donnell Aware in Medicine, Engineering, and Science (not awarded).
2019	Clock Award, Services for Students with Disabilities. In recognition of positive contributions, support, and guidance to students with disabilities at The University of Texas at Austin.
2018	Dean's Faculty Fellow, University of Texas at Austin, Appointed a Dean's Faculty Fellow for Spring 2020 by the Dean of the Moody College of Communication, The University of Texas at Austin.
2018	Searle Scholars Nominee. Nominated to represent the University of Texas at Austin in the Searle Scholars Program for 2019 (not awarded).
2017	Winner, NVIDIA GPU Grant. Winner of Titan XP GPU through NVIDIA's GPU Grant Program, Academic Programs Team (co-PI)
2014-2017	Postdoctoral F32 - Ruth L. Kirschstein National Research Service Award (1F32DC014192)
2009-2013	National Science Foundation Graduate Research Fellowship (GRFP) recipient

C. Contributions to Science

1. *Uncovering the functional organization of the human speech cortex*

Human speech perception involves mapping a highly variable acoustic signal onto a more variation-tolerant linguistic representation (phonemes, syllables, or words). Uncovering the spatial organization and feature maps for speech in the auditory cortex has important implications for sensory coding, since it is thought that map representations may underlie efficient coding and permit effective sensory discrimination (Kaas *Brain Research Bulletin* 1997). As both a lead author (Hamilton et al. 2021, Hamilton* & Edwards* et al. 2018, and Cheung* & Hamilton* et al. 2016), co-author (Tang et al. 2017, Hullett et al. 2016), and senior author (Kurteff et al. 2024), I have shown that the human auditory cortex shows an anterior/posterior organization for sentence and phrase onsets (Hamilton* & Edwards* et al. 2018) that is unique to the lateral temporal cortex (Hamilton et al. 2021) and is suppressed during speaking (Kurteff et al. 2024). We also showed that pitch intonation – how we emphasize words to change the meaning of a sentence – is represented by entirely different populations of neurons than phonetic information, which explains how we are able to identify what was said, who said it, and how it was said when communicating in the real world (Tang et al. 2017). Finally, we most recently showed that the primary auditory cortex may not be required for speech perception, and that speech is routed through a posterior temporal pathway that is activated in parallel to primary auditory cortex (Hamilton et al. 2021).

Relevant publications:

a. Kurteff GL, Field AM, Asghar S, Tyler-Kabara EC, Clarke D, Weiner HL, Anderson AE, Watrous AJ, Buchanan RJ, Modur PN, **Hamilton LS**. Spatiotemporal mapping of auditory onsets during speech production. Journal of Neuroscience. 2024 Oct 22.
b. **Hamilton LS**, Oganian Y, Hall J, Chang EF (2021). Parallel and distributed encoding of speech across human auditory cortex. ***Cell.*** 184(8):4626-4639.e13. PMC8456481.
c. **Hamilton LS***, Edwards E*, Chang EF (2018). A spatial map of onset and sustained responses to speech in the human superior temporal gyrus. ***Current Biology***. 28(12): 1860-1871.e4. *Co-first authors. PMID 29861132.
d. Tang C, **Hamilton LS**, Chang EF (2017). Intonational speech prosody encoding in human auditory cortex. ***Science***. 357(6353): 797-801. PMID 28839071 (PMC ID request in process).

2. *Understanding the neural processing of natural sounds*

A large portion of my work involves using natural speech or other sounds to probe auditory cortical function. While much previous research has focused on using tightly controlled, simple stimuli such as single syllables, new statistical methods and better computational resources have allowed for the expansion of research questions into using natural stimuli that are more ethologically relevant and may provide more generalizable results. The work here includes a review of the advantages of using natural stimuli over more simplistic stimuli – they engage a wider area of the cortex, they provide more repeatable responses, and tasks using natural stimuli are more interesting for participants and thus can be used in longer tasks (Hamilton & Huth 2018). Many of the papers in contribution (1) also used natural sentence or narrative stimuli in addition to more controlled stimuli to answer specific questions. In Desai et al. (2021), we directly compared encoding of controlled speech stimuli from the TIMIT corpus to annotated audiovisual movie clips, and shows that responses to one stimulus generalize to the other. We have also determined dataset size considerations for using different types of natural stimuli, showing that the minimum amount of training data depends on the type of stimulus used as well as the type of model fitted (Desai et al. 2022). We take naturalistic tasks to another extreme in Ashmaig et al. (2021), which describes using a Sony Playstation to investigate multiple cognitive processes in epilepsy patients undergoing surgical monitoring.

a. Desai M, Field AM, **Hamilton, LS** (2022). Dataset size considerations for robust acoustic and phonetic speech encoding models in EEG. ***Frontiers in Human Neuroscience***, *16*.
b. Desai M, Holder J, Villarreal C, Clark N, **Hamilton LS** (2021). Generalizable EEG encoding models with naturalistic audiovisual stimuli. ***Journal of Neuroscience.*** 9 September 2021. PMC8549533.
c. Ashmaig OE, **Hamilton LS**, Modur P, Buchanan RJ, Preston AR, Watrous AJ (2021). A platform for cognitive monitoring of neurosurgical patients during hospitalization. ***Frontiers in Human Neuroscience*** 15: 726998. November 2021. PMC8645698.
d. **Hamilton LS**, Huth AG (2018). The revolution will not be controlled: natural stimuli in speech neuroscience. ***Language, Cognition, and Neuroscience.*** 2018 Jul 22;35(5):573-582. eCollection 2020. Free PMC article.

3. *Methods development for electrocorticography research*

I have spearheaded the development of a free, open source software package for electrode localization and labeling for use by other researchers in epilepsy and those who work with electrocorticography data (Hamilton et al. 2017). While many laboratories use in house software to localize ECoG electrodes, there is not a widely available, well-documented way of doing this across laboratories. This software was developed in conjunction with software to perform automated detection of interictal discharges in focal epilepsy, such that interictal discharges may be detected and displayed on the brain's surface (Baud et. al 2018 and Kleen et al. 2021). We hope that development of these methods will aid in future epilepsy research as well as eventual clinical adoption, to decrease the burden of cumbersome manual detection of epileptiform activity from intracranial recordings. In addition, I am working with a large consortium of ECoG researchers to improve methods for data sharing across laboratories, including expanding the use of the Brain Imaging Data Structure (BIDS) to intracranial electrophysiology data.

Relevant publications:

a. Kleen J, Speidel BA, Baud MO, Rao VR, Ammanuel SG, **Hamilton LS**, Chang EF, Knowlton RC (2021). Accuracy of omni-planar and surface casting of epileptiform activity for intracranial seizure localization. ***Epilepsia*** 2021;00:1-13. (Featured on the cover of April 2021 issue of ***Epilepsia***). Free PMC article.

b. Holdgraf C, Appelhof S, Bickel S, Bouchard K, D'Ambrosio S, David O, Devinsky O, Dichter B, Flinker A, Foster BL, Gorgolewski KJ, Groen I, Groppe D, Gunduz A, **Hamilton L**, Honey CJ, Jas M, Knight R, Lachaux J-P, Lau JC, Lundstrom BN, Lee-Messer C, Miller KJ, Ojemann JG, Oostenveld R, Petridou N, Piantoni G, Pigorini A, Pouratian N, Ramsey NF, Stolk A, Swann NC, Tadel F, Voytek B, Wandell BA, Winawer J, Zehl L, Hermes D (2019). IEEG-BIDS, extending the Brain Imaging Data Structure specification to human intracranial electrophysiology. ***Scientific Data*** 6: 102. Free PMC article.
c. Baud MO, Kleen JK, Anumanchipalli GK, **Hamilton LS**, Tan Y-L, Knowlton R, Chang EF (2018). Unsupervised learning of spatiotemporal interictal discharges in focal epilepsy. ***Neurosurgery***. 2018 Oct 1;83(4):683-691. PMC6454796.
d. **Hamilton LS**, Chang DL, Lee MB, Chang EF. Semi-automated anatomical labeling and inter-subject warping of high-density intracranial recording electrodes in electrocorticography (2017). ***Frontiers in Neuroinformatics***. 2017; 11:62. PMC5671481.

4. *Uncovering the role of inhibition in auditory cortical representations*
Studies on the role of inhibition in sensory representations have shown that balanced excitatory and inhibitory activity is critical to the normal functioning of neural circuits. In my PhD research in the laboratory of Dr. Shaowen Bao, I combined optogenetic manipulations with *in vivo* recordings in the mouse auditory cortex to investigate how stimulating inhibitory parvalbumin-positive (PV+) neurons influences functional connectivity in the auditory cortex during sound perception. Using simultaneous multi-electrode recordings in the auditory cortex, I fit computational models to elucidate interactions between sites recorded from different layers and columns of the auditory cortex as well as modulation of these sites by sound stimuli. Increasing inhibitory PV+ activity enhanced the signal-to-noise ratio of cortical responses to sound, and also preferentially increased vertical columnar functional connectivity, but not lateral connectivity within cortical layers. This work has implications for how disruptions in inhibitory circuitry lead to sensory deficits in multiple neurological disorders.
Relevant publications:
a. **Hamilton LS**, Sohl-Dickstein J, Huth AG, Carels VM, Deisseroth K, Bao S (2013). Optogenetic activation of an inhibitory network enhances feedforward functional connectivity in auditory cortex. ***Neuron*** 80:4 1066-1076. PMC3841078.

5. *Multimodal structural and functional neuroimaging of schizophrenia, ADHD, and bipolar disorder*
Prior to graduate school, I investigated structural and functional changes resulting from neurological disorders including attention-deficit hyperactive disorder (ADHD), bipolar disorder, and schizophrenia. This involved using structural MRI, functional MRI, and diffusion tensor imaging (DTI) to compare brain data in patients to healthy controls. This work with patient populations in a Neurology and neuroimaging research group has informed my current work with both pediatric and adult patient populations. Our results have also led to better knowledge of endogenous biomarkers for disease. During my time as a Research Assistant at UCLA and in the early years of my graduate career at UC Berkeley, I was lead author on many of these publications, performing data collection, analysis, and manuscript preparation.
a. **Hamilton LS**, Altshuler LL, Townsend J, Bookheimer SY, Phillips OR, Fischer J, Woods RP, Mazziotta JC, Toga AW, Nuechterlein KH, Narr KL (2009). Alterations in Functional Activation in Euthymic Bipolar Disorder and Schizophrenia During a Working Memory Task. ***Human Brain Mapping*** 2009 Dec;30(12):3958-69.
b. Luders E, Narr KL, **Hamilton LS**, Phillips OR, Thompson PM, Valle JS, Del-Homme M, Strickland T, McCracken JT, Toga AW, Levitt JG (2009). Decreased Callosal Thickness in Attention-Deficit/Hyperactivity Disorder. ***Biological Psychiatry***. 2009 Jan 1; 65(1): 84-88. PMC2773144
c. **Hamilton LS**, Levitt JG, O'Neill J, Alger JR, Luders E, Phillips OR, Caplan R, Toga AW, McCracken J, Narr KL (2008). Reduced white matter integrity in attention-deficit hyperactive disorder. ***Neuroreport***. 2008 Nov 19; 19(17):1705-8. PMC2819371
d. **Hamilton LS**, Narr KL, Luders E, Szeszko PR, Thompson PM, Bilder RM, Toga AW (2007). Asymmetries of cortical thickness: effects of handedness, sex, and schizophrenia. ***Neuroreport*** 18(14): 1427-1431. PMC3197832.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/jessica%20liberty.hamilton.1/bibliography/public/

OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 01/31/2026)

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: Sabharwal, Ashutosh

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

POSITION TITLE: Fellow

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)	START DATE MM/YYYY	COMPLETION DATE MM/YYYY	FIELD OF STUDY
Indian Institute of Tech., Delhi	BS		06/1993	Electrical Engineering
The Ohio State University, Columbus, OH	MS		03/1995	Electrical Engineering
The Ohio State University, Columbus, OH	PHD		09/1999	Electrical Engineering
Rice University, Houston, Texas	OTH		06/2001	Electrical Engineering

A. Personal Statement

I work in two broad research areas: (a) digital health and (b) mobile wireless systems.

(a) I am the founding director of the Rice Digital Health Initiative, which has 16 faculty members with research focus spanning bioelectronics, device development, imaging, robotics, and machine learning. My research focus broadly falls into three areas in digital health: (i) **health data science**, where we develop and deploy new data science methods for projects spanning diabetes, mental health, pulmonology, and surgery, (ii) **health speech AI**, where we have and continue to develop novel AI-based methods to process speech data to understand context for projects in mental health and neuro-cognitive disorders, and (iii) **novel wearables**, where the aim is to develop wearable devices to measure novel bio-behavioral markers identified from the first two focus areas. In all three areas, we regularly combine modern artificial intelligence methods with traditional methods from signal processing, statistical learning and computer engineering. Overall, my lab is currently on 10+ projects spanning mental health, children's health, cognitive attention, neuro-cognitive disorders, chronic pulmonary conditions, and cardiovascular health. In our research in mental health, we have developed methods for quantifying transdiagnostic dimensions of sociability and impulsivity. In our research on diabetes, we have identified (i) interpretable bio-behavioral markers that show how dietary behaviors impact HbA1c, (ii) personalized recommendations on diet-exercise combinations that lead to improved glycemic control and (iii) identifying dietary rhythms that can be used for novel intervention strategies to alter habitual patterns. In addition to research contributions, our research has led to translational outcomes in the form of a medical device spinoff – Cognita Labs (2013), which has developed to FDA-approved digital health devices, and two patents have been licensed by Stryker.

Critically, my expertise in health speech AI will contribute to Melissa's growth as a language neuroscientist and will help her execute the proposed work. My lab has developed methods to objectively measure human sociability using wearable audio sensors. These devices capture patient's speech in real-world settings, similar to the methods Melissa is proposing to capture patient and others' speech in the hospital's Epilepsy Monitoring Unit. Together, Melissa and I will employ similar methods for isolating and transcribing speech so she can discover the neural alignment of word semantics and speaker identity as discussed in her proposal. Finally, having successfully mentored six postdoctoral fellows in my lab who transitioned into faculty roles, I look forward to offering the same dedicated guidance to Melissa

(b) I also lead the Rice Wireless group with 8 faculty members. My research is on theory, practical protocols, and their experimental evaluation for next-generation mobile communications and systems (since 1995). In 2009 I received the Hershel M. Rich Invention Award for WARP (Wireless open-Access Research Platform). The WARP project is now in use at over 125 research organizations worldwide and has been used in more than 250 publications. I co-invented full-duplex wireless in 2010, which has been adopted in global communication standards. I currently lead Rice RENEW, an NSF-funded national wireless testbed project, which has developed the world's first open-source massive MIMO wireless testbed. RENEW is now publicly deployed and is being used by the global community of researchers.

Ongoing and recently completed projects that I would like to highlight include:

NIH 1UH3NS136631-01**,** Goodman (PI), 09/01/2024 – 08/31/2029, Role: Co-I, Building mood state classifiers to inform DBS of Treatment-Resistant Bipolar Depression (TRBD)

NIH 1R01DA059925-01, Sano (PI), 06/01/2023-05/31/2027 Role: Co-I, SCH: Multidimensional Data Science Approach: Measuring and Characterizing Craving and Affective Profiles in Substance Use Disorders

NSF CNS-2215082 Sabharwal (PI) 10/01/2022-09/30/2025 Collaborative Research: CNS Core: Large: 4D100: Foundations and Methods for City-scale 4D RF Imaging at 100+ GHz

NSF CNS-2148313 Javidi (PI), Role: Co-PI 05/01/2022-04/30/2025 RINGS: LARA: Layering for Active Resiliency and Awareness in Next-generation Wireless Networks

NSF CNS-2106993 Sabharwal (PI) 10/01/2021-09/30/2025 Collaborative Research: CNS Core: Medium: Information Freshness in Scalable and Energy Constrained Machine to Machine Wireless Networks

NSF CNS-2120363 Sabharwal (PI) 10/01/2021-9/30/2025 Collaborative Research: CCRI: New: RFDataFactory: Principled Dataset Generation, Sharing and Maintenance Tools for the Wireless Community

NSF CNS-2016727 Lin (PI), Role: Co-PI 10/01/2020-09/30/2025 CCRI: Medium: Collaborative Research: 3DML: A Platform for Data, Design and Deployed Validation of Machine Learning for Wireless Networks and Mobile Applications

NSF CNS-1827940 Melodia (PI), Role: RENEW Lead PI 04/01/2018-03/31/2025 PAWR Platform POWDER-RENEW: A Platform for Open Wireless Data-driven Experimental Research with Massive MIMO Capabilities

NSF EEC-1648451 Cote (PI), Role: Co-PI 10/01/2017-09/30/2027 Engineering Research Center for Precise Advanced Technologies and Health Systems for Underserved Populations (PATHS-UP)

Rice University 23-1179 Arroyave (PI), Role: Co-I 06/15/2023-06/14/2025 Development and Validation of a Quantitative Behavioral Rating Scale for Parkinson's Patient Evaluation

1. Chen W, Sabharwal A, Taylor E, Patel AB, Moukaddam N. Privacy-Preserving Social Ambiance Measure From Free-Living Speech Associates With Chronic Depressive and Psychotic Disorders. Front Psychiatry. 2021;12:670020. PubMed Central PMCID: PMC8385275.
2. Lamichhane,Bishal,, Moukaddam,Nidal,, Patel,Ankit,, Sabharwal,Ashutosh,. ECoNet: Estimating Everyday Conversation Network From Free-living Audio for Mental Health Applications. IEEE Pervasive Computing, Special Issue - Mental State, Mood, and Emotion [Preprint]. 2021 July.

B. Positions and Honors

Positions and Scientific Appointments

2025-	Co-Director, Methodist-Rice Digital Health Institute
2020 –	Fellow, National Academy of Inventors, Tampa, FL
2019 -	Ernest Dell Butcher Professor of Engineering, Dept. of Electrical and Computer Engineering, Rice University, TX
2019 - 2024	Department Chair

2015 - 2015	Visiting Professor, University of California, Los Angeles, CA
2014 -	Fellow, Institute of Electrical and Electronics Engineers
2012 -	Professor, Rice University, Houston, TX
2012 -	Director, Scalable Health Initiative, Rice University, Houston, TX
2012 -	Chair, ECE Corporate Affiliates, Rice University, Houston, TX
2011 - 2011	Visiting Professor, Intel-NTU Connected Context Computing Center, National Taiwan University
2010 - 2012	Associate Professor, Rice University, Houston, TX
2010 - 2010	Visiting Professor, Institute of Communication Engineering, National Taiwan University
2009 - 2009	Visiting Professor, Department of Computer Science and Communication Engineering, National Chia-Tung University
2007 - 2010	Assistant Professor, Rice University, Houston, TX
2007 - 2008	Visiting Professor, School of Computer and Communications Sciences, EPFL
2006 -	Senior Member, IEEE
2006 - 2011	Director, Center for Multimedia Communication, Rice University, Houston, TX
2001 - 2007	Faculty Fellow (Research Faculty), Rice University, Houston, TX
1991 - 2001	Post-Doctoral, Research Associate, Rice University, Houston, TX

Honors

2023	Alumni Award for Academic Excellence, College of Education, The Ohio State University
2023	Distinguished Alumni Award, Indian Institute of Technology, New Delhi
2023	Best Paper Award for “Unsupervised Wireless Diarization: A Potential New Attack on Encrypted Wireless Networks, ICC
2022	Fellow, Association for Computing Machinery (ACM)
2021	ACM, Sigmobile Test-of-time Award
2020	Fellow, National Academy of Inventors (NAI)
2020	Best Paper Award (Honorable Mention), ICCP 2020 for High-resolution Sub-surface Tomography
2019	ACM, Sigmobile Test-of-time Award
2019	ACM Community Contribution Award, HealthSense
2018	Society Award for Advances in Communication, IEEE Communications
2017	Jack Neubauer Memorial Award, IEEE
2017	CameraVitals: Non-contact Clinical-grade Vital Signs Using Cameras, Hershel M. Rich Invention Award,
2015	Finalist, Vodafone Wireless Innovation Project, Global Competition
2014	Fellow, Institute of Electrical and Electronics Engineers (IEEE)
2011	Best Demo, where we demonstrated first patient-operated spirometer, which automatically detects maneuver errors, and provides context-based audio-visual coaching to the patients, mHealthSys Workshop
2009	WARPnet: A High-Performance Platform for Research on Deployed Wireless Networks, Hershel M. Rich Invention Award

C. Contribution to Science

1. Quantifying Trans-diagnostic Behavioral Dimensions: One of the foundational challenges in systematically studying behavior-biology pathways is the lack of a dimensional approach to quantifying human behavior. In our recent work, we have made significant progress to quantifying sociability. Sociability impairment, such as decreased social network size and socialization, is implicated in mental health disorders. To complement the existing self-reports-based assessment of sociability measures, which could be error-prone and burdensome, we propose to estimate an individual’s everyday conversational network from free-living speech recordings obtained with a wearable. Our first contribution is ECoNet, an automatic method to estimate the everyday conversational network using a modular audio processing architecture. Our second contribution is using ECoNet to analyze multiday egocentric audio recordings from 32 individuals

representing diverse mental health conditions (healthy controls, depressive disorders, and psychotic disorders). Specifically, we discover that the conversational network size as a sociability measure has a significant correlation with mental health scores. Audio-based estimation of conversational network size using ECoNet, therefore, could provide a pervasive computing solution to complement existing mental health assessment methods.

a. Lamichhane B, Patel A, Sabharwal A, Moukaddam N. Dyadic Interaction Assessment from Free-living Audio for Depression Severity Assessment. Interspeech 2022. 2022 September 18; :2493-2497.
b. Chen W, Sabharwal A, Taylor E, Patel AB, Moukaddam N. Privacy-Preserving Social Ambiance Measure From Free-Living Speech Associates With Chronic Depressive and Psychotic Disorders. Front Psychiatry. 2021;12:670020. PubMed Central PMCID: PMC8385275.
c. Lamichhane,Bishal, Moukaddam,Nidal,, Patel,Ankit,, Sabharwal,Ashutosh,. ECoNet: Estimating Everyday Conversation Network From Free-living Audio for Mental Health Applications. IEEE Pervasive Computing, Special Issue - Mental State, Mood, and Emotion [Preprint]. 2021 July .

2. Smartphone and Online-Usage-Based Evaluation for Depression (SOLVD): Depression is one of the most common mental disorders that carries significant emotional and financial burden for modern society. However, depression is often monitoring through clinician psychometric instruments, and there is still a lack of an effective method to automatic and continuously track the patient's mental health status. We developed and validated the Smartphone- and OnLine-usage-based eValuation for Depression (SOLVD), which is a new tool for continuous and real-time monitoring of the patient's depression state. We develop the SOLVD mobile app and the backend cloud platform, for data collection, storage, analysis and sharing. In the study, we collect three types of data from clinically depressed patients: (i) smartphone sensor and usage data, including accelerometer, location, steps, screen status, call log, text messages, and apps, (ii) self-reported mood and activity level on daily basis, and (iii) psychometric data from biweekly in-clinic exams, including PHQ-9 (Patient Health Questionnaire), HamiltonD (Hamilton Rating Scale for Depression) and HamitonA (Hamilton Anxiety Rating Scale). Our pilot study shows a correlation between smartphone sensor data and psychometric scores. The passive phone sensor and usage, including their number of steps, number of text messages and the amount of time spent messaging, correlate with clinical assessments.

a. Moukaddam N, Truong A, Cao J, Shah A, Sabharwal A. Findings From a Trial of the Smartphone and OnLine Usage-based eValuation for Depression (SOLVD) Application: What Do Apps Really Tell Us About Patients with Depression? Concordance Between App-Generated Data and Standard Psychiatric Questionnaires for Depression and Anxiety. J Psychiatr Pract. 2019 Sep;25(5):365-373. PubMed PMID: 31505521.

3. Non-contact Tissue Imaging: In many important scenarios, it is desirable to have a method to estimate vital signs (heart rate, heart rate variability, blood pressure, breathing rate and SpO2) without a contact probe. Towards that end, we have developed a method, labeled distancePPG, to estimate heart rate, heart rate variability and breathing rate from normal (selfie-) videos that achieves clinical grade accuracy. DistancePPG improves significantly over all prior methods, and increases overall signal-to-noise ratio by 4-6 dB. That level of improvement allows the system to operate in very low light conditions (as low as 100 lux), for all skin tones and can even tolerate natural motion. Currently, we are working on novel methods to estimate blood pressure from selfie-videos, and in the process estimate blood perfusion maps.

a. Kumar M, Veeraraghavan A, Sabharwal A. DistancePPG: Robust non-contact vital signs monitoring using a camera. Biomed Opt Express. 2015 May 1;6(5):1565-88. PubMed Central PMCID: PMC4467696.

4. Quantification of Inhaled-Drug Use Errors: For Asthma and COPD patients, one of the the most effective method of medication delivery is metered dose inhalers. However, metered dose inhalers are hard to use due to large number of vaguely defined steps. In fact, it is well documented that more than 70% of the patients use their inhalers incorrectly in at least one of the steps, despite regular training. Our contributions till date have been four-fold. First, we have developed a method to collect detailed parameters during inhaler maneuver during normal use of the inhalers. A preliminary data-set from 30 adult patients is the first to quantify the exact form and amount of error. All prior work research has relied on human observers for

error evaluation and many steps are only qualitatively evaluated. Second, we developed a novel testbed to quantify the impact of specific errors in the loss of overall drug deposition. This is the first study that has performed such quantification as a function of most common error, and is possible only because of our first contribution. Third, our results strongly point to the fact that the current recommendations for inhaler use may need to be revisited. If true, this could have significant ramifications on inhaler use for all patients using metered dose inhalers. Lastly, our results have inspired a new product being developed by Rice spinoff Cognita Labs, that will aid inhaler users to improve their technique.

a. Biswas R, Hanania NA, Sabharwal A. Factors Determining In Vitro Lung Deposition of Albuterol Aerosol Delivered by Ventolin Metered-Dose Inhaler. J Aerosol Med Pulm Drug Deliv. 2017 Aug;30(4):256-266. PubMed Central PMCID: PMC5564031.
b. Biswas R, Chang P, Dharmasiri H, Patel G, Sabharwal A. AsthmaGuru: a framework to improve adherence to asthma medication. WH '13: Proceedings of the 4th Conference on Wireless Health; 2013; Baltimore, MD, United States.

5. Retinal Imaging: We developed a portable, robust, smartphone-based ophthalmoscope, mobileVision, intended to reduce the barriers to ocular pathology screening in developing and underserved regions. In contrast to currently available retinal imaging solutions, mobileVision provides the portability of a handheld ophthalmoscope without sacrificing retinal field-of-view or resolution. Through tight integration with a smartphone and ergonomic design, we developed automatic compensation for patient refractive error, voice-activated multi-shot retinal image acquisition without pupil dilation (non-mydriatic), and touch-gesture based control of patient fixation and accommodation. We further demonstrated a computational lucky imaging and retinal stitching pipeline which not only increases overall retinal field-of-view, but also makes the system robust to patient saccades, blinks, device jitter, and imaging artifacts such as noise or unintended scattering from ocular surfaces.

a. Samaniego A, Sabharwal A, Veeraraghavan A. MobileVision: A Face- mounted, Voice-activated, Non-mydriatic “Lucky” Ophthalmoscope. Frontiers in Optics. 2014. DOI: 10.1364/FIO.2014FW3F.1
b. Samaniego A, Porter J, Sabharwal A, Twa M, Veeraraghavan A. mobileVision: Towards a patient-operable, at-home, non-mydriatic retinal imaging system. Journal of Vision. 2013; 13(15). DOI: 10.1167/13.15.63

PHS Fellowship Supplemental Form

OMB Number: 0925-0001
Expiration Date: 01/31/2026

Introduction

1. Introduction to Application (for Resubmission applications)	Introduction_final.pdf

Fellowship Applicant Section

2. Applicant's Background and Goals for Fellowship Training*	F32_trainingPlan_MF_resubmit1.pdf

Research Training Plan Section

3. Specific Aims*	F32_specificAims_final_resubmit.pdf
4. Research Strategy*	F32_researchPlanBest_resubmit1.pdf
5. Respective Contributions*	Respective_Contributions.pdf
6. Selection of Sponsor and Institution*	Selection_of_Sponsor_and_Institution.pdf
7. Progress Report Publication List (for Renewal applications)	
8. Training in the Responsible Conduct of Research*	RCR_F32.pdf

Sponsor(s), Collaborator(s) and Consultant(s) Section

9. Sponsor and Co-Sponsor Statements	Sponsor_Statement_F32_resubmit1.pdf
10. Letters of Support from Collaborators, Contributors and Consultants	CombinedSupportLetters.pdf

Institutional Environment and Commitment to Training Section

11. Description of Institutional Environment and Commitment to Training	Franch_DESC_INST_ENVIRO__AND_COMM_TO_TRAINING_2.pdf
12. Description of Candidate's Contribution to Program Goals	

Other Research Training Plan Section

Vertebrate Animals

The following item is taken from the Research & Related Other Project Information form and repeated here for your reference. Any change to this item must be made on the Research & Related Other Project Information form.

Are Vertebrate Animals Used? ☐ Yes ☑ No

13. Are vertebrate animals euthanized?

If "Yes" to euthanasia
Is method consistent with American Veterinary Medical Association (AVMA) guidelines?

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

14. Vertebrate Animals

PHS Fellowship Supplemental Form

Other Research Training Plan Information

15. Select Agent Research

16. Resource Sharing Plan Resource_Sharing_Plan.pdf

17. Other Plan(s)

18. Authentication of Key Biological and/or Chemical Resources

Additional Information Section

19. Human Embryonic Stem Cells

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), using the registry information provided within the agency instructions. Or, if a specific stem cell line cannot be referenced at this time, please 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):

20. Alternate Phone Number:

21. Degree Sought During Proposed Award:

Degree:	If "other", indicate degree type:	Expected Completion Date (MM/YYYY):

22. Field of Training for Current Proposal*: 160 Neurosciences & Neurobiology

23. Current or Prior Kirschstein-NRSA Support?* ☑ Yes ☐ No

If yes, identify current and prior Kirschstein-NRSA support below:

Level*	Type*	Start Date (if known)	End Date (if known)	Grant Number (if known)
Predoctoral	Individual	07/04/2022	12/31/2023	1F31MH125451

24. Applications for Concurrent Support?* ☐ Yes ☑ No

If yes, describe in an attached file:

25. Citizenship*

U.S. Citizen U.S. Citizen or Non-Citizen National? ☑ Yes ☐ No

Non-U.S. Citizen ☐ With a Permanent U.S. Resident Visa

☐ With a Temporary U.S. Visa

If you are a non-U.S. citizen with a temporary visa applying for an award that requires permanent residency status, and expect to be granted a permanent resident visa by the start date of the award, check here: ☐

Name of Former Institution:*

26. ☐ Change of Sponsoring Institution

PHS Fellowship Supplemental Form

Budget Section

All Fellowship Applicants:

27. Tuition and Fees*:

☑ None Requested ☐ Funds Requested

Year 1	
Year 2	
Year 3	
Year 4	
Year 5	
Year 6 (when applicable)	
Total Funds Requested:	$0.00

28. Childcare Costs*:

☑ None Requested ☐ Funds Requested

Year 1	
Year 2	
Year 3	
Year 4	
Year 5	
Year 6 (when applicable)	
Total Funds Requested:	$0.00

Senior Fellowship Applicants Only:

29. Present Institutional Base Salary:	Amount	Academic Period	Number of Months

30. Stipends/Salary During First Year of Proposed Fellowship:

a. Federal Stipend Requested:	Amount	Number of Months
b. Supplementation from Other Sources:	Amount	Number of Months
	Type (e.g.,sabbatical leave, salary)	
	Source	

Appendix

31. Appendix

Introduction

I thank the reviewers for their time and constructive feedback. The reviewers were overall enthusiastic about the research proposal and my mentoring team and environment, but weaknesses were noted with the training plan and research plan. Specifically, they highlighted two major concerns: (1) lack of novelty of my training goals and (2) lack of support for our hypothesized neural mechanism for binding semantics and speaker identity. I agree with the reviewers, and I made the following changes to address their concerns.

FELLOWSHIP APPLICANT: Reviewer 1 noted that I don't have prior experience in human neuroscience research. Since the time of my initial application, I have completed my first study of language processing; this study is now on bioRxiv (Franch et al., 2025). I have added this paper to my Biosketch.

SPONSOR: Reviewer 1 expressed concern about a lack of sufficient mentoring in automatic speech recognition and transcription. I have now added another consultant, Dr. Ashutosh Sabharwal (Rice University / BCM), who is an expert in speech recognition and will provide additional training. Dr. Sabharwal's laboratory is a five-minute walk from my office in the Texas Medical Center where I will attend our meetings. Reviewer 2 suggested having mentorship in LFP processing. I added additional training in LFP data processing from my mentors, Dr. Sheth and Dr. Hamilton, and colleague Dr. Bartoli, to my training plan. Reviewer 3 noted that my primary mentor, Dr. Hayden, is not an established investigator of human neuroscience research. In the revised training plan, I emphasize that I will receive equal co-mentorship from Dr. Sheth, a leader in human neuroscience research and neuromodulation since 2012. Moreover, Dr. Hayden's experience in the field has grown, as is indicated by his three new publications, now found on his revised Biosketch.

TRAINING PLAN: Reviewer 1 is concerned that my goals are only an extension of existing knowledge in electrophysiology and computational methods instead of learning new skills. In the revised Training Plan, I more clearly delineate the new skills to be learned, which include (1) performing human intracranial research, (2) designing experiments suitable for human participants and a hospital environment, (3) automatic speech recognition and transcription, (4) analysis of data related to language and to gain knowledge in language neuroscience, and (5) professional training to prepare me for an independent research career.

RESEARCH PLAN: **Insufficient support for the study hypothesis:** I added a new paragraph to the significance section providing additional support and rationale for the binding hypothesis. **Not enough neurons or brain regions:** In response to this suggestion, I added a fuller power analysis and now increase the number of patients from 15 to 20. Also, I added justification in the significance section for focusing the analysis on ACC given its critical and established role in social cognition and communication. **Unclear whether the subspaces in ACC are crucial for binding**: I added a new analysis in the "neural analysis" section of Aim 2 that gets at the question of causality by including measures of misbinding and its trial-by-trial neural correlates (Johnston et al., *Nature Neuroscience*, 2024). **Lack of LFP analysis is a missed opportunity:** Although my hypothesis can only be tested at the level of single neurons, I agree that not analyzing the LFP data is a missed opportunity and I added a future directions section in Aim 2 that includes LFP analysis. **Combining data across participants may be invalid:** I now include some additional justification for the pseudopopulation approach. In short, none of our hypotheses rely on the statistical properties of single participants or on simultaneous collection. (For example, if different patients have different representational schemes for language, that will not affect our ability to adjudicate between our hypotheses). Indeed, our previous work combined neurons across monkeys to test the neural subspace and hypothesis in a different context. The proposed analysis explicitly aligns neural data into a common representational space across subjects, thus preserving neural representational structure while mitigating individual differences. Thus, our approach represents a widely accepted and methodologically rigorous solution to the inherent sparsity and variability of human single-neuron recordings. I added this rationale to the methods section of the research plan.

DESCRIPTION of INSTITUTIONAL ENVIORNMENT and COMMITMENT to TRAINING (DIECT): Reviewer 1 mentioned that my research plan has implications for BCI development, but the support is not discussed in the environment description. Since the time of the original application, our research team has joined BrainGate, a pre-eminent cross-institutional research team focused on BCI. I will now attend weekly BrainGate meetings. In addition, I will meet monthly with Dr. Nishal Shah, a member of the Rice Neuroengineering Initiative and the BCM Neurosurgery department. I added these details to the DIECT and Facilities and Other Resources.

Applicant's Background and Goals for Fellowship Training

A. Doctoral Dissertation and Research Experience

My curiosity about neural mechanisms behind social behavior and communication drove me to pursue research positions during and after college. I acquired a broad scientific skillset before entering graduate school by working with a variety of animal models (mouse, pig, and human) and performing various techniques in molecular, behavioral, clinical, and neuroscience research. During these experiences, I valued the ability to communicate and conduct research effectively, motivating me to pursue my goal of becoming an academic researcher and professor. These ambitions led me to conduct my dissertation work under Dr. Valentin Dragoi, where I used innovative experimental and computational methods to study the neural basis of social learning in monkeys. Now, through my postdoctoral work in the Hayden lab, I am broadening my study of social cognition to include the neuroscience of language comprehension. In the future, I aim to combine the computational and language neuroscience training gained through this fellowship with my background in social and visual neuroscience. By bringing these disciplines together in the Franch lab, I plan to study the multi-modal integration of language and social visual cues during natural conversations and social interactions.

Undergraduate Research

Thrall Lab, Pacific Northwest National Laboratory, Richland, WA. *June – September 2010*

During my first research experience as an intern in the Thrall lab, I conducted my own project testing the ability of a proline rich polypeptide to restore hematopoietic stem cells and increase survival in lethally irradiated mice. My goal was to develop a prophylactic that could mitigate harmful effects from exposure to external ionizing radiation. I hypothesized that the polypeptide would be radioprotective due to its ability to regulate immune functions in the body. I wrote the IACUC protocol, determined animal groups and treatment regimens, irradiated the mice, and collected body weights daily. My results revealed that mice who received treatment repeatedly post-irradiation had significant increase in body weight and survival rate, and an increase in white blood cells, lymphocytes, and neutrophils. I concluded that this polypeptide, when administered repeatedly post-irradiation, mitigates effects of external ionizing radiation. The Department of Energy selected me to present my poster at the Department of Energy's Science and Energy Research Challenge at Argonne National Lab. Most notably, this internship taught me the importance of developing meaningful scientific questions and thoughtful experiments for productive research and began molding me into an independent researcher.

Post-graduate Research

Thrall Lab, Pacific Northwest National Laboratory, Richland, WA. *June 2013 – August 2014*

After college, I continued working in the Thrall lab during the summer while teaching high school biology in NC. Even though I had to move across the country to live in WA each summer, it was important to me to remain active in research while teaching. I continued studying radiation research, where I used a porcine animal model to 1) investigate the effects of hematopoietic acute radiation syndrome on cell proliferation and 2) test the efficacy of a therapeutic agent to restore cell growth post-radiation exposure. I conducted enzyme-linked immunosorbent assays (ELISAs) to measure levels of flt-3 ligand, d-dimer, and endotoxin in plasma samples that received treatment or control after exposure to ionizing radiation. I found that treatment could significantly reduce radiation-induced cell death, but was unable to mitigate cellular protein degradation entirely. This experience solidified my aptitude for research and motivated me to pursue full-time employment in research.

Franks Lab, Duke University, Durham, NC. *June 2015 – July 2016*

My scientific interest in autism and social behavior led me to develop neuroscience expertise as a research assistant in the Franks lab, where I studied stable odor representations in mouse piriform cortex. We hypothesized that odor coding relied on the strength and timing of neuronal responses. I performed stereotaxic surgeries to inject Cre-dependent viral opsins, enabling cell-type-specific optogenetic manipulation. Using optogenetics and electrophysiology, I recorded neural activity during odor presentation and analyzed spike data in MATLAB. Our work, now published in *Science*, showed that recurrent piriform circuits support concentration-invariant odor coding. This experience gave me foundational training in neuroscience methods and solidified my commitment to a neuroscience research career.

Neurosurgery research team, UTHealth – McGovern Medical School, Houston, TX. *July* 2016 *– August 2017*

Before beginning graduate school, I wanted to experience the benefits and challenges of conducting neuroscience research in a clinical setting. As a clinical research coordinator, I used fMRI and biospecimen data

to investigate how traumatic brain injury affects neuromodulators, proteins, and ultimately the circuitry of the human brain. I enrolled 78 patients with mild to severe traumatic brain injury, and collected and processed their data. Additionally, we wanted to determine the optimal treatment for elderly patients (70 years or older) presenting with acute traumatic subdural hematoma. Our multivariable logistic regression analysis revealed that age, Glasgow Coma Scale score, and surgery type had a significant impact on mortality, resulting in my authorship on a publication. Clinical research exposed me to novel methods for studying neuroscience. For the first time, I understood how research done in powerful animal models could translate to a clinical population.

Graduate Research
University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences (GSBS)

Dragoi Lab, Dissertation lab, UTHealth, Houston, TX *May 2018 – December 2023*

When I started at GSBS, I was most eager to rotate in the Dragoi lab, which is why it was my first rotation. I knew there were many opportunities and resources in the lab to study social cognition in a relevant animal model, rhesus macaques. I helped the lab develop and validate a novel experimental paradigm to study social behavior, specifically, cooperation. For this, I worked closely with the electrical engineers in our lab to design the correct circuits and code to run the task. I collected preliminary behavioral data from a pair of freely moving animals as they used the novel paradigm to cooperate. Through my analysis of their movement and choice behavior, I found that animals coordinate their actions to cooperate, and their motivation to cooperate is sensitive to reward value and inequity. Therefore, we concluded this paradigm provides a dynamic and effective way to study cooperation, and I enthusiastically joined the lab in May 2018 to continue this project as my doctoral work.

Social interactions are a ubiquitous aspect of our everyday life that typically require interpreting and responding to visual cues, such as body language and expressions, from others. However, the underlying neural mechanisms of *learning* advanced social concepts, such as cooperation, remain unknown. During my PhD, I hypothesized that visual brain areas, such as the visual cortex, as well as executive regions in the prefrontal cortex were improving their processing of visual information to guide decisions during social learning. If confirmed, this would expand our knowledge of social cognition to include regions like the visual cortex, which was not previously considered as part of the 'social brain'.

I developed a novel experimental paradigm that combines behavioral monitoring with wireless eye tracking and single neuron recordings from visuo-frontal brain areas to study how pairs of freely moving, interacting rhesus monkeys learn cooperation for food reward. I performed all experiments recording behavioral, neural, and eye tracking data from two monkey pairs as they learned to cooperate across weeks. Animals could freely move and visually but not physically interact. Each monkey had their own button and cooperation occurred when monkeys simultaneously pushed and held buttons, delivering a food reward to them. I found that animals learned to cooperate by improving their action coordination and reaction times. Notably, animals became more likely to cooperate after viewing a social cue, such as the reward or partner monkey. As animals learned cooperation, both visual and executive brain regions improved coding of social cues, such as viewing the partner monkey or reward, confirming my hypothesis. Neural encoding of each monkey's decision to cooperate was greatest when animals viewed social cues during decision-making. Moreover, learning social events increased coordinated spiking between visual and prefrontal cortical neurons. These results indicate that the visual-frontal cortical network prioritizes relevant sensory information to facilitate learning social interactions.

My dissertation provided the first evidence for the role of visual cortex in encoding socially relevant information and suggests that learning cooperation emerges from improved communication between visuo-frontal circuits during social viewing and improved population coding within areas. By allowing animals to move freely during social interaction, my work represents a pioneering effort toward studying the neural underpinnings of naturalistic behavior. I earned a NIMH F31-Diversity Award to fund this research. Additionally, this project received the 2019 Society for Neuroscience "Hot Topic" Award for innovative science and I published a first-author manuscript that summarizes these findings (Franch et al., *Nature* 2024).

B. Training Goals and Objectives

Transition to Postdoctoral Research

Hayden Lab, Postdoctoral lab, Baylor College of Medicine, Houston, TX *January 2024 – present*

Driven by my long-term commitment to autism research, I want to run a laboratory collecting electrophysiological data from humans to understand social decision-making, language, and communication with an emphasis on autism spectrum disorders. To achieve this goal, I will need to develop a full suite of skills related to collecting

and analyzing electrophysiological data from humans. This includes experience doing clinical and language neuroscience research.

Mentoring team: Several factors motivated me to choose Drs. Benjamin Hayden (PhD; primary mentor/sponsor) and Sameer Sheth (MD/PhD; cosponsor) as post-doctoral mentors in the Neurosurgery Department at Baylor College of Medicine (BCM). The Hayden lab has long been a leader in naturalistic decision-making and advanced statistical analysis of physiological data; the Sheth lab is likewise a leader in intracranial data related to human cognition and psychiatric disease. Moreover, I am mentored by my consultants, Dr. Ashutosh Sabharwal at Rice University/BCM, and Dr. Liberty Hamilton, associate professor in the Department of Speech, Language and Hearing Sciences at UT Austin, who are both experts in automatic speech recognition and transcription. Dr. Hamilton also collaborates with neurosurgeons here in the Texas Medical Center (TMC) at Texas Children's Hospital. Dr. Hamilton has extensive experience studying language neuroscience in adult humans and children with epilepsy, and her expertise in modeling speech and neural signals during language comprehension will provide relevant and critical support during this fellowship. Additionally, some of the children with epilepsy and intracranial implants also have autism, providing a unique opportunity to examine neural changes in language comprehension and communication in healthy and autistic adolescents. Drs. Hamilton, Sabharwal, Hayden, Sheth, and I plan to pursue this research opportunity later together under a K99/R00 award or as co-PIs.

Notably, all of my post-doctoral advisors have a strong track record of post-doctoral training. My primary mentor, Benjamin Hayden, has trained 4 postdocs who earned tenure-track faculty positions. My co-sponsor, Dr. Sameer Sheth, MD/PhD, has trained 3 junior faculty, 4 residents and a postdoc who has a faculty position. Dr. Hamilton has trained 2 PhD students and 2 master's students. Dr. Sabharwal has trained 6 postdocs who are now faculty. Additionally, I have a positive and healthy relationship with each of my postdoctoral mentors. Leadership is built on relationships, and I trust that my mentors are shaping my research goals and directions in ways that will have a lasting impact on both the field and the quality of life for individuals with communication deficits. In addition to our weekly joint Hayden-Sheth lab meetings, both sponsors have offices located in the same lab suite as mine, making it easy to meet with them anytime. I meet weekly with Dr. Hayden to discuss my latest scientific results and short-term and long-term professional goals. Frequent conversations with Dr. Sheth and Dr. Sabharwal (whose office is across the street) inform my research questions, methods, and practice. Although Dr. Hamilton is based in Austin, TX, we meet on Zoom and she is in Houston at least once per month for her research. I meet with her during this time, and she discusses new literature with me, provides feedback on my computational methods, and suggests ways to establish collaborations within the medical center for future research opportunities.

I have incorporated insights and feedback from discussions with my mentors, as well as results from my IDP (individual development plan), to create the following training objectives that will promote my success both during and after my postdoc. All mentors encourage me to pursue a career in academia, motivating me to present my work at both local and external neurosurgery and neuroscience conferences that provide networking with clinicians and autism researchers at other institutions for my future work in The Franch Lab. Together, this team of veteran professors and physicians will support my development during this fellowship and beyond.

Goal 1: Learn human intracranial electrophysiology and speech processing. Success of my F32 and future research program is dependent upon interdisciplinary collaborations between the hospitalized patients, clinicians, and researchers. During this fellowship, I will learn how to initiate and maintain these relationships. Furthermore, the proposed experiments are truly unique as they require scientists to set up lab and research equipment in the hospital and patient's room. Therefore, I will also master technical skills in recording neural and language data from humans in a hospital.

Clinical research. BCM is located in the Texas Medical Center (TMC), the largest medical center in the world. Impressively, the Neurosurgery research group at BCM is a major leader in human intracranial research, with proficiency in examining neural activity from patients during naturalistic behaviors. The group has one of the highest numbers of patients with single-unit recordings in the U.S., which will allow me to test specific hypotheses about the neuronal mechanisms of real-time communication. Patients with epilepsy reside in the Epilepsy Monitoring Unit (EMU) during their time in the hospital. The BCM neurosurgery group has a research office in the EMU that is adjacent to the patient's room, making it easy to stabilize equipment and monitor the patient during experiments. I have described my F32 research project and performed experiments with 5 adult patients, learning how to run experiments around their schedule and ensuring they are comfortable. I will continue to learn the names of the hospital staff, so I can find a patient's nurse or clinician when they have a medical related need. Certainly, I will continue to advocate for my patients during research. Additionally, my mentors will help me build

connections with other scientists and clinicians for future collaborations. For example, during this fellowship, Dr. Sheth will introduce me to other clinicians at neurosurgery conferences (ASSFN) and I will shadow Dr. Hamilton when she conducts her experiments in the TMC so I can network with neurosurgeons from nearby hospitals. For example, Dr. Sheth and Dr. Hamilton have identified Dr. Erich Storch (psychologist) and Dr. Howard Wiener (neurosurgeon) here at BCM whom I could also collaborate with as a PI, given my interest in autism. Additionally, Dr. Hamilton uses a mobile neural and speech recording system that she can move from room to room, so this training will show me alternative methods for how to conduct language neuroscience research in a hospital.

Recording speech and natural conversations. The hospital is filled with the sounds of equipment and people moving in and out of the patient's room, making it essential to record speech with minimal noise interference. I will continue to learn about different types of microphones and how to position them properly for recording sounds in the patient's room, particularly from my consultant, Dr. Sabharwal. Dr. Sabharwal has created wireless, wearable audio sensors to record patient's everyday speech to assess sociability, making him an expert in speech recognition and transcription. I will learn how to remove noise from audio files using software like Adobe Audition and Praat. My other consultant, Dr. Hamilton, and an experienced medical student, Katie, have used this data to analyze emotional state and they have also begun teaching me these skills. Additionally, I am learning how to synchronize speech signals with neural data from our group's operational technologist and will refine these abilities during this fellowship.

Neural recordings. My knowledge in electrophysiology and study of action potentials from single neurons in graduate school has been helpful for my postdoctoral work, but I am still learning how all behavioral data is synchronized to the neural system, how to troubleshoot noise, and how to process the neural signals. To learn this, I am and will continue to perform the electrode setup on the patient's implant day. I am learning the nuances of our recording system by connecting the electrodes on the patient's head, along with behavioral recording equipment to our neural recording system. Further, Dr. Bartoli, a junior PI in our group, will continue to train me on both hardware and software resolutions to remove noise from the neural signals. She is also teaching me how to use spike sorting programs and filters to obtain high quality data offline after experiments. Finally, from my graduate work, I have established a professional relationship with the engineers at Blackrock Neurotech, the company that develops our neural recording device, so I will continue to contact them for assistance.

Goal 2: Develop computational methods to study the neuroscience of language. An important goal of this fellowship is to become knowledgeable in linguistic concepts and speech and language research so that I can develop a framework for my experiments and adequately constrain my hypotheses. Through this goal, I will learn how the neuroscience of language has been studied and how to apply computational tools to answer relevant scientific questions in this field.

Knowledge in the neuroscience of language. I have and will continue to read manuscripts that use a variety of neuroimaging (FMRI, MEG) and intracranial (LFP, single cell) neural recording techniques to study the neural basis of language. I will focus my study on papers involving the neural processing of semantics, speaker identification, and language comprehension, especially during natural conversations. I completed the *"Language and the Brain*" course that Dr. Hayden taught at Rice University in 2023. Also, I have presented four neurolinguistic papers on lexico-semantics and dialogues in our monthly journal club this year and I will continue to present relevant papers. Additionally, I have and will continue to attend conferences and workshops for language neuroscience. In May 2024, I attended the Neurobiology of Language workshop at MIT where myself and leaders in the field engaged in whole group discussions about the definition of language, the purpose of language, and the theories of language representation in the brain. During this award, I will attend The Society for the Neurobiology of Language (SNL) Conference held in Washington, DC in 2025 and the Society for Neuroscience Conference each year to learn about recent studies in the field. My consultant, Dr. Hamilton, also suggests relevant and important literature for me to review.

Word transcription and linguistic feature extraction. I am learning how to use new tools in Artificial Intelligence (AI) to improve the efficiency and accuracy of speech transcription. I developed a pipeline for processing speech in Python through AssemblyAI, a state-of-the-art AI model to transcribe and understand speech, whereby we input the audio file from natural conversations or podcasts and the model returns each word and its corresponding timestamp. These txt files are then passed in Montreal Forced Aligner, where they are further corrected, and then loaded into Praat where the timestamps are checked and manually corrected. This process is significantly faster and more accurate than manual transcription from the original file. Moreover, I am learning how to use Assembly AI's diarization feature, to extract transcripts with speaker labels from natural conversations with 2 or more speakers. During this fellowship, I will learn and improve these skills with mentorship from my

consultants, Dr. Hamilton and Dr. Sabharwal, experts in automatic speech recognition. Additionally, I will learn how to extract word embeddings from Large Language Models and use the Natural Language Processing Toolkit in Python to access lexical databases like WordNet to extract semantic relationships from words such as word polysemy. I will also use the English Lexicon Project and Praat to extract word frequency and acoustic feature like word pitch, respectively. To learn these skills, I will be trained by Dr. Hamilton and two linguistic experts in the lab who recently graduated with degrees in neurocognitive linguistics and are proficient at using these tools to study language.

Neural coding of semantics and speaker. The proposed research requires mathematical skills for analyzing the representational geometry of neural activity to test hypotheses for neural binding of semantics and speaker identity. Throughout my career I made great strides in developing computational neuroscience literacy through coursework, coding, and Neuromatch Academy's online content. The Hayden lab is an excellent environment to further these skills and test the proposed hypotheses as our laboratory has developed a mathematical framework for subspace orthogonality, binding, and generalization that was recently published (Johnston et al., 2024). During this fellowship, I will receive mentorship from Dr. Hayden and two first authors on the study, Dr. Johnston and Dr. Fine. While they both work remotely, Dr. Fine travels to Houston at least 3x/year, and I have and will continue to meet with each of them over Zoom when I have specific questions about the analysis. Preliminary results in the research plan demonstrate my ability to test the proposed neural theories and elucidate neural coding of word meanings and speaker identity in the ACC. Additionally, to further my knowledge of modeling linear and nonlinear neural interactions with language, I will take the "*Regression and Linear Models*" course, STAT 615, at Rice University in the Fall of 2025. I will also attend and present my findings at the Rice Neuroengineering Interface Symposium and at Cosyne (Computational and Systems Neuroscience conference) during this Fellowship, where I will receive valuable and relevant feedback. Although my proposed hypothesis is not testable with LFP data, LFP is informative, and I've added additional analyses of LFP to the research plan. My mentors, Dr. Sheth, Dr. Hamilton, and Dr. Bartoli, will teach me LFP analysis, and I will learn LFP computational skills from taking the *Fourier Transform and Time Series* course by Mike X Cohen on YouTube. Finally, I will take the *BCM Rigor and Reproducibility Workshop* to ensure robust and unbiased analysis and interpretation of my results.

Goal 3: Prepare for an independent research career. A key aim of my postdoctoral training is to prepare for an independent research career in academia. Through this fellowship, I will fully leverage the numerous professional development opportunities at BCM and the Texas Medical Center, and my outstanding team of postdoctoral mentors, to build the skills essential for establishing The Franch lab and my career in academia.

Oral Communication. I enjoy presenting my work at various stages of its progression. Discussing my research with the scientific community deepens my knowledge of the material and creates stimulating conversations with useful feedback. Specifically, my presentations at research-specific conferences provide meaningful advice from relevant scientists who also study the neurobiology of language, communication, and social cognition. I often return from conferences with an improved understanding and new ideas for analysis. Therefore, I will continue to present my work in oral and poster presentations at various local and global conferences. For example, I have already presented preliminary findings from my postdoctoral work at 4 conferences this year, including the Society for Neuroscience annual meeting and the NIH BRAIN Initiative conference as a *Scholar Spotlight*. Such recognition from the NIH highlights my ability to communicate research effectively. During this fellowship, I will continue to present my work at these conferences, at lab meetings, and the Society for the Neurobiology of Language Conference in 2025.

Written Communication. Establishing excellent scientific writing skills is necessary for success as a scientist. Dr. Hayden also realizes this importance, and regularly provides opportunities to work on grant writing. For example, he held a "mock study section" where BCM neuroscience faculty reviewed my Specific Aims page for this proposal, and he sends me his grants and proposals of graduate students in the lab to review and edit. Additionally, I completed a grant-writing course and the NIH Fellowship Proposal Development course during graduate school, and, although I did not receive it, I gained more experience in grant writing this year when I applied for the HHMI Hanna H. Gray Fellowship. During the last year of this fellowship, I will apply for a K99/R00 Pathway to Independence award and I will prepare for this submission by reviewing others' applications and attending the K99/R00 workshop here at BCM. Besides grant writing, I look forward to improving my scientific communication skills for manuscripts. To this end, I will refine my Adobe Illustrator skills to create interpretable, unambiguous figures for papers and presentations. I will also peer edit manuscripts by other lab members and collaborators. Moreover, I also review manuscripts from other labs for journals and will continue to do so during this fellowship. Finally, I will gain writing skills when preparing two manuscripts that summarize findings from the

proposed research.

Inclusive Leadership. One of our greatest accomplishments in academia is the people we teach, who will go on to excel and make impactful contributions to research beyond our own lab. I will continue to develop connections with students I mentor and provide them opportunities to connect with resources and professionals who benefit them. I currently mentor 2 graduate students, 2 research technicians, and 2 undergraduate students. I help them design experiments and develop hypotheses, teach them how to process and analyze neural data, and I review their presentations and abstracts. I created a designated Slack channel where we share fellowship opportunities, graduate school advice, and new papers on topics that interest them. Throughout this fellowship, I will continue to mentor these students and new people who join the lab. I also interview prospective lab members. Additionally, I am a volunteer audio editor and interviewer for the "*Stories of Women in Neuroscience*" podcast, showcasing and uplifting other women and their experiences in the field. I will also continue to teach two lectures on language neuroscience in 2026 for Rice University's undergraduate course, *Systems Neuroscience* (NEUR 380). Moreover, I will attend the "Mentoring up" workshop held here at BCM. Overall, I help others enjoy and build skills in science, which will be invaluable when I recruit and mentor as a PI in the Franch lab.

Transition to Faculty. I have selected a team of mentors with a strong track record of guiding postdoctoral fellows into faculty positions, who will review my progress throughout this fellowship and provide feedback on my manuscripts and grants, including this proposal and the K99/R00 Pathway to Independence Award. When I begin applying for faculty positions, I will practice my interview presentation and chalk talk with these mentors and colleagues, and I will review application materials from successful applicants who were recently hired. Moreover, working with these mentors and conducting the proposed research in the TMC provides networking with other scientists and physicians whom I can collaborate with as a PI, should I remain in TX. I am confident that I will accomplish my long-term goal of becoming a productive neuroscientist and educator through the exceptional training and mentorship I will receive during this award, outlined in the timeline below.

C. Activities Planned Under This Award

	Year 1 (2025-2026)	**Year 2** (2026-2027)	**Year 3** (2027-2028)
Research	- Data collection for both aims & preliminary analyses	- Complete analyses & controls - Submit manuscript 1 (semantics, speaker, and other linguistic feature encoding)	- Finalize analyses - Submit manuscript 2 (semantics and speaker neural alignment)
Goal 1 (experimental & clinical skills)	- Mentorship from Drs. Sabharwal and Hamilton for learning speech recognition and translation.	- Meetings with Dr. Hamilton and Dr. Bartoli for processing neural and language data - Present at ASSFN (neurosurgery conference)	- Networking with Drs. Hamilton and Sheth to meet other professionals in the TMC
Goal 2 (computational & language research skills)	- complete STAT 615 course - Learn from YouTube videos, Dr. Hamilton, and lab members for language processing and feature extraction - Present research at SNL conference and lab meetings - Present language neuroscience papers at journal club	- Apply knowledge from STAT 615 to analysis in both aims. - Meetings with Drs. Fine, Johnston, and Hayden for computational methods in Aim 2 - Rigor & Reproducibility course at BCM - LFP and time series YouTube course and meetings with Drs. Hamilton, Sheth, and Bartoli for LFP analysis	- Present research at COSYNE - Present research at SNL and SfN conferences.
Goal 3 (professional skills)	- Mentor undergraduates, graduate students, & techs in the Hayden lab - Taught two lectures NEUR 380	- Present research at SfN, Rice Interface, WSSFN conferences - Review papers for Journals - K99/R00 workshop at BCM - Teach two lectures NEUR 380	- "Mentoring up" workshop at BCM - Apply for K99/R00 - Teach two lectures NEUR 380

Specific Aims: Neural coding of language semantics and speaker identity during speech comprehension

Amid the lively buzz of conversation with friends, our brains effortlessly track not just what is said, but who says it, weaving meaning and identity together in real time. Effective communication relies on a mutual understanding of meaning, also known as *semantics*. In conversation, we draw on our knowledge of others' identities to make sense of their words. For example, hearing “we should talk” from a friend might be less concerning than if said by one’s boss. Disruptions in communication, resulting in failure to infer semantic information in a social context, are diagnostic of many neurological conditions like autism and aphasia[1,2]. Understanding how the brain navigates the process of aligning semantics with speaker identity is crucial for social interactions and improving quality of life for individuals with communication deficits. Resolving this problem requires, first, a basic understanding of how meaning is represented in the brain, and second, an understanding of how meaning is aligned with identity.

The anterior cingulate cortex (ACC) is closely involved with both language and social cognition[3–6]. While the human brain has been shown to integrate speech content and speaker identity very rapidly during listening[7], how single neurons from hub-like regions such as the ACC integrate speaker identity and semantic content remains unknown. Single-neuron recordings provide the temporal precision needed to capture the rapid integration of speaker identity and semantics during speech. **The central premise of this proposal is that ACC serves as a key site for the integration of semantic and social information**.

One *theory for how the brain combines different features* that arise from a single object together, such as the meaning and speaker identity of a perceived word, is through distinct population subspaces[8]. A *neural subspace* refers to a lower-dimensional space within the high-dimensional activity of a neural population, that represents patterns of neural activity for specific features or functions. The arrangement of neural activity patterns for semantics and speaker identity in the subspace can reveal how the brain binds these elements. Recent work from our lab indicates that ACC uses subspace alignment to register reward and action information[9]; here, we propose to extend this idea to the sociolinguistic domain of semantics and identity. We hypothesize that ACC encodes semantics from different speakers in distinct, semi-orthogonal neural population subspaces. To test this hypothesis, we will use electrophysiology to record from single neurons in the healthy ACC of human patients with epilepsy (who maintain healthy language function) during speech comprehension and natural conversations.

Aim 1: Delineate the functional role of ACC neurons in language semantics and speaker identity during speech comprehension and natural conversations. Patients will listen to forty-five minutes of podcast stories chosen to be both interesting and linguistically rich. Patients will also naturally engage in unscripted conversations with the doctors, visitors, and researchers. We will precisely transcribe all words and conversations and align word onsets with neural data. We will extract word embeddings using natural language processing models, and then perform unsupervised learning to identify natural semantic categories (we expect these to include categories like “people”, “objects”, “actions”, and “places”). For each ACC neuron, we will compute evoked firing rate responses. Thus, each word is associated with a speaker, a semantic category, and a neuron’s response. We will assess neuronal tuning for semantics and speaker identity by fitting linear regression models. We hypothesize that: (1) that neurons will be selective for multiple semantic categories and (2) both semantic categories and speaker identity can be decoded from ACC population activity. Completion of this aim will reveal how meaning and speaker identity are represented in ACC, which can be used for assessing their alignment in the next Aim.

Aim 2: Determine how ACC populations align semantics with speaker identity. We will use coefficients from the regression models in Aim 1 to create a semantic population subspace vector for each speaker, and we will examine the geometry (correlation) of these vectors to determine alignment. We hypothesize that: (1) semantics will generalize across speakers, meaning the word “dog” should evoke similar neural responses whether it is said by the patient or by someone they are conversing with, and that (2) ACC populations will bind speaker identity to semantics by encoding the words of different speakers along semi-orthogonal dimensions - creating a subspace that ensures separability and binding alongside generalizability during conversations. Alternative outcomes could be a subspace that is completely orthogonal, suggesting separate representations for speaker and semantics and the inability to generalize, or a subspace that is collinear, which would enable identity coding but would not be able to disentangle the speaker from semantics. Identifying the ACC's coding regime will reveal how it supports communication, enhancing our understanding of neural processes behind flexible language comprehension in real-world conversations.

Overall, this proposal is an unprecedented opportunity to study single neuron dynamics in communication, informing development of assistive technologies and neural prosthetics to address language deficits.

RESEARCH STRATEGY

SIGNIFICANCE

Effective communication is fundamental to human interaction. Aligning speaker identity with semantics helps listeners understand intent and respond appropriately - skills that are particularly essential in complex social environments[7,10,11]. Unfortunately, difficulties in understanding the semantics of spoken words are widespread, especially among individuals with developmental (Autism and Social Communication Disorder), acquired neurological (Aphasia), or neurodegenerative conditions (Alzheimer's), affecting millions globally[1,2,12]. Therefore, studying the neural basis of semantics and speaker recognition during communication is imperative for advancing assistive technologies and neural prosthetics, which could help address language deficits and significantly enhance the quality of life for those affected. Despite the critical role of this alignment in social communication, the neural mechanisms that integrate speaker identity with word meaning remain poorly understood. My research proposal aims to address this gap by elucidating the neural binding of speaker identity and semantics, offering new perspectives on how humans achieve nuanced, contextually accurate communication.

We posit that the anterior cingulate cortex (ACC) has an important role in processing semantics and social cues like speaker gestures and identity during language comprehension. Lexical-semantics (word meanings) and semantic knowledge (general world knowledge about people, objects, facts, etc.) are encoded across many regions of the human brain, including the anterior cingulate cortex[4–6,13–15.] For example, Zhao et al. show that ACC, alongside the anterior temporal lobe, functions as a hub for multimodal semantic integration[4]. ACC is also implicated in the semantic encoding processes necessary for remembering and manipulating socially relevant information[15], and can even signal the saliency of a speaker, such as a mother's voice compared to another woman's[16]. Moreover, ACC supports social cognition including agent identity[17,18] and inferring self and other's emotions and actions[3,19–21]. More broadly, ACC is a processing hub that integrates multiple forms of information to generate flexible, abstract control signals[3,22,23]. Based on these data, **the central premise of this proposal is that ACC serves as a key site for the integration of semantic and social information.** For example, while semantics generalizes across speakers (meaning we can understand the word "dog" regardless of who said it), meanings of the same words can mean different things depending on the speaker. Thus, we postulate ACC is involved in evaluating semantic content and speaker characteristics to keep track of what was said, who said it, and what it means during language comprehension.

How is the brain binding, or integrating, semantics and speaker identity? Speech processing relies on precise temporal dynamics, and the human brain rapidly integrates both speech content and speaker identity during listening[7,24]. Therefore, single neuron dynamics can support such rapid and fine-scale processing. One theory for how populations of single neurons combine different features that arise from a single object together, such as the meaning and speaker identity of a perceived word, is through distinct population subspaces[9,25]. A **neural subspace** refers to a lower-dimensional space within the high-dimensional activity of a neural population, that represents patterns of neural activity for specific features or functions[8,26,27]. The arrangement of neural activity patterns for semantics and speaker identity in the subspace can reveal how the brain binds these elements. For example, information related to semantics of the words said by speaker 1 (the visitor) may be put into one shared subspace. Then, they are effectively bound. Information relating to semantics from words spoken by speaker 2 (the researcher) can exist in an orthogonal subspace (see **Fig. 6** for schematic).

Recent work from our lab indicates that ACC uses this subspace alignment to register reward and action information[9]; what we propose here, therefore, is an extension of this idea to the domain of semantics and identity, especially given the prominent role of the ACC in representing multiple features essential to social cognition[3,4,18–20,28,29]. Indeed, **subspace orthogonalization** is a concept that comes from population approaches to understanding and analyzing neurophysiological data[25,30]. Although these ideas originated in motor physiology[26,31,32], studies have shown that they apply to cognitive neuroscience as well[8,33–35]. Based on this growing body of empirical studies[34–39], we propose that subspace alignment serves as a unifying computational principle for binding co-occurring features - including semantic content and speaker identity - within brain regions like the ACC that support social cognition[16–18,28]. We hypothesize that ACC encodes semantics from different speakers in distinct, semi-orthogonal subspaces. This encoding would allow for both generalization (across speakers) and specification (identification with specific speakers). These semi-orthogonal representations have been observed in many other binding studies[33–35,37,38,40,41]. To test this hypothesis, we will use electrophysiology

to record from single neurons in the healthy ACC of human patients with epilepsy (who maintain healthy language function) during speech comprehension and natural conversations.

These results will answer several outstanding questions in the field: (1) what lexical-semantic features of words are represented at the single neuron level, (2) how speaker identity is represented, (3) and how semantic and speaker features are organized and integrated. Our findings will have important implications for basic science research and understanding of communication disorders. Uncovering the neural representation of semantics and speaker integration will increase our understanding of how semantics and speaker recognition are disrupted in disorders such as aphasia and autism. In addition, it will improve development of brain-computer interfaces (BCI) for speech perception and production[42,43]. By understanding the specific semantic features that are encoded by the ACC, BCI decoders can be trained to more accurately infer intended speech content. Aphasia often disrupts the ability to understand who is speaking, especially in environments where multiple speakers are involved. This work can inform novel encoding models of semantic and speaker perception, whereby brain stimulation is used evoke or enhance language comprehension[43]. Collectively, this proposal aims to elucidate single neuron dynamics in communication and will provide me with the skills needed to continue social communication and language neuroscience research as a PI.

INNOVATION

This proposal offers several advances in providing a novel mathematical framework for understanding language representations from single neuron recordings in humans during real-life, in-person conversations.

1) Intellectual innovation: subspace orthogonalization is a concept that comes from population approaches to understanding and analyzing neurophysiological data[25]. Although these ideas originated in motor physiology[25,31], we have shown that they apply to cognitive neuroscience as well[8,34,44].

2) Surgical innovation: using human neurophysiology to answer outstanding questions in cognitive neuroscience: In recent years, revolutions in clinical practice for identification of the site of seizure generation have led to the use of stereo-EEG approaches, which allow for the collection of single neuron data in targeted brain regions. This work is targeted to the site of epileptic origin, but in practice nearly always involves the prefrontal cortex. More recently, our team, led by co-sponsor Dr. Sameer Sheth at Baylor St. Luke's Hospital, has expanded our efforts to include recordings from the ACC to localize sites of hyperactivity, even in cases where they may originate from the medial temporal lobe. My research proposal makes use of these innovations.

3) Task innovation: **natural storytelling and conversations:** Stories from *The Moth* Podcast have been previously used to effectively study the neural basis of language comprehension[14,45], and this proposal is the first study to examine single neuron responses to language during natural conversations between two or more people. Through development of novel language transcription and analysis pipelines in this proposal, we aim to enable and inspire other researchers in neuroscience to study speech and neurolinguistics during natural behavior.

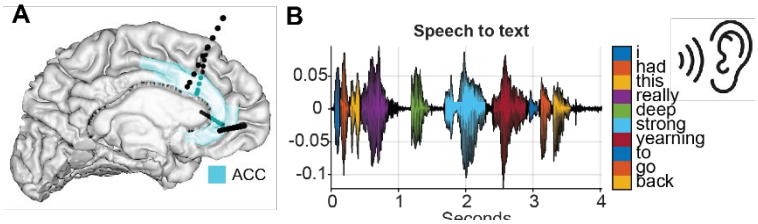


Figure 1. Single neuron recordings during natural language comprehension. **A**) Medial view of one patient's left hemisphere with blue color showing the anterior cingulate cortex (ACC) and Behnke-Fried recording electrodes from both hemispheres. **B**) Different colors reflect the transcribed words from each sound heard in the podcast stories (also applies to conversations).

APPROACH

General Methodology

Human intracranial neurophysiology. For adults with drug-resistant epilepsy, neurosurgeons implant intracranial electrodes to localize seizure foci. During their 7-14 day stay in the Epilepsy Monitoring Unit (EMU), patients often participate in cognitive tasks that do not interfere with clinical care. We will record from patients with intact language using Behnke-Fried-style sEEG electrodes (AdTech, PMT Corp.), which include both macro contacts for LFPs and microwires for single-neuron recordings. Neural data will be acquired using a 512-channel Blackrock Neuroport system, with simultaneous LFP and spike recordings collected throughout the patient's stay. We will obtain single neuron recordings from the anterior cingulate cortex (**Fig. 1**), and locations will be confirmed via co-registered MRI and CT scans.

Overview and timeline. To date, I have collected story listening and natural conversation data on six subjects for a total of 156 ACC neurons. I performed a statistical power analysis based on these data and I also examined

our own previous macaque-based dataset on subspace orthogonalization in economic choice[33,34]. From these data, assuming similar effect sizes of subspace correlation values between 0.2 and 0.6, I will need 400 neurons to complete both Aims ($\alpha = 0.01$, power = 0.8). The proposed analysis of subspace orthogonalization and binding in Aim 2 requires analyzing relationships across many neurons simultaneously[25,31,32]. Our previous subspace binding study, as well as many others in both humans and animals, accomplish this by combining neurons across subjects to create a pseudopopulation[34,35,38,39,41,46,47]. A pseudopopulation provides the dimensionality needed to observe these geometric properties. Pseudopopulations can reliably reflect the statistical structure of true population activity, especially with normalization procedures like using z-scored firing rates[26,48]. This makes them suitable for the dimensionality reduction, decoding, and subspace analyses in this proposal. I currently record ~25 neurons/patient, so I will record from 20 patients to account for sufficient statistical power and effect size[47,49,50]. With our hospital averaging 10 ACC research patients/year, I should finish data collection in the first 1.5 years of the proposal, and finish analyses by end of year two. I plan to submit a manuscript on semantic coding in ACC during year 2 and another manuscript on semantic and speaker neural alignment in year 3.

Classifying single neuron activity. Recordings from all microwires are sampled at 30 kHz. To identify single neuron action potentials, the raw traces will be spike sorted using the *WaveClus* sorting algorithm[51]. I will classify spike waveforms as usable clusters by ensuring they have physiologically valid shapes, consistent mean spiking rates, and interspike intervals of at least 3 ms for over 95% of spikes[51]. Any patients whose ACC is a seizure focus area will be excluded from analysis.

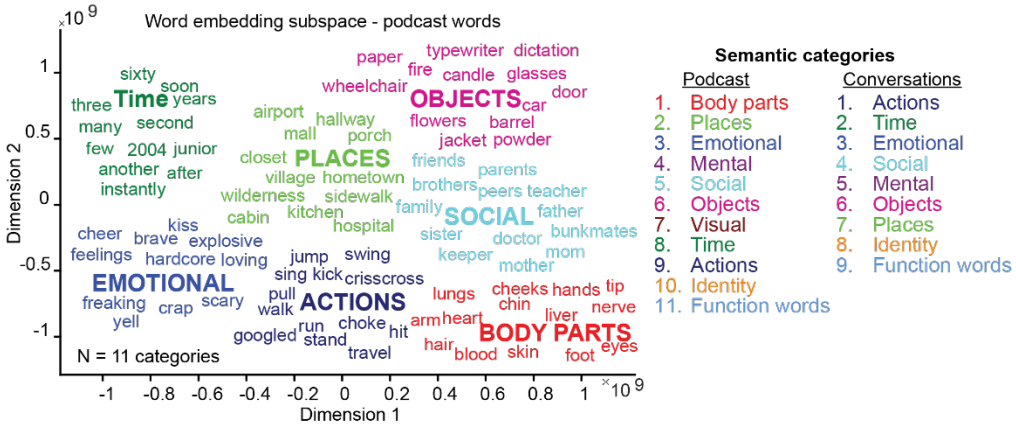


Figure 2. Semantic categories. Left - the semantic subspace shows how words with similar meanings have similar coordinates and cluster near one another after dimensionality reduction of their embeddings values (see *Methods*). The semantic category labels we gave to each cluster are capitalized. Right - the semantic categories we extracted from the podcast stories and a 30-minute conversation with one patient and two researchers.

Natural language stimuli and conversations. Participants will be asked to watch and listen to a selection of continuous narrative stories from *The Moth Radio Hour* podcast: 6 stories/monologues from 6 different speakers, totaling 47 minutes and 7,346 words. Stories will be played through the TV and speakers in the patient's room, and all patients will listen to the same stories. Surveillance cameras in the patient's room will be used to ensure they do not fall asleep while listening. We will also use high-quality microphones (Logitech, Blue Yeti, lavalier mics) to record unscripted conversations that patients naturally have with the doctors and visitors, and at least 3 conversations (20-30 minutes each; ~ 5,000 words) of myself and/or another researcher speaking with the patient. We will ask the patient questions about their family, career, favorite movies and food, etc. during these conversations.

Neural and audio data synchronization. The microphone in the patient's room and the audio from story monologues are directly synchronized with the neural recording system via BNC cables, providing analog input to the system. All signals, neural and audio, are recorded at 30kHz.

Control experiments with Jabberwocky stimuli. After story listening or conversations, patients will listen to 17 minutes of Jabberwocky stories (1,890 words) to assess neural specificity for semantics. Jabberwocky stimuli are words that are altered from the real words to become words that have no meaning, for example, "toom" or "skook". We will use the software, *Wuggy*, to transform podcasts and conversation transcripts into jabberwocky[52]. This program matches the subsyllabic segment length of each word and replaces words with letters that match phonetic probabilities of orthographic English. Jabberwocky preserves syntactic structure by retaining function words and morphemes, even though it lacks coherent semantics.

Audio transcription. All audio .wav files of natural conversations and storytelling will be automatically transcribed using Assembly AI, which also provides speaker diarization for conversations. Transcripts with word-level timestamps are imported into *Praat* software alongside the original audio, where spectrograms and timings are manually reviewed and corrected for word onset/offset and speaker attribution, then used in Matlab/Python.

Linguistic feature extraction. Semantic categories: To identify natural semantic categories, we will extract 300-dimensional word embeddings using a pre-trained *fastText* Word2Vec model in MATLAB[53,54]. Semantic similarity will be captured via cosine distance by t-SNE for dimensionality reduction and K-means clustering (k chosen via silhouette score)[55]. Clusters will be manually labeled and refined as needed. This method aligns with prior semantic studies[14,47,56] and has produced expected results on initial datasets (**Fig. 2**). For pitch, we will extract each word's mean pitch using *Praat* to assess neural sensitivity to speaker identity vs. vocal pitch.

Aim 1: Delineate the functional role of ACC neurons in language semantics and speaker identity.

Rationale: Effective communication relies on a mutual understanding of meaning, or semantics, as well as our ability to draw on knowledge of others' identities to interpret their words. The ACC supports the processing of both semantic and social information[4,15,17,19,57]. However, the computations used by single ACC neurons and their populations to code for features like semantics and speaker identity remain unknown. Here, we will address this gap in knowledge by characterizing neural responses to listened words during natural, continuous speech.

Hypotheses: We hypothesize that: 1) There is robust encoding of semantic features in ACC neurons - the same neuron in the ACC can encode many semantic categories and speaker identities. These neurons will be a mix of linear and nonlinear mixed selectivity neurons, determined from their best fit by different linear regression models. 2) Single neurons distinguish words from non-words (Jabberwocky stimuli). 3) Both semantics and speaker identity can be decoded from ACC population activity.

Experimental design: Patients will listen to a consistent suite of podcast stories and engage in natural conversations with researchers, visitors, and doctors. We will extract semantic categories from word embeddings (see *General Methodology*). Together, these activities provide a robust study of language comprehension to one's own spoken words and that of others.

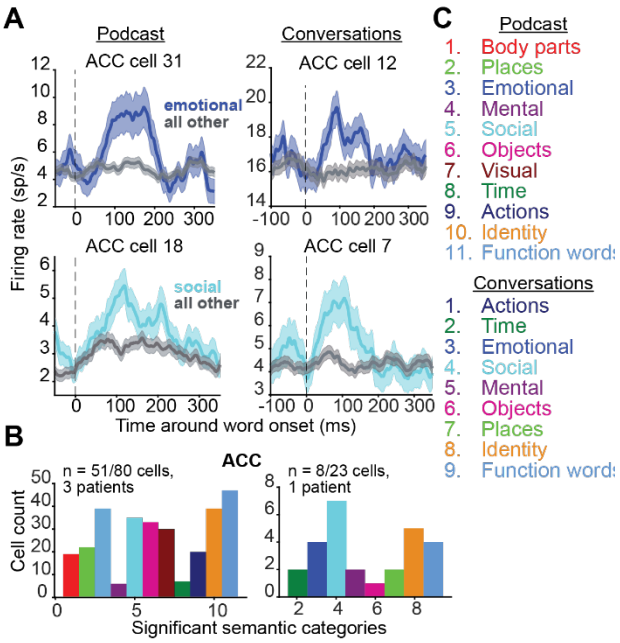


Figure 3. Single cell responses to semantic categories. **A**) Four distinct example ACC neurons with significant responses to the emotional and social words from podcast stories and conversations (rank-sum test comparing category response to all other words response with FDR correction across categories, $P < 0.05$). **B**) A summary of all ACC neurons with significant responses to one or more semantic categories, in both podcasts and conversations. Statistical test described in A. 45 out of 51 responsive neurons coded more than one semantic category in podcasts (left) and 7 out of 8 responsive neurons coded more than one semantic category in conversations (right). **C**) The semantic category legend for the colors shown in B.

Neural analysis: To determine whether ACC neurons are sensitive to distinct semantic categories and speakers, we will first use a Wilcoxon Rank-Sum significance test to compare firing rate responses between each semantic category and all others or a specific speaker and all others. For all analyses, a neuron's response to each word is the average firing rate across its duration (with an 80 ms delay, as observed in **Fig. 3**), normalized by word duration (and z-scored when appropriate). Thus, each word is associated with a speaker, a semantic category, and a neuron's response. To determine whether ACC neurons are sensitive to word meanings, we will use the same t-test to compare evoked responses to words and non-words. To investigate the role of linear vs. nonlinear interactions between semantics and identity, we will fit two linear regression models with lasso regularization[9,14]: **Equation 1**) a model with the semantic category labels (**Fig. 2**) and the speaker identity as categorical variables to predict a neuron's firing rate for each word and **Equation 2**) a model with terms for semantics, identity, and the pairwise interaction (product) between them. We will identify the model that best fits each neuron through a Bayesian model stacking analysis based on approximate leave-one-out cross-validation. Lastly, we will use a linear support vector machine (SVM) decoder to classify each word's semantic category or speaker identity from the normalized firing rates of all neurons, employing separate models for each[58]. I will use 10-fold cross-validation to assess the accuracy of predicting semantic category or speaker identity from unseen neuronal activity, comparing results to chance levels from shuffled models. The computational methods in this aim will closely follow recent publications from myself and our lab[9,59].

Equation 1 (linear model):

$$Firing\ rate\ (words, n) = \beta_0 + \beta_1 SemanticID + \beta_2 SpeakerID$$

Equation 2 (nonlinear interaction model):

$$Firing\ rate\ (words, n) = \beta_0 + \beta_1 SemanticID + \beta_2 SpeakerID + \beta_3 (Interaction)$$

Here, β is the coefficient/weight for each predictor, and a separate model is fitted for each neuron (n) on its firing rates for all words.

Expected outcomes: We expect ACC neurons to show significantly modulated firing rates during nonsensical, jabberwocky stimuli. This aligns with preliminary data from three patients showing 73% of ACC neurons (n = 80 neurons) had significantly higher firing rates during story listening than jabberwocky (**Fig. 4**). In both podcasts and natural conversations, results portray diverse responses across neurons to semantic categories and speaker identity (**Figs. 3 & 5**). Together, these preliminary findings support our hypothesis that ACC neurons are encoding the meanings of each word as well as who spoke them. From regression, we expect that the nonlinear interaction model will provide the best fit for most neurons, as nonlinear mixed selectivity has been shown to support a population subspace that can bind and generalize features (tested in Aim 2)[60–63]. Finally, preliminary results suggest that both semantics and speaker identity can be decoded from population activity using SVM models, with highest performance for speaker identity (**Fig. 5**).

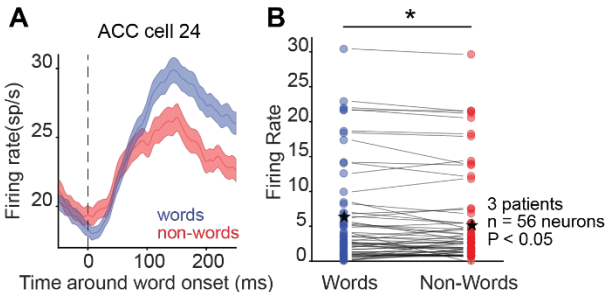


Figure 4. Single cell responses to words and non-words. **A**) A single ACC neuron firing rate response to the onset of listened words in the podcast and jabberwocky (nonsense) words. **B**) Firing rates for ACC neurons across 3 patients that exhibited a significant difference in firing rate between words and non-words (58/80 neurons total; rank-sum test; P< 0.05). Mean firing rate across neurons is shown as a black star- 6.13 for words and 5.78 for non-words.

Alternative approaches: 1) Word pitch and duration are features that we will also include in our models and can regress them out by using residuals in our analysis. Preliminary results from one patient indicate that even when pitch is included as a predictor (**Eq. 1**), the model retains significant coefficients for semantics and speaker identity (21/23 significant neurons). 2) Here, we transcribe speech from natural conversations using a semi-automated method with AI models (*Assembly AI*), but we will test other transcription models such as *Whisper* and *NeMo* to improve efficiency and accuracy.

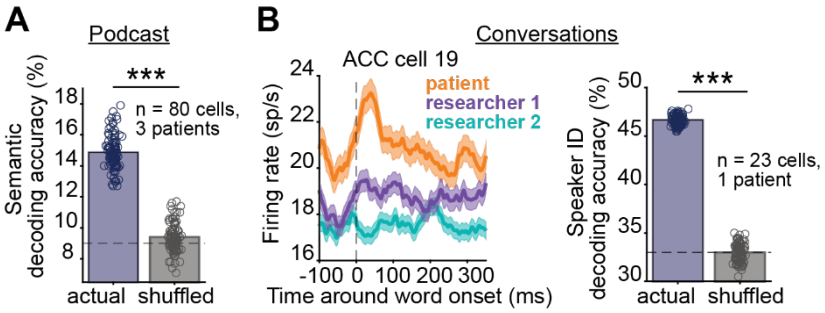


Figure 5. Decoding semantics and speaker identity in ACC. **A**) Decoding performance for each semantic category (one vs all) from linear SVM models using actual and shuffled data (chance =9%, Wilcoxon signed-rank test P < 0.001). **B**) Left - An example cell with different firing rate responses to all words spoken by each speaker. Right **-** Decoding performance for speaker identity from linear SVM models using actual and shuffled data (chance = 33%, Wilcoxon signed-rank test P <0.001). Dashed lines represent chance.

Aim 2: Determine how ACC populations align semantics with speaker identity.

Rationale: During natural conversations, we must bind the meaning of each word with the identity of the person who spoke them to monitor dialogue and respond in an appropriate manner. One implementation of binding lies in the coding power of neural populations[8,64], partly due to 'nonlinear mixed selectivity', where a neuron's response depends on not just the sum but the interactions between multiple features[60–62]. We recently discovered that neural systems bind value to action by encoding the value of options in semi-orthogonal subspaces of the population space, generated by neurons with both linear and nonlinear mixed selectivity[9]. Testing this hypothesis requires responses of single neurons, rather than local field potentials or neuroimaging signals. Here, we aim to test whether these neural mechanisms underlying value–action binding could also apply to other forms of binding, such as integrating semantic content with speaker identity.

Hypotheses: We hypothesize that: 1) The semantic-identity functions from Aim 1 will produce semi-orthogonal subspaces for semantics (as shown in **Fig. 6**, middle). 2) Semantics will generalize across speakers. A decoding model trained using semantics in speaker 1 should predict semantic categories of words spoken by speaker 2.

However, some words may carry speaker-specific meanings, while others are broadly consistent across different speakers. For example, the word “water” should have very similar representations between speakers, but the word “problem” might have strongly distinct representations when spoken by the doctor and not generalize well.

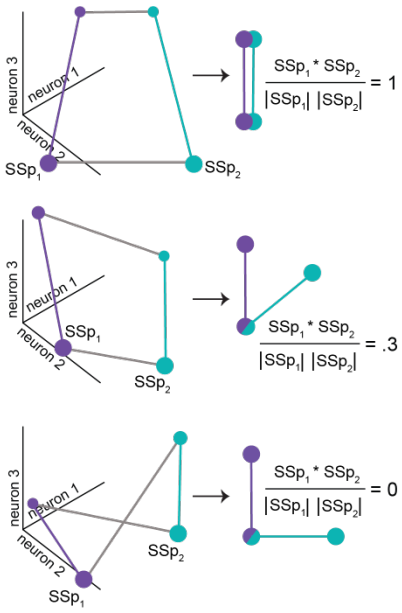


Figure 6. Illustration of subspace options for binding. Schematic of three different representational geometries that would lead to different subspace correlation results. **Top**: Two perfectly aligned semantic vectors for each speaker (SSp_1 and SSp_2) in population space (left) would produce a subspace correlation close to 1 (right), and would not achieve the goal of binding, as their respective features would be confusable. **Middle**: Two partially aligned (semi-orthogonal) semantic-speaker vectors would produce a subspace correlation between 0 and 1. These would also achieve the goals of binding and generalizing. **Bottom**: Two unaligned semantic vectors would produce a subspace correlation close to 0, and would produce strong decoding and binding but no generalization.

Experimental design: Patients will engage in natural conversations with researchers, visitors, and doctors. We will extract semantic categories from word embeddings (see *General Methodology*).

Neural analysis: To quantify the degree of overlap between speakers’ semantic subspaces, we will use the coefficients from the regression models in Aim 1, which define a semantic-encoding subspace for each speaker (SSp_1 and SSp_2, **Fig. 6**). To determine alignment, we will compute cosine similarity between vectors, reflecting their correlation. For example, a correlation of 1 reflects two parallel vectors that cannot implement binding, a correlation between 0 and 1 reflects semi-orthogonal vectors that permit binding and generalization, and a correlation of 0 reflects orthogonal vectors that have reliable decoding and binding but no generalization. We will also use the same SVM models discussed in Aim 1 to test generalization performance of semantics across speakers. We will train models from semantic categories of speaker 1 and test their ability to classify semantic categories of words from speaker 2. Validating the contribution of subspace alignment for binding: We will repeat the analyses in Aims 1 & 2 using a noise model and models fit to shuffled data and check that our correlations are significantly less than noise ceiling and more than the shuffle-based floor. Additionally, we’ve shown that the rate of misbinding errors depends on the degree of subspace separation[34]: as subspaces become more orthogonal, binding errors decrease, enhancing decision accuracy and reinforcing the notion that the geometric arrangement of neural subspaces plays a critical role in the binding process.

Expected outcomes: Since preliminary results in Aim 1 suggest semantics and speaker identity are both decodable from ACC population activity (**Fig. 5**), we expect subspaces between semantics from each speaker to be semi-orthogonal or orthogonal (**Fig. 6,** middle or bottom). If we find that the subspace correlation is 0 (orthogonal alignment) then we should also find nonsignificant generalization performance for decoding semantics across speakers. However, if our subspace correlation is semi-orthogonal, the generalization performance should also be significant. If this is the case, we expect to find words or semantic categories that are more speaker dependent and less generalizable (as suggested in our hypotheses).

Alternative approaches: 1) Because mixed selective neurons provide linear readouts in the population, we expect SVM models with linear kernels to yield the best performance, but we will also train models with nonlinear kernels and assess changes. 2) Another possible subspace outcome not shown in Figure 6 is a negative correlation, with vectors in opposite directions. This geometry would result in poor generalization of semantics across speakers.

Future directions with LFP analysis: Semantic classification models trained on LFP data can also be used to elucidate semantic generalization across speakers[38,39,61,63]. We will use SVM models to predict semantic categories from gamma power in brain regions where we record LFP signals, typically areas of the temporal and prefrontal cortex. We will test whether a model trained on words from speaker 1 can predict semantic categories from speaker 2 to assess the Cross-Condition Generalization Performance (CCGP)[38,39,63] of these models from different brain regions. Although we cannot identify the semantic-speaker selectivity of single neurons in these areas, the CCGP can provide insight into the subspace alignment and population geometry of these brain regions, complementing our binding discoveries in the ACC, and enabling us to assess whether similar population-level coding motifs exist throughout the brain's language and social processing networks.

Respective Contributions

Concept and project design: The proposal was designed to teach me how to study the neuroscience of language. Prior to becoming a postdoc, my work focused on understanding the neural basis of social learning and the use of wireless eye tracking to determine visual cues important for social interactions. Given my interest in social cognition, adding the study of language and communication to my research enterprise is a natural progression. To become knowledgeable of current research in the field of neurolinguistics, I took my sponsor, Dr. Hayden's class titled "Language and the Brain" at Rice University in Fall 2023. I also performed an extensive literature review, reading studies from prominent neuroscientists in the field, and specifically noted the tools they used for audio transcription and how they correlated linguistic features with neural data. Conversations with my consultant, Dr. Hamilton, were also very helpful. Together, Dr. Hayden and I decided to focus on studying semantics during speech comprehension. Given Dr. Hayden's years of background and expertise in studying and understanding the anterior cingulate cortex, we hypothesized that this brain region could be aligning both semantics and speaker identity to keep track of what was said and who said it. With my background in wirelessly recording neural and eye data from freely behaving animals, it was my goal to design an experiment to test our hypothesis that was as naturalistic as possible. Fortunately, due to the established and proficient research environment and team at BCM, recording neural and audio data during natural conversations and story listening is extremely feasible. Since we decided on the neural question and experiments, I recorded neural and audio data from 5 patients and will continue to record all experiments during this proposal.

Fellowship Application: Through numerous insightful discussions, Dr. Hayden, Dr. Hamilton, Dr. Sheth, and I developed the scientific and training goals for this project in a way that uses skills learned in graduate school, such as single neuron electrophysiology and computational modeling, and allows me to learn new techniques and analytical methodologies. I performed all the experiments and generated all the preliminary data in the research plan. From these results, I formed specific hypotheses for each aim. I wrote the first draft of this proposal and continued to refine the components, especially the specific aims page and research plan, after reviews from both sponsors and Dr. Hamilton, incorporating scientific and editorial suggestions.

Future Contributions: If funded, Dr. Hayden and Dr. Sheth will guide the implementation of the project, both from a theoretical perspective and in the acquisition and analysis of sEEG data from patients. Indeed, Dr. Sheth has experience overseeing more than 20 clinical trials, with 10 clinical trials currently active. Since I have just begun to analyze and extract linguistic features from language, Dr. Hamilton's guidance in transcription methods and programs for getting word embeddings and semantic categories will be very helpful. Though I have some background in computational modeling of electrophysiological data, Dr. Hayden (and our colleagues Dr. Fine and Dr. Johnston) will provide added expertise and support in computational analysis as well as knowledge of computational principles of ACC neurons. All of my mentors have published research that is relevant to the current proposal in journals including Nature Human Behavior, Cell, Neuron, and Nature Neuroscience. I will gather feedback from all mentors as I prepare and submit two manuscripts during this fellowship. The training described here will provide me with the tools necessary to further my career goal to become an independent researcher.

Selection of Sponsor and Institution

Sponsor (Hayden): Dr. Hayden is a McNair Foundation Scholar and Associate Professor within the Neurosurgery department at Baylor College of Medicine. Like me, Dr. Hayden began his career studying the neuroscience of decision-making using electrophysiology in monkeys. With over a decade of experience as a neuroscience professor, he has cultivated a lab and research environment that fosters creative and impactful work, a culture that has inspired and energized the entire neurosurgery research team at BCM. In just these two years that he has been at BCM, he has worked closely with human data and has published three empirical papers, two review papers, and two preprints (currently under review) in the field. He is also a co-PI on one project that is exclusively devoted to human neurophysiology (MH129439). Dr. Hayden is an advocate for his trainees and makes decisions with their best interests in mind. For example, given my interest in social cognition, Dr. Hayden suggested I add neuroscience of language and communication to my research pillars, and I knew his undergraduate degree and interest in linguistics would benefit me in this pursuit. He has also connected me with other mentors in the language neuroscience and speech processing field, such as my consultant, Dr. Hamilton. Dr. Hayden is also an expert in studying and understanding single neurons and population computations in the ACC, providing excellent support for accomplishing my analysis goals for neural alignment in this proposal. Dr. Hayden's commitment to my postdoctoral work and eventual transition to faculty in unparalleled. He encourages me to share my postdoctoral work through presentations and publications, and he helps me refine my research vision for the Franch lab. I look forward to continue working and learning from him under this fellowship. I cannot think of a mentor and lab environment better suited for me to achieve my research and training goals in this proposal and my ultimate goal of becoming an independent investigator.

Co-Sponsor (Sheth): Dr. Sheth has been an equal pillar of knowledge and support. Dr. Sheth is a world expert in functional neurosurgery, has conducted cutting-edge research in the neuroscience of mental health and mood disorders, and determined novel neurostimulation protocols for remediating negative feelings in people with treatment resistant depression and OCD. Because I am interested in language representation and fast temporal dynamics not measurable by noninvasive methods such as fMRI, I chose to work with Dr. Sheth, who is an accomplished neurosurgeon and scientist who has published many important papers in the field. I wanted to select a mentor with experience in recording and interpreting neural signals from the human brain, especially as it relates to neurological disorders, as I plan to continue working with physicians throughout my postdoc and career as a principal investigator. Dr. Sheth supports this mission, and he is helping me develop collaborations with other scientists, neurosurgeons, and clinical populations in the medical center and beyond. Dr. Sheth is incredibly down to earth and easy to have honest conversations with. I feel incredibly fortunate that he supports my postdoctoral work under existing clinical trials and that he is so dedicated to helping me realize my research and career goals in the Franch lab.

Institution: BCM is located in the Texas Medical Center, the largest medical center in the world - a 700-acre complex home to 19 academic institutions. BCM has primary affiliations with six teaching hospitals, each with national and international reputations for medical excellence. Basic scientific research covering a range of topics related to human health and disease built the foundation of BCM's name in research, which has since expanded into many interdisciplinary research facilities. Given my interest in social cognition and autism, I chose to switch to human neuroscience for my postdoctoral work and future career as I am not confident that complex social behaviors and disorders can be effectively studied in animal models. I wanted to switch to conducting neuroscience in humans with the goal to eventually study or identify neural changes in individuals with autism. I chose to complete my postdoctoral work at BCM because of the incredible faculty, clinicians, and medical and research environment that BCM has to offer. BCM offers significant opportunities for my growth and development, and even if I am not able to stay here for faculty, the connections I make here will position me well to secure a faculty role at a similar research and medical institution. The department of Neurosurgery hosts bi-weekly seminars with invited speakers, giving me access to experts in a broad range of topics. Together, BCM, the Department of Neurosurgery, and the TMC make an ideal environment in which to train me as a neuroscientist and carry out the proposed work.

Responsible Conduct of Research

As part of the America COMPETES Act of 2007, all trainees, fellows, participants, and scholars receiving support through any NIH or NSF training, career development, research education, or fellowship grants must receive instruction in responsible conduct of research at least once every four years during each career stage (undergraduate student, graduate student, postdoctoral associate).

For postdocs, there are annual training sessions held each spring in the months of March, April, and May. This training takes place via four training modules, each including lecture topics and small-group case study discussions. I have already completed this Responsible Conduct of Research course through CITI Program that included the following modules:

Module 1	Module 2	Module 3	Module 4
Data Acquisition & Record Keeping	Research Misconduct & Safe Practices in the Lab	Authorship, Peer Review, & Conflicts of Interest	Ethics in Research with Human Subjects
Responsible Authorship	Ethics in Biomedical Studies involving Animals	Collaboration in Research and with Industry	The Scientist as Responsible Member of Society
Mentorship & The Mentor-Mentee Relationship	Rigor & Reproducibility – Topics A	Rigor & Reproducibility – Topics B	The Impact of Diversity & Representation to Science

I will continue to practice RCR in the laboratory as I continue onwards in my science.

Other completed training:

Training	Format	Subject matter	Faculty participation	Duration of Instruction	Frequency of Instruction
Research Mentor Training Workshop via Gulf Coast Consortia (GCC)	In-person	Maintaining Effective Communication, Aligning Expectations, Fostering Independence, Addressing Equity and Inclusion, Cultivating Self-Efficacy. Participants benefit from case study and group discussions.	Robert Tillman, PhD, a Master Trainer with the National Research Mentoring Network (NRMN), is the lead facilitator for the GCC workshops and trainings	6 hours	Yearly – Completed on August 4, 2023
GCC Rigor and Reproducibility (R&R) Publication and Reporting Workshop	In-person	- Publication and Reporting through the Lens of Rigor and Reproducibility - Scientist – More than Just a Job. Responsibility to Public: Examples linked to Strategies - From Avoidance to Transparency in Research Behavioral Strategies to R&R in Publication and Reporting	- Suzanne Tomlinson, Gulf Coast Consortia, - Natasha Kirienko,PhD, Rice University - Stacey Gorniak, PhD, University of Houston	4 hours	Yearly – Completed on August 8, 2023

Sponsor Statement

A. Research Support Available

Sponsor Dr. Hayden:

Funding Source	Title	PI	Period	Total Costs
NIMH 125377 (R01)	Neural basis of behavior in freely moving macaques	Hayden	07/21-04/26	$3,467,676
NIMH 124687 (R01)	Modeling circuit-specific psychiatric deep brain stimulation and its cognitive effects in macaques	Widge, Hayden	09/20-07/25	$3,505,508
NIDA 038615 (R01)	Neuronal basis of persistence	Hayden	04/20—01/26	$1,993,244
NIMH129439 (R01)	Posterior cingulate cortex and executive control of episodic memory	Foster, Hayden, Sheth	04/22-03/27	$1,112,773
McNair Foundation	Intracortical studies of decision-making and executive control	Hayden	03/23-03/31	$2,400,000

Funds are currently and will continue to be available for the entire duration of Melissa's training. Grants expiring next year will go into no cost extension until at least 2027. Additionally, I have funds from the McNair Foundation that can support this research until 2031. Finally, I have four grants under review.

Co-sponsor Dr. Sheth:

Funding Source	Title	PI	Period	Total Costs
NINDS NS136631 (UH3)	Building Mood State Classifiers to Inform Deep Brain Stimulation (DBS) of Treatment-Resistant Bipolar Depression.	Sheth, Goodman	09/24-08/29	$9,742,839
NIMH MH130597 (R01)	Intracranial Investigation of Neural Circuitry Underlying Human Mood	Sheth	06/23-03/28	$4,664,155
NINDS NS121472 (U01)	Mapping Algorithmic State Space in the Human Brain	Sheth	06/21—03/26	$7,277,458
NINDS NS103549 (UH3)	Deep Brain Stimulation for Depression Using Directional Current Steering and Individualized Network Targeting	Sheth	09/17-08/26	$8,900,691

B. Sponsor's Prior Fellows/Trainees

Sponsor, Dr. Hayden:
Total prior fellows/trainees:

- 6 postdoctoral fellows, including 1 currently in the lab (Dr. Franch herself)
- 18 predoctoral trainees, including 2 currently in the lab
- 9 research assistants
- 30 undergraduate students, including 6 currently in the lab

Since establishing my lab in 2011, I have served as PhD advisor for 6 post-doctoral fellows including one who is still in my laboratory (Dr. Franch). All post-doctoral fellows in my laboratory publish at least one first-authored publication, and generally finish with several high-impact papers in prestigious journals such as *Nature Neuroscience* and *Neuron*. Below are five representatives who have trained in my laboratory:

Trainee	Position in Lab	Years in Lab	Current Position
Michael Yoo PhD	Postdoctoral Fellow	2015-2021 (includes PhD)	Assistant Professor, Tenure Track, IBS, Sungkyunkwon University
Pragathi Pryadharsini Balasubramani, PhD	Postdoctoral Fellow	2007-2014	Assistant Professor, Tenure Track, IIT Kanpur
R. Becket Ebitz, PhD	Postdoctoral Fellow	2006-2013	Assistant Professor, Tenure Track, Université de Montréal
Ruyuan Zhang, PhD	Postdoctoral Fellow	2011-2014	Assistant Professor, Tenure Track, Jiao

			Tong University
Justin Fine, PhD	Postdoctoral Fellow	2012-2016	Assistant Professor, Non-tenure Track, Baylor College of Medicine

Co-Sponsor, Dr. Sheth:

Dr. Sheth has mentored 6 predoctoral individuals and 12 postdoctoral individuals. Additionally, Dr. Sheth has mentored 27 Medical Students, 9 Medical Residents and Fellows, and 4 Undergraduates.
Below are five representatives who have trained in his laboratory:

Trainee	**Position in Lab**	**Years in Lab**	**Current Position**
Nicole Provenza, PhD	Postdoctoral Fellow	2021-2023	Assistant Professor, Tenure Track, Baylor College of Medicine
Elliot Smith, PhD	Postdoctoral Fellow	2013-2017	Assistant Professor, Tenure Track, University of Utah
Garret Banks, MD	Fellow in functional neurosurgery	2022-2023	Assistant Professor, Tenure Track, Baylor College of Medicine
Jiayang Xiao, PhD	Graduate student in neuroscience	2020-2024	Postdoctoral Fellow at Cedars-Sinai
Ben Shofty MD,PhD	Fellow in functional neurosurgery	2020-2022	Assistant Professor, Tenure Track, University of Utah

C. Training Plan, Environment, and Research Facilities

Drs. Ben Hayden and Sameer Sheth together designed this training plan as the next step in Dr. Melissa Franch's development as an independent researcher and professor at a research university.

Career goals: Melissa's long-term career goal is to become a full professor with an independent research lab, where she wants to continue investigating the neural computations of language during communication and social cognition, especially as it relates to autism spectrum disorder. I will ensure that she receives a thorough, comprehensive training in order to position her for her this career path. First, I will help her acquire skills to achieve her short-term career goal of obtaining grants and publishing papers to further develop into a productive, independent researcher and acquire a faculty position. I will use my diverse expertise in neuroscience and linguistics, as well as my vast network of collaborators and consistent funding to facilitate Melissa's growth of scientific knowledge in language neuroscience, ability to study neuroscience in humans, and computational and communication skills during this fellowship. Furthermore, Melissa works closely with and learns from my collaborators, such as her co-sponsor Dr. Sameer Sheth and consultants Dr. Liberty Hamilton and Dr. Ashutosh Sabharwal, among many other faculty here at BCM. This is highly important, as human intracranial research requires synergy and cooperation with patients, surgeons, and research and clinical teams. Her development of experimental, computational, and communication skills will enable her to effectively conduct, evaluate, and share research, positioning her for a highly competitive job in academia. Melissa's previous training using electrophysiology and computational neuroscience methods in her PhD work has prepared her well for her postdoctoral research, with many transferable skills in addition to the new ones she will develop during this fellowship. In summary, our training plan will facilitate Melissa's achievement of both her short and long-term career goals.

Individual Development Plan (IDP): Melissa, Dr. Sheth, and I use results from her IDP assessment (taken annually) to create and update her training plan. Based on Melissa's previous experiences and current expertise, we have developed a comprehensive plan with detailed activities for enhancing her knowledge in linguistics and language neuroscience, and computational and professional skills, discussed in further detail below.

Professional and Academic Mentorship: Since her initial inquiry of joining our team and my lab as postdoc, Dr. Sheth and I have maintained a positive and productive mentorship with Melissa. We communicate effectively with each other, which leads to successful research. She will continue to have unrestricted access to both of us as mentors, as I have an open-door policy and individually meet with each of my trainees weekly. I will also provide the technical and educational resources she needs to complete her proposed project and develop into an independent scientist. As my office is right next to hers and Dr. Sheth's, we often discuss and formulate ideas through organic day-to-day interactions. We also have formal discussions on a weekly basis to examine experimental progress, address potential obstacles, and review background literature. Through these regular meetings, Melissa will learn how to design and continually refine experiments, which will help achieve her goals

and answer important scientific questions. Moreover, we have weekly Hyaden-Sheth joint lab meetings where Melissa presents her data on a rotating basis. These presentations not only enhance her communication skills, but also provide constructive criticism from myself and other lab members to improve her research. Importantly, in addition to meeting with me, the lab, and Dr.Sheth, Melissa discusses her findings with consultant and language neuroscientist, Dr. Hamilton, every month.

Feasibility and Timeline: Melissa's proposed work is part of our current clinical trial for patients with intractable epilepsy patients to undergo neural monitoring to determine epileptic tissue. Melissa has already recorded the proposed experiments and neural data from six patients. Dr. Sameer Sheth and I will continue to oversee this project and her clinical trial. Melissa will record from 20 patients to account for sufficient statistical power and effect size, so she should finish data collection in the first 1.5 years of the proposal, and finish analyses by end of year two. We plan to submit a manuscript on semantic coding in ACC during year 2 (Aim 1) and another manuscript on semantic and speaker neural alignment in year 3 (Aim 2) of this fellowship.

Goal 1: Learn human intracranial electrophysiology and speech processing. The success of Melissa's research and her future research program relies heavily on interdisciplinary collaboration among hospitalized patients, clinicians, and researchers. To support this, I am committed to providing her with comprehensive mentorship - not only from myself but also from physicians and other principal investigators. This guidance will equip her with the skills needed to conduct impactful research, both here at the Texas Medical Center (TMC) and at any institution where she may serve as faculty in the future.

Clinical research: Impressively, the Neurosurgery research group at BCM is a major leader in human intracranial research, with proficiency in examining neural activity from patients during naturalistic behaviors. The group has one of the highest numbers of patients with single-unit recordings in the U.S., allowing Melissa to test specific hypotheses about the neuronal mechanisms of real-time communication. During this fellowship, Melissa will be working closely with physicians such as co-sponsor, Dr. Sameer Sheth. She will attend and present her research at functional neurosurgery conferences, such as ASSFN and WSSFN, providing her with opportunities to connect with neurosurgeons and explore institutions for potential future collaborations and career opportunities. Moreover, Melissa will shadow Dr. Hamilton as she conducts her experiments at the Texas Children's Hospital, allowing her to network with neurosurgeons from nearby hospitals while gaining hands-on experience with Dr. Hamilton's mobile neural and speech recording system, which can be moved between rooms – showing Melissa alternative approaches for conducting language neuroscience research in a hospital setting. Certainly, this training will provide Melissa with professional connections and clinical skills to support her current and future research. Technical skills. While Melissa is already familiar with recording neural activity from single neurons, she is learning how to record and analyze both neural and audio data during this fellowship. I have suggested Dr. Bartoli, a junior PI in our group, to train Melissa on hardware and software resolutions to remove noise from the neural signals. Additionally, Melissa will meet with her consultants, Drs. Hamilton and Sabharwal, to learn processing and transcription of speech recorded from wearable and room microphones. Melissa will learn how to implement this technology and synchronize it with neural data during this fellowship.

Goal 2: Develop computational methods to study the neuroscience of language. Melissa will gain insight into how the neuroscience of language has been studied and learn to apply computational tools effectively to address significant scientific questions in this area.

Knowledge in the neuroscience of language: To learn about previous studies, Melissa took my class, "Language and the Brain" at Rice University in 2023 where we reviewed ten different papers from various labs on the neuroscience of language. Melissa will continue to read manuscripts on the neural basis of language and present them at journal clubs. She already presented one paper this year that analyzed neural data during natural conversations and another one about neural representations of semantics. Additionally, Melissa will continue to attend conferences and workshops for language neuroscience. In May 2024, she attended the Neurobiology of Language workshop at MIT where we engaged in whole group discussions with leaders in the field about the definition of language, the purpose of language, and the theories of language representation in the brain. During this award, my entire lab will attend The Society for the Neurobiology of Language (SNL) Conference held in Washington, DC in 2025 and Melissa attends the Society for Neuroscience Conference each year to learn about recent studies in the field. Dr. Hamilton also suggests relevant and important literature for Melissa to review. Word transcription and linguistic feature extraction: I have been really impressed with Melissa's ability to leverage new tools in AI to improve speech transcription. Melissa will learn how to extract linguistic features like pitch, semantics, and speaker identity during this fellowship. Melissa will learn these skills from Hayden lab members who have degrees in linguistics and from Drs. Hamilton and Sabharwal, who are experts in using Praat. forced

aligners, and WordNet.
Computational neuroscience: My lab has developed a mathematical framework for subspace orthogonality, binding, and generalization that was recently published. During this fellowship, Melissa will receive mentorship from myself and the two first authors on the study, Dr. Johnston and Dr. Fine. While they both work remotely, Dr. Fine travels to Houston at least 3x/year, and Melissa meets with each of them over Zoom when she has questions. Melissa's prior research experience and analytical skills make her exceptionally well-prepared to carry out the alignment analyses outlined in this proposal. Preliminary results in the research plan demonstrate her ability to test the proposed neural theories and elucidate neural coding of word meanings and speaker identity in the ACC. To further her knowledge of modeling linear and nonlinear neural interactions with language, she will take the "*Regression and Linear Models*" course, STAT 615, at Rice University in the Fall of 2025. Melissa will also present her findings at the Rice Neuroengineering Interface Symposium and at Cosyne (Computational and Systems Neuroscience conference) during this fellowship. For additional LFP analyses, Melissa will be mentored by Drs. Sheth, Hamilton, and Bartoli, who are experienced in analyzing these neural signals and she will review the Mike X Cohen *Time Series Analysis* course on YouTube. Finally, Melissa will take *the BCM Rigor and Reproducibility Workshop* to ensure robust and unbiased analysis and interpretation of her results.

Goal 3: Prepare for an independent research career. A key aim of Melissa's postdoctoral training is to develop the necessary skills to run her own lab and research enterprise.

Oral & written Communication: Melissa presented preliminary findings from her postdoctoral work at 4 conferences this year and will continue to present her work in oral and poster presentations at various local and global conferences. Moreover, I recommended that Melissa teach two lectures on language neuroscience in Spring 2025 and 2026 for Rice University's undergraduate course, *Systems Neuroscience* (NEUR 380). Melissa will also develop her writing skills for grants and manuscripts. To improve her grantsmanship, I held a "mock study section" where BCM neuroscience faculty reviewed her Specific Aims page for this proposal, and I send her my grants and proposals to review and edit. I encourage Melissa to apply for all funding opportunities and during the last year of this fellowship, she will apply for a K99/R00 Pathway to Independence award. Melissa also peer edits by other lab members and collaborators. Moreover, I have Melissa review manuscripts from other labs for journals and she will continue to do so during this fellowship. Notably, Melissa has already written a postdoctoral manuscript on language processing in the human hippocampus, now on bioRxiv. Finally, she will gain writing skills when preparing manuscripts that summarize findings from the proposed research. Leadership and transition to faculty: Melissa currently mentors 2 graduate students, 2 research technicians, and 2 undergraduate students. She oversees most aspects of their projects and created a designated Slack channel where we share fellowship opportunities, graduate school advice, and new papers on topics that interest them. Throughout this fellowship, Melissa will continue to mentor these students and new people who join the lab. Melissa also interviews prospective lab members. Moreover, I encouraged Melissa to apply for the *Leading-Edge Fellows Program* that provides community and resources for women in academia, and she did so in February 2025. Importantly, Melissa attends chalk talks and research seminars from postdocs being considered for faculty in neuroscience at BCM. Melissa will also participate in BCM Postdoc Career workshops, where she will learn tips for mentoring, writing an impressive manuscript, and developing her CV. The team of mentors we have curated for Melissa have a strong track record of guiding postdoctoral fellows into faculty positions, who will, together with these activities, offer Melissa focused mentorship for this proposal and for becoming an independent investigator.

Environment and Research Facilities:

Located in the Texas Medical Center (TMC), the largest medical center in the world, my lab offers Melissa unmatched opportunities to take advantage of our technical and funding resources, diverse training programs, and strong collaborative network. Melissa has access to a unique collegiate environment where experts across neurosurgery, electrophysiology, engineering, computer science, and psychology, including Dr. Sheth's lab, collaborate closely - an atmosphere that will undoubtedly support her growth. Our lab and the Baylor College of Medicine neurosurgery research team are fully equipped for her project, with resources such as Behnke-Fried electrodes, sophisticated data acquisition systems, and high-performance computing tools. We have two Neural Signal Processor systems located in the Epilepsy Monitoring Unit (EMU) at Baylor St. Luke's Hospital, allowing us to conduct experiments directly adjacent to patient rooms. This setting, along with Melissa's strong relationship with the hospital staff and her completion of all required institutional research training, will enable her to seamlessly collect data from the roughly 10 patients we enroll each year. Certainly, Melissa has an arsenal of resources – available patients, supporting lab members and clinical staff, recording technology, data analysis software, and consistent funding to successfully complete her project.

D. Number of Fellows/Trainees to be Supervised During the Fellowship

Sponsor, Dr. Hayden:

Trainee	Position	Entry	Trainee	Position	Entry
Assia Chericono	Graduate student	2023	Ana Guadalupe Chavez	Graduate student	2023
Lizzie Mickiewicz	Post-bachelors associate	2024	James Belanger	Undergraduate assistant	2024
Amay Parmar	Undergraduate assistant	2024	Brian Kim	Undergraduate assistant	2024

Co-Sponsor, Dr. Sheth:

Trainee	Position	Entry	Trainee	Position	Entry
Vigi Katlowitz MD, PhD	Neurosurgery resident	2023	Daniko Paulo	Fellow in functional neurosurgery	2024
Shraddha Shah	Postdoc	2022	Habiba Azab	Postdoc	2020
Kat Kabotyanski	Graduate student	2015	Holden Bentley	Medical student	2024
Kasra Mansourian	Medical student	2024	Davin Devara	Medical student	2024

E. Applicant's Qualifications and Potential for a Research Career

(Sponsor, Dr. Hayden):

I offer my strongest possible recommendation for Melissa for the NIH Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral F32 Fellowship. Quite simply, Melissa is one of the strongest post-doctoral fellows I have met, and I consider myself very lucky that she decided to join my lab. I am highly confident that she is a major star and will make a significant contribution to the scientific community. I met Melissa when I was visiting the Texas Medical Center before I was recruited. At that point, she was finishing her Ph.D. in Valentin Dragoi's lab. During my discussion with her about her research I was highly impressed by her deep and impressive knowledge of the field she was working in, but also by her creativity in thinking about new problems in that field. When I moved to BCM, she interviewed in my new laboratory for a joint position working with myself and Sameer Sheth.

Melissa is eminently qualified for a high-impact research career, and has the highest possible potential. I will delve into her major strengths. **Work ethic**: Melissa is a highly committed scholar. Although her original background (as a high school teacher) did not provide her a standard preparation for a research career, she devoted herself diligently to overcoming that lack of training, and worked harder than anyone else in her graduate school class. It is this commitment to working hard that led to her to succeed in graduate school, and that will lead to her continued success as a post-doctoral fellow. **Broad vision**: In addition to hard work, success in science depends critically on the ability to understand a problem in a detailed way and then take the birds eye view and see the most important points, and the areas of limitation that need to be addressed. In my year working with Melissa, I have been consistently impressed by her ability to read papers and attend talks and immediately grasp the big picture implications and see its relationship to the rest of the major questions in the field. **Analysis skills**: But of course, success requires more than just an understanding of what needs to be done, in an abstract way. It requires the ability to implement solutions. Nowadays, in the field of electrophysiology, that means the ability to write good, high quality computer code that can analyze increasingly large and complex datasets. It also requires a commitment to following the literature on neural statistics and understanding and implementing new analyses. Of course, it also requires having enough of a broad understanding of the field that one can decide which analyses to apply. Melissa has already demonstrated each of these, in spades. **Creativity**: But of course it also involves having the creative vision to have new and original thoughts. Indeed, this is perhaps Melissa's greatest strength. It has been a great pleasure to collaborate with her, because she is able to come up with excellent new ideas. This is true not only for her own project, but also for other projects that she helps with, including several junior members of the lab.

Indeed, Melissa's **leadership** is another great strength, and one that will surely benefit her greatly as she moves to her own lab. As my lab has expanded to include language (Melissa's area of focus) she has taken on a leadership role, and has begun helping other students, both undergraduate and junior graduate

students, in all the aspects. That includes developing projects, thinking through analyses, and preparing their work for presentations. Indeed, Melissa has been acting almost as a co-mentor with me in this domain, which is highly gratifying, but also gives her additional training. But most of all, it's a demonstration of her leadership skills – the students in the lab come to her for advice and counsel because she already has the major skills needed to run her own lab.

Based on her performance in my lab, I have no doubt that Melissa will continue doing extraordinary work on this project and develop into a productive academic researcher and professor. Melissa's genuine enthusiasm for research questions, particularly those related to language, and to social neuroscience more broadly, drives her to learn many complicated techniques (for both data acquisition and data analysis) in a short time span. On a personal note, Melissa is a pleasure to work with. She is well liked by all colleagues and is a great asset to the social environment of my lab. She is a team player, and always welcomes a collaborative project in order to develop new ideas. I am confident that Melissa will complete the proposed research, and ultimately contribute significantly to the field in future years. Recognizing Melissa's work with the Kirschstein-NRSA Individual Postdoctoral Fellowship (F32) will be a significant step towards her goal of becoming an independent investigator.

(Co-sponsor, Dr. Sheth):

I enthusiastically recommend Melissa for the NIH Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral F32 Fellowship. From our very first interaction during her postdoctoral interview with Dr. Hayden and our group, Melissa made a strong impression on me. Her dissertation work laid an excellent foundation for her postdoctoral research with us, and her current and future research goals align seamlessly with the direction of our projects. Over the past year, I have thoroughly enjoyed collaborating with Melissa, and I am excited to continue our work together throughout her postdoc and beyond.

Melissa has been an asset to the group, as she brings her expertise in using electrophysiology to record and study single neurons in the primate brain. She is also a team player and does the micro- and macroelectrode setup in the EMU on the evening of the patient's surgery. The setup involves connecting the implanted hardware on the patient to our recording devices. This setup and ensuring the neural signal quality is clean truly benefits the entire team, as many labs in our group will collect data and perform research tasks with the patient. She has also developed an extensive knowledge of our system and the code and software that supports it, allowing her to troubleshoot issues and help others when problems arise. I think Melissa's prior roles as a teacher and clinical research coordinator prepared her well for human research, as she is incredibly patient, kind, and empathetic when working with the patients and clinical care team.

I have been thoroughly impressed by Melissa's exceptional scientific reasoning skills, particularly her ability to quickly understand unfamiliar research projects and provide insightful interpretations of results. Melissa consistently demonstrates this acumen during our Hayden-Sheth joint lab meetings, where her contributions stand out for their depth and impact. She offers constructive, valuable feedback to graduate students, medical students, and research fellows, often suggesting crucial modifications to experimental designs, innovative analyses, or more effective ways to visualize data. The productivity of our lab meetings significantly increases when Melissa is present - her contributions drive meaningful progress, and her insights elevate the quality of the research we discuss.

Melissa's clear vision for her future research lab as a principal investigator is one of her most distinguishing qualities. She has used this vision to deliberately shape the skills and experience she pursues during her postdoctoral training. Melissa has thoughtfully connected her current research on language comprehension with her past expertise in eye-tracking, laying the groundwork to study human communication and social interaction in a truly integrated and comprehensive way as a PI. Her long-term goal is to extend this research to individuals with autism, an area she feels passionately about. I fully support Melissa's research aspirations, and we are already taking steps to turn her vision into reality. Through our collaborations with Dr. Hamilton and the neurosurgeons at Texas Children's Hospital, we plan to leverage our ongoing work with children with epilepsy who are undergoing intracranial recordings, many of whom also have autism, to advance these important studies.

I am fully committed to supporting Melissa's research and her future success as a PI. With more than 10 years of experience in clinical trials and translational research, I am well-equipped to guide her through the proposed research and the next stages of her career. Melissa's passion, dedication, and scientific acumen make her an exceptional candidate, and I am confident that she will make significant contributions to our understanding of communication and social interaction. It is my pleasure to recommend her without reservation for the NIH F32 Fellowship, and I look forward to seeing the impact of her research in the years to come.

The University of Texas at Austin
Speech, Language, and Hearing Sciences
Moody College of Communication

2504 A Whitis Ave., A1100
Austin, Texas 78712-1074
512-471-4119
slhs.utexas.edu

March 20, 2025

To Whom It May Concern:

I am pleased to serve as a consultant on Dr. Melissa Franch's NRSA post-doctoral application, and to offer my strong support during her training with Drs. Benjamin Hayden, Sameer Sheth, and Ashutosh Sabharwal. I met Melissa earlier this year while giving a talk at Rice University, and right off the bat, I was impressed with her motivation to study the neuroscience of language to inform our understanding of communication and social cognition in humans. Melissa has made many research accomplishments in just this first year of her postdoc, and the skills she gains in this proposal will be instrumental to her contributions to the field. Her prior work on social interactions in freely moving macaques is also particularly unique, and positions her well to perform the research outlined here.

Melissa's training goals to expand her knowledge of the literature on language neuroscience and to use intracranial electrophysiology to study the neural dynamics of semantics and identity during language comprehension fit well within the context of the collaborative research I conduct with nearby neurosurgeons at Texas Children's Hospital (TCH) in Houston. I have been working with my collaborators at TCH since 2019, and received NIH R01 funding for a collaboration with them in 2020 (R01 DC018579), followed by DoD funding from the Congressionally Directed Medical Research Projects (CDMRP) in 2024 for a project related to language development in children with tuberous sclerosis complex (TSC), many of whom are also on the Autism Spectrum (TS230003). This new DoD grant is through a partnering PI mechanism for which my lab and BCM are the two funded sites, so we already have a fruitful ongoing and growing collaboration. I look forward to consulting with Melissa on theories and research in the neural processing of speech, particularly as it relates to semantics. To help Melissa gain expertise in this broad literature, I send her papers to read and we discuss them during my monthly visits to Houston or in my lab's journal club that Melissa can attend virtually. Indeed, although my lab is based in Austin, I am in Houston monthly for research and I am fully committed to mentoring Melissa during this fellowship. In addition, my lab holds a weekly "mini course" in which we discuss research methods related to the lab, including language, linguistics, and phonetics, neurophysiology and intracranial recordings, and more. By shadowing my experiments at TCH, Melissa will gain expertise in studying the neural basis of language in children, including those with autism. This experience - and exposure to potential collaborations with clinicians - will enhance her research abilities beyond those needed for this fellowship, preparing her for success as a principal investigator.

I have an excellent professional relationship with Melissa's sponsors, Dr. Hayden and Dr. Sheth. I am already collaborating with Dr. Ben Hayden on new work related to the current project, and have active grants with Dr. Howard Weiner (Neurosurgeon at TCH/Baylor College of Medicine) and Dr. Anne Anderson (epileptologist at TCH/Baylor College of Medicine). I plan to consult with Melissa not only on theoretical issues, but also on experimental design and data analysis. I will provide direct training in concepts such as automated transcriptions and analysis of conversation data (including use of forced aligners for transcribing language data, Praat, and other methods). I

will also provide support for analysis of neural recordings – given my prior work in human intracranial recordings (LFP) as well as multi-unit/single-unit recordings in mice and rats during my PhD, I have appropriate expertise in this area. I will also be sure to connect Melissa with other postdocs, graduate students, and research assistants in my lab who can provide additional assistance and supplement her work with me. I am also willing to co-author manuscripts as appropriate. Melissa is a highly promising scientist and I think she will have extensive training opportunities at Baylor College of Medicine. I am delighted to help in any way I can to facilitate her research and training.

In summary, it is a great pleasure to work with Melissa and her sponsors to be a part of this pioneering project that I believe to be a first step in Melissa's long and productive research career. The environment at Baylor College of Medicine is excellent for intracranial recordings as I can attest from years of collaboration with clinicians in the Texas Medical Center hospitals, the strong support for research, and highly collaborative environment. Melissa's research is exciting and interdisciplinary, and I believe this proposal represents a strong plan and commitment to training that will bolster her future plans.

Sincerely,

Liberty Hamilton, PhD
Associate Professor
Department of Speech, Language, and Hearing Sciences, Moody College of Communication
and Department of Neurology, Dell Medical School
The University of Texas at Austin
Adjunct Faculty, Department of Neurosurgery, Baylor College of Medicine

March 25, 2025

To Whom It May Concern,

I am delighted to serve as a consultant on Dr. Melissa Franch's NRSA postdoctoral application and to offer my full support throughout her training with Drs. Benjamin Hayden, Sameer Sheth, and Liberty Hamilton. Having interacted with Melissa during joint lab meetings at BCM, I was particularly impressed by her dedication to understanding the neural computations underlying social interaction and communication. She has thoughtfully assembled an exceptional mentorship team, reflected in her promising preliminary findings and remarkable productivity - highlighted by a manuscript on bioRxiv within her first postdoctoral year. Clearly, Melissa's mentorship team and research environment are ideally suited to support her continued success in language neuroscience research during this fellowship and beyond, and I look forward to contributing to her career development.

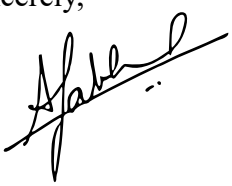
My research intersects engineering, behavioral sciences, and medicine. My lab integrates AI techniques with classical signal processing, statistical learning, and computer engineering methods to develop novel wearables to capture bio-behavioral makers and to create novel AI-based approaches to analyze speech data to inform mental health and neuropsychiatric disorders. For example, we developed the Social Ambiance Measure (SAM), which analyzes unconstrained audio recordings to assess social environments by detecting the number of concurrent speakers, serving as a proxy for social ambiance. We also developed RACER, which utilizes large language models to automate the generation of transcripts and emotional content from semi-structured interviews in healthcare settings. Methods used in SAM and RACER are analogous to Melissa's speech detection and processing goals. I am looking forward to being available as a mentor for her in this area.

To mentor Melissa with skills related to automatic speech recognition and transcription, I will continue to meet with her weekly in our joint lab meetings, where we discuss the ongoings of her project. I have seen her equipment set up in the hospital and recommended using specific recording technologies - such as wearable lavalier microphones - to capture speech from researchers, family members, or physicians during their interactions with patients, and I will continue to offer relevant advice. Outside of weekly lab meetings, it's easy to meet with Melissa as my lab is just across the street from her office. We will schedule additional meetings where I will teach her how to transcribe speech using AI language models and how to manually identify phonemes of words from the spectrograms in Praat. While AI transcription models such as Whisper/Assembly AI/RACER can automatically detect words, knowing how to also manually

detect words in Praat is especially helpful during overlapping speech, which often occurs during natural conversations when two speakers may be talking simultaneously. Certainly, we will continue this mentorship throughout the course of her fellowship.

Overall, I am eager to collaborate with Melissa and her mentors on this innovative project, which will result in an impactful research career for her. I have helped six postdocs in my lab earn and transition into faculty positions and will provide the same guidance for Melissa. I have an excellent professional relationship with Melissa and her sponsors, Dr. Hayden and Dr. Sheth, which is crucial to effective communication and high productivity. Melissa is an exceptionally promising scientist, and Baylor College of Medicine will provide her with outstanding training opportunities. It is my pleasure to support her in any way possible as she embarks on this important phase of her scientific journey.

Sincerely,



Ashutosh Sabharwal, PhD
Ernest Dell Butcher Professor of Electrical and Computer Engineering, Rice University
Adjunct Faculty, Department of Neurosurgery, Baylor College of Medicine
Director, Rice Digital Health Initiative
Co-Director, Methodist-Rice Digital Health Institute

Description of Institutional Environment and Commitment to Training

Institutional Environment

Baylor College of Medicine (BCM) encompasses cutting-edge technologies, collaborative faculty, and outstanding shared facilities, making its institutional environment the ideal setting for completion of my proposed research plan. Located in the largest medical center in the world, the Texas Medical Center, BCM is optimally positioned to collaborate with other prestigious research institutes to construct novel techniques, advance scientific discovery, and address complex topics related to human health and disease. Coordination among several educational offices with the Graduate School for Biomedical Sciences (GSBS) program and the Office of Postdoctoral Affairs ensures students and post-doctoral fellows receive individualized, reliable support. The Office of Postdoctoral Affairs within the Graduate School of Biomedical Sciences supports nearly 600 postdoctoral trainees who come from across the United States and 46 countries. Postdoctoral associates and fellows conduct research within eight basic sciences departments, 17 clinical departments or eight academic centers with over $500 million in research funding. Access to resources spanning career development, academic success, poster-printing services, Responsible Conduct of Research courses, and additional workshops and training opportunities exemplify the level of commitment BCM has to training. BCM also offers a multitude of Advanced Technology Labs, including the Center for Advanced Magnetic Resonance Imaging (CAMRI), a state-of-the-art imaging facility.

Resources for Career Development

BCM places high value on maintaining accessible resources for students and postdocs in career development. Specifically, the Career Development Center, located within the Office of Student and Trainee Services, is devoted to help students and postdocs explore, identify, and achieve professional aspirations through meaningful careers. Further, the Career Development Center hosts many workshops and events supportive of postdocs establishing a scientific network. Additionally, postdocs can review curated, program specific career resources and templates through the "*Career Hub*" database. Several guides and videos are readily accessible for postdocs wanting to learn how to generate professional contacts, conduct informational interviews, effective resume/CV writing, develop research proposals, or launch an independent academic research career. Moreover, students and postdocs can schedule individual career coaching appointments with professional experts. These institutional resources for trainees help transition students and postdocs into the subsequent chapter of their career.

Department of Neurosurgery

At all levels within the Department of Neurosurgery, commitment to training persists as an integral component to the department. With more than 6000 square feet of laboratory space, collaborative research flourishes. Neurosurgery faculty are heavily involved in the training of postdocs and students in the Neuroscience Graduate Program. Multiple faculty members are either course directors or lecturers as part of the first-year core curriculum. With the arrival of my sponsor, Dr. Hayden, to the department, trainee resources and support have expanded even further. Dr. Hayden has established consistency in bi-weekly journal clubs, bi-weekly data presentations, and spearheaded multiple programming learning opportunities. Paired with frequent visiting speakers and consistent seminars featuring prominent neurosurgeons and neurosurgical researchers from across the country, these additions foster a motivational environment where trainees are exposed to a variety of research topics and provided with opportunities to forge nation-wide connections.

Department of Neuroscience

The Department of Neuroscience is dedicated to training future leaders in neuroscience research through the Neuroscience Graduate Program. With an aggregated total of approximately $30 million in annual research funding, the Department of Neuroscience has the capacity to support trainees in their research endeavors. Neuroscience department faculty members actively participate in both the research and academic development of students within the Neuroscience Graduate Program, acting as both lecturers and course directors for neuroscience program curriculum. Further, the department exhibits their continued commitment to student training through holding the annual Rush and Helen Record Neuroscience Research Forum, a department-wide symposium highlighting student research through student-led talks and poster presentations.

Intellectual Environment

With educational backgrounds and research spanning the fields of biology, psychology, chemistry, genetics, physics, mathematics, engineering, computer science, medicine, and more, the collective intellectual environment accessible to the student is top tier. Trainees spend much of their time conducting research,

attending seminars, and actively participating in journal clubs. Along with other topic-specific journal clubs specializing in machine learning and theoretical neuroscience, trainees have multiple venues for participating and learning from interaction with students, other postdoctoral fellows, and faculty.

Neurotechnology Development: This research has direct implications for developing speech neuroprosthetics. Our research team is a member of BrainGate, a pre-eminent cross-institutional research team focused on BCI. I will attend weekly BrainGate meetings. In addition, I will meet monthly with Dr. Nishal Shah, a member of the Rice Neuroengineering Initiative and the BCM Neurosurgery department to support the clinical application of our findings.

PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001

Expiration Date: 12/31/2027

Use of Human Specimens and/or Data

Does any of the proposed research in the application involve human specimens and/or data *

● Yes ❍ No

Provide an explanation for any use of human specimens and/or data not considered to be human subjects research.

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

Other Requested Information

Human Subject Studies

Study#	Study Title	Clinical Trial?
1	Neural coding regimes for language comprehension in human cortex	Yes

Section 1 - Basic Information (Study 1)

1.1. Study Title *

Neural coding regimes for language comprehension in human cortex

1.2. Is this study exempt from Federal Regulations * ❍ Yes ● No

1.3. Exemption Number ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8

1.4. Clinical Trial Questionnaire *

1.4.a. Does the study involve human participants?	● Yes	❍ No
1.4.b. Are the participants prospectively assigned to an intervention?	● Yes	❍ No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	● Yes	❍ No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	● Yes	❍ No

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 1)

2.1. Conditions or Focus of Study

- Epilepsy

2.2. Eligibility Criteria

Epilepsy Cohort: adult patients scheduled to undergo intracranial seizure monitoring who provide informed consent.

2.3. Age Limits	Min Age: 18 Years	Max Age: 70 Years
2.3.a. Inclusion of Individuals Across the Lifespan	Inclusion_of_Individuals_Across_the_Lifespan.pdf	
2.4. Inclusion of Women and Minorities	Inclusion_of_Women_and_Minorities.pdf	
2.5. Recruitment and Retention Plan	Recruitment_and_Retention.pdf	
2.6. Recruitment Status	Recruiting	
2.7. Study Timeline	Study_Timeline.pdf	
2.8. Enrollment of First Participant	02/05/2024	Actual

Inclusion of Individuals Across the Lifespan

Studies in this project occur in patients undergoing intracranial monitoring for the surgical treatment of refectory epilepsy. Subjects will be asked to volunteer their time to participate in the research activities described in this proposal during their inpatient monitoring. Children can certainly be candidates for intracranial epilepsy monitoring, but young ones especially would not easily be able to participate in the behavioral tasks.

There is no upper age limit for this study. Practically, however, these implants are rarely if ever done in patients over the age of 70 for the following reasons; 1) typically their epilepsy would have manifested and been treated much earlier; 2) increased risk of the intracranial monitoring procedure; and 3) increased risk of any subsequent therapeutic procedure after the intracranial monitoring.

Inclusion of Women and Minorities

We will not discriminate with respect to gender, race, or ethnicity. Intracranial recordings depend on clinical factors, and every effort will be made to equally recruit women and minorities into the study but cannot be predetermined. Based on the patient populations and prior experience, we anticipate roughly equal numbers of male and female subjects. Similarly, we anticipate that approximately 30% of the research subjects will be drawn from ethnic and racial minorities. The racial and ethnic character of the subjects closely reflect the population of Texas and neighboring states that are the primary sources of patients. Economic status should not affect recruitment since respective hospitals make accommodations for patients with limited financial resources. Because of the smaller sample size of this study population some groups may not be included by chance. Spanish language translators will be made available for patients not fluent in English, so that English fluency will not be a cause of exclusion for Spanish-speaking groups.

Recruitment and Retention

Recruitment

Sufficient recruitment relies on busy intracranial monitoring programs with experience in human neuroscience research. Our epilepsy program is very busy, and the Neurosurgery Research Team, led by Dr. Sameer Sheth, has significant experience with this type of research. Based on several years' worth of track record, BCM expects to perform 20 implants in 2025 and subsequent years. Of all implants, >90% include at least 2 Behnke-Fried electrodes in dACC, OFC, vmPFC, or MTL. (Each such electrode has multiple contacts). Of patients with this appropriate coverage, >90% consent to research and are able to perform our tasks, based on extensive previous experience. We therefore project to be confidently able to recruit at least 12 subjects per year.

Our recruitment procedures follow the most rigorous neuroethical standards. Decisions regarding sEEG electrode number and location are determined by the clinical team in consensus meetings involving the entire epilepsy neurology/neurosurgery multi-disciplinary group. This decision is made purely on clinical grounds. The informed consent process ensures that patients know that participation is entirely voluntary, that their decision to participate or not in research does not impact their clinical care, and that they can withdraw from participation at any time. Further details regarding these procedures are available in the Protection of Human Subjects section. Sheth is a member of the NIH/BRAIN Research Opportunities in Humans (ROH) Neuroethics Working Group and member of the NIH Neuro Ethics Working Group (NEWG).

Retention

Retention is not an issue with any of the subjects, as the study activities end upon electrode explant and discharge from the hospital.

Study Timeline

We expect to be able to recruit 10 subjects per year in the Epilepsy Cohort without difficulty (see Protection of HS). The study timeline is illustrated in the table below.

	Year 1 (2025-2026)	**Year 2** (2026-2027)	**Year 3** (2027-2028)
Research	- Data collection for both Aims & preliminary analyses	- Finish data collection - Complete analyses for each Aim including control experiments (jabberwocky) - Submit manuscript 1, from Aim 1 (semantics, speaker, and other linguistic feature encoding)	- Finalize analyses for Aim 2 - Submit manuscript 2 from Aim 2 (semantics and speaker neural alignment)

2.9. Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location
Study 1, IER 1	Domestic	Baylor College of Medicine

OMB Number: 0925-0770

Expiration Date: 12/31/2027

Inclusion Enrollment Report 1

1. Inclusion Enrollment Report Title* : Neural coding regimes for language comprehension in human cortex.

2. Using an Existing Dataset or Resource* : ❍ Yes ● No

3. Enrollment Location Type* : ● Domestic ❍ Foreign

4. Enrollment Country(ies): USA: UNITED STATES

5. Enrollment Location(s): Baylor College of Medicine

6. Comments:

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	0
Asian	1	1	0	0	2
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	2	1	0	0	3
White	2	2	2	2	8
More than One Race	0	0	0	0	0
Total	5	4	2	2	13

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	1	0	0	0	0	0	0	1
White	0	2	0	1	1	0	0	0	0	4
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	0	2	1	1	1	0	0	0	0	5

Tracking Number:

Received Date:

Section 3 - Protection and Monitoring Plans (Study 1)

3.1. Protection of Human Subjects	Protection_of_Human_Subjects_F32_rev.pdf
3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?	❍ Yes ● No ❍ N/A
Single IRB plan attachment	
3.3. Data and Safety Monitoring Plan	Data_safety_monitoring.pdf
3.4. Will a Data and Safety Monitoring Board be appointed for this study?	❍ Yes ● No
3.5. Overall structure of the study team	Overall_Structure_of_the_Study_Team.pdf

Protection of Human Subjects

All studies will be carried out with the highest ethical considerations. Neurosurgeon/Neuroscientist Co-sponsor Dr. Sheth is an invited member of the NIH Neuroethics Working Group (NEWG) and a member of the BRAIN Initiative Research Opportunities in Humans (ROH) Neuroethics working group. He has extensive experience with ethical conduct of intracranial research in human subjects (Hendriks et al., 2019) and will ensure adherence to these standards across the project.

1. Risk to Human Subjects

1.a. Human Subjects Involvement, Characteristics, and Design

Our patient cohort consists of a clinical cohort of patients with medically refractory epilepsy undergoing intracranial monitoring for seizure localization. The studies described in this project simply “piggyback” on the existing opportunity for intracranial investigation available through this cohort. The intracranial electrodes are implanted for the sole clinical purpose of evaluation of epilepsy. At the time of participation in this study, the subject is in the epilepsy monitoring unit (EMU) waiting to have seizures, with the electrodes already implanted. At no time does the research enter into any clinical decision-making process. In particular, decisions regarding the placement of electrodes are based solely on clinical grounds during discussions in the multi-disciplinary epilepsy conference. We will include participants 18 years or older who are scheduled to undergo surgical implementation of stereo-electroencephalography (sEEG) electrodes for the purposes of investigation of their seizures. Intracranial investigation using sEEG electrodes is extremely common in the U.S. and within our Comprehensive Epilepsy Center. During the informed consent process, patients are clearly told that participation in the proposed research has no impact on their clinical treatment. All patients undergoing invasive monitoring at BCM/Baylor St. Luke’s Comprehensive Epilepsy Center will be asked whether they would like to volunteer for research experiments. Several procedures are in place to ensure a separation and primacy of clinical care before, during, and after invasive monitoring. The proposed research activities are covered within and approved by our existing BCM IRB (H-18112).

1.b. Study Procedures, Materials, and Potential Risks

Study Procedures

Subjects will participate in the study during their intracranial monitoring period. As described above, this study will have no influence over the selection of subjects or over the placement of intracranial electrodes. Subject participation generally requires recording from the implanted electrodes during passive and active periods. Passive periods include periods of rest and periods of unstructured activities the subject is electing to perform (e.g., talking on the phone, watching TV, etc.). Active periods include participation in the behavioral tasks described in the Research Strategy. There are no study procedures before or after the inpatient monitoring period.

Materials

All materials necessary for this study can be de-identified. Materials consist of demographics, baseline scores on neuropsychological assessments, electrophysiological data recorded from the intracranial electrodes, and behavioral data (performance on the tasks).

Potential risks

Potential risks from this study can relate to the recordings and to the stimulation studies. The risks related to the surgical procedures are not part of this study, as they are covered in the clinical decision-making.

Based on the Dr. Sheth’s prior experience (>100 patient recordings over 10+ years), there are no anticipated risks associated with performing the recordings and associated behavioral tasks. None of the tasks are designed to be noxious or make the subject feel uncomfortable. All have been used before at BCM. Patients and their families are continually informed that participation is voluntary, free of cost, and in no way related to their clinical care. Their participation in the proposed experiments does not change or extend their inpatient stay. In addition, all experiments are performed in the patient’s personal room at the bedside using

customized recording equipment that is designed to allow simultaneous clinical and research recordings. Therefore, these experimental recordings do not pause or alter clinical monitoring in any fashion.

Intracranial stimulation carries a small risk of eliciting seizures. Measures to mitigate this risk are described below. We estimate this risk to be <2% based on our recent report across a large cohort of >700 intracranial, research-related electrical stimulation sessions in epilepsy patients (Goldstein et al., 2019).

2. Adequacy of Protection Against Risks

2.a. Informed Consent

Participants will be recruited from the pool of patients evaluated at the Baylor St. Luke's Comprehensive Epilepsy Center, which provides a comprehensive program for the care of people with epilepsy (Level 4 accreditation). New patients who are planned for admission for intracranial monitoring will be given information regarding ongoing research studies that could relate to their clinical monitoring. Patients who express interest in participating will be interviewed, and if they fulfill the inclusion criteria (as determined during initial screening by Co-sponsor Sheth), they will be given a copy of the informed consent documents that detail the general purposes and procedures of the experiment. Patients are also instructed by their clinical team that the research is fully independent of their clinical care and they may choose to withdraw from research at any time. Then a full informed consent discussion is conducted by a study research coordinator who is independent from the patient's clinical care, and consent is obtained. Any questions patients may have regarding the study or consent form will be answered. The consent form clearly states that the patient may quit participation at any time without affecting their medical treatment and seizure monitoring. All patients will be assured that their data will be kept confidential, and that their decision regarding participation will in no way affect their ability to receive health care. Everyone has completed appropriate training in the treatment of humans as experimental subjects and in HIPAA guidelines. Co-sponsor Sheth is an active proponent of maintaining the highest ethical standards in human intracranial research (NEWG member, ROH Neuroethics group member, co-author in Hendriks et al. *JAMA Neurol* 2019; Feinsinger et al., 2022) and will ensure that the consent process follows the most rigorous ethical guidelines.

2.b. Protections Against Risk

To further ensure patient safety and mitigate any undue influence of our research goals on patient clinical care, several procedures will be implemented: i) Non-clinical research team members will have no contact with patients until after the implantation surgery and only if written and verbal consent for research has been provided. ii) Non-clinical research team members will not influence clinical decision-making during case conferences in which patient surgery planning occurs. It is important to note that while Contact PI Sheth will attend such meetings as part of his clinical duties, all decisions about patient electrode implantation (e.g. number & location of probes) are formed via consensus with the primary epileptologist and other clinicians. Together, these steps will ensure a firewall between clinical practice and the research goals of our project.

Planned experiments will produce electrophysiological recording and stimulation data obtained during intracranial monitoring. These data are locally stored at the site of experimentation and can only be accessed by personnel identified on the relevant research consent forms. All identifiable patient data is handled under HIPAA regulations and only individuals with HIPAA certification will be allowed access to the data. For subsequent data analysis, all data will be de-identified and given unique code identifiers. All data will be stored with high-level encryption in the neurosurgery research team server, *Elias*, maintained to HIPAA standards by Baylor College of Medicine. Only the PI and Co-I's and will have access to the identifying participant codes. Upon study completion data will be archived onto DVD.

3. Potential Benefits of the Proposed Research to Research Participants and Others

The proposed study does not provide any anticipated direct benefit to the individual participant. The findings from the proposed research will contribute to understanding the brain circuits underlying depression and other related mental health disorders.

4. Importance of the Knowledge to be Gained

Understanding human brain function is relevant not only to basic science since this remains one of the enigmas of science, but also to treating those with disorders of mental health. Given the tremendous impact of psychiatric illness on daily functioning and well-being, the knowledge potentially gained by this project about cognitive processes core to communication disorders and their potential treatments are extremely important.

The large number of people affected by psychiatric illness and/or communication disorders combined with the potential to benefit their symptoms provides a reasonable justification for exposure to the minimal potential risks.

References

Feinsinger, A., Pouratian, N., Ebadi, H., Adolphs, R., Andersen, R., Beauchamp, M. S., Chang, E. F., Crone, N. E., Collinger, J. L., Fried, I., Mamelak, A., Richardson, M., Rutishauser, U., Sheth, S. A., Suthana, N., Tandon, N., & Yoshor, D. (2022). Ethical commitments, principles, and practices guiding intracranial neuroscientific research in humans. *Neuron*, *110*(2), 188–194.

Goldstein, H. E., Smith, E. H., Gross, R. E., Jobst, B. C., Lega, B. C., Sperling, M. R., Worrell, G. A., Zaghloul, K. A., Wanda, P. A., Kahana, M. J., Rizzuto, D. S., Schevon, C. A., McKhann, G. M., & Sheth, S. A. (2019). Risk of seizures induced by intracranial research stimulation: analysis of 770 stimulation sessions. *Journal of Neural Engineering*, *16*(6), 066039.

Hendriks, S., Grady, C., Ramos, K. M., Chiong, W., Fins, J. J., Ford, P., et al. (2019). Ethical Challenges of Risk, Informed Consent, and Posttrial Responsibilities in Human Research With Neural Devices: A Review. *JAMA Neurology*, *76*(12), 1506–1514.

Data and Safety Monitoring Plan

Data and Safety Monitoring Board

Based on the nature of the proposed studies, none of which are more than minimal risk or involve a therapeutic intervention, we believe that creation of a Data and Safety Monitoring Board (DSMB) is not needed. We would of course be happy to create one or appoint an Independent Medical Monitor (IMM) should NIH request it. Short of those designations, the PI (Sheth) will ultimate serve the role of ensuring safety for all participants.

Monitoring Procedures

As detailed in Protection of Human Subjects, the proposed study carries only minimal risk since it is merely piggybacking on a clinical opportunity in which intracranial electrodes are already implanted for the purpose of chronic inpatient epilepsy monitoring (Epilepsy Cohort). At no time does the research enter into any clinical decision-making process. The Co-sponsor (Sheth) will closely monitor all study procedures carefully on a per-participant and per-day basis to make sure everything is carried out according to the IRB approved planned protocol. Specifically, the PI and sponsors will ensure that informed consent is obtained prior to beginning any research procedures and that all participants meet eligibility criteria. Data will be immediately accessible to the PI and sponsors to review. Dr. Sheth will review any adverse events in real-time. Serious AEs (SAEs) will be reviewed by the PI immediately in real-time. Dr. Sheth will ensure that any AEs or SAEs as well as any protocol deviations are reported to the NIH, FDA, and IRB in a timely fashion and according to regulatory requirements.

Adverse Events

For this study, the following standard AE definitions are used:

Adverse event: Any unfavorable and unintended sign, symptom or disease temporally associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure.

Serious Adverse Event: Any AE that results in any of the following outcomes:
• Death
• Life-threatening event
• Event requiring inpatient hospitalization or prolongation of existing hospitalization
• Persistent or significant disability/incapacity

Overall Structure of the Study Team

Administrative Site

Baylor College of Medicine

Data Coordinating Site

Baylor College of Medicine

Enrollment/Participating Sites

Baylor College of Medicine

Analysis Sites

Baylor College of Medicine

Baylor College of Medicine:

Dr. Hayden (Sponsor): Neuroscientist (study design and analysis)

Sheth (Co-sponsor): Neurosurgeon/Neuroscientist (surgery, data collection)

Hamilton (Consultant and collaborator): Neuroscientist (analysis)

Franch (PI, applicant): Neuroscientist (study design and analysis)

The study team will consist of myself, the fellowship applicant, sponsors, Dr. Ben Hayden and Dr. Sameer Sheth, and consultant Dr. Liberty Hamilton. Dr. Hayden is an expert in using electrophysiology to understand the neural circuitry of cognition, especially reward, decision-making, and executive control, especially in naturalistic contexts and therefore will oversee my execution of data collection, analysis, and manuscript publication. Dr. Sheth is the neurosurgeon of our research team at BCM and directs the neurosurgery research program – he will support and oversee this clinical trial and my training goals in clinical research. Dr. Hamilton is an expert in intracranial recordings in humans during speech comprehension and will guide my development into a language neuroscientist, assisting with transcription and extraction of linguistic features from natural conversations and advise analysis of these features with neural data. I will be responsible for all data collection and analyses across both aims with assistance from Drs. Hayden and Hamilton as needed. I will meet individually with my sponsors regularly to communicate study decisions and keep all team members informed on progress.

Section 4 - Protocol Synopsis (Study 1)

4.1. Study Design

4.1.a. Detailed Description

4.1.b. Primary Purpose

4.1.c. Interventions

Type	Name	Description

4.1.d. Study Phase

Is this an NIH-defined Phase III Clinical Trial? ❍ Yes ❍ No

4.1.e. Intervention Model

4.1.f. Masking ❍ Yes ❍ No

❑ Participant ❑ Care Provider ❑ Investigator ❑ Outcomes Assessor

4.1.g. Allocation

4.2. Outcome Measures

Type	Name	Time Frame	Brief Description

4.3. Statistical Design and Power

4.4. Subject Participation Duration

4.5. Will the study use an FDA-regulated intervention? ❍ Yes ❍ No

4.5.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.6. Is this an applicable clinical trial under FDAAA? ❍ Yes ❍ No

4.7. Dissemination Plan

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
The form does not have any delayed onset studies			

Resource Sharing Plan

Baylor College of Medicine adheres to the NIH policy on Sharing Research Data and on Sharing Model Organisms.

The PIs, sponsors, and investigators acknowledge their willingness to share data and materials with other eligible investigators through established means. Particularly, given the uniqueness of the study population, all study team members fully intend to participate and collaborate with other investigators in this field to maximize opportunities for collection, curation, and analysis of data from this unique population of human subjects. The research coordinator budgeted for BCM will be responsible for uploading data to nationally funded repositories such as DABI.

Data will be shared with collaborators immediately upon availability and with the scientific community at large after initial analysis and publication. Three years after initial publication, the data generated by this proposal will be available to the academic community at large upon request to the PIs and sponsors accompanied by a sound plan for novel analysis and interpretation. All requests will be reviewed and, if appropriate, approved by the PIs. We recognize that we are building a very comprehensive and extensive behavioral and multi-scale physiological dataset that can be used to probe many more questions than we specifically seek to address. Once requests for data sharing are approved by the PIs, the investigators will provide access to requesting individuals/institutions via secured server access. Only fully anonymized and deidentified data will be shared.

Results will be shared by presentations at local, regional, national and international scientific meetings. Finally, data will be brought to the widest audience possible via publication. Press interviews on important publications will be arranged through study sites' media offices.

The plans for data sharing will be submitted to institutional IRBs and all sharing of de-identified data will be IRB compliant.