A. Objectives and Significance

Learning a second language as an adult is a notoriously demanding task, and outcomes vary substantially across individuals. One of the most challenging aspects of second language acquisition is appropriate categorization of novel speech sounds. In English, for example, the sounds /ɹ/ and /l/ differentiate the words *ramp* and *lamp*, and English speakers can easily tell these sounds apart. However, in Japanese, these sounds do not differentiate words, and thus Japanese speakers have difficulty perceiving and producing these sounds in English.

Substantial research has examined why second language learning is challenging and how it can be made easier. However, these efforts have been limited because theories of language learning are not well-integrated with cognitive science broadly, and with neuroscience-based approaches more specifically. Here, we propose bridging these fields, using a mouse model to investigate the fine-grained neural processes underlying speech sound learning. We capitalize on an intriguing finding[89], which demonstrates that periods of passive stimulus exposure to unfamiliar speech sounds, which are less effortful than periods of active practice, yield learning in some situations. Specifically, passive exposure alone did not result in robust category learning, but yielded improvements when combined with active practice. This suggests that multiple learning mechanisms drive speech sound learning, and that a less-effortful path toward speech sound acquisition can be designed with detailed understanding of these mechanisms. Through a series of experiments in mice and humans, we will investigate the roles of active practice and passive exposure on speech sound learning. Our **overall goals** are to determine the changes in neural coding of speech sounds that result from active training and passive exposure, and to test predictions about learning behavior in humans that arise from this knowledge.

The specific **objectives** of this work will determine (1) the conditions in which passive exposure is beneficial for learning speech sounds, (2) the changes in neural coding of speech sounds by populations of auditory cortical neurons as a result of active training *vs.* passive exposure, and (3) the interaction between active training and passive exposure. The **significance** of the proposed work stems from the potential to achieve a detailed understanding of the neural processes that underlie speech sound learning, allowing for the development of powerful models of second language learning, and inspiring novel approaches for teaching and learning.

A.1 Intellectual Merit

This proposal is innovative in that it combines physiological and behavioral experiments in mice with experiments in humans to explore questions critical to our understanding of language acquisition. Moreover, our approaches go beyond traditional analyses of single neuron responses, focusing instead on how populations of neurons interact to provide effective coding strategies for the categorization of speech sounds, and how these strategies change with learning. Our proposal capitalizes on these techniques to allow insight from neuroscience to influence the design of human training experiments. Further, it allows for insights from human behavior to direct physiological experiments in mice to better understand the underlying neural mechanisms of speech sound learning. These approaches enable a cycle of prediction generation at different levels of analysis, allowing us to examine increasingly complex human behavior and the underlying neural mechanisms of auditory cognition.

A.2 Broader Impacts

An improved understanding of how language learning works, from neurons to behavior, will enable the development of efficient learning strategies that take into account differences across individuals. Efficient language learning has the potential to revolutionize business, government, and communication around the world. Because our project is relevant to a wide audience, we find it is crucially important to disseminate our findings broadly (including non-academic audiences), and to include a diverse population of individuals in this research. Therefore, we have devised four specific outreach objectives: (1) we will pilot a program for first-year college students to develop cross-disciplinary educational programs; (2) we will work with established programs to broaden participation in STEM for underrepresented groups; (3) we will work with the Eugene Science Center to develop new exhibits on neuroscience and acoustics; and (4) we will bridge theory and practice in language learning, through education and outreach to practicioners.

A.3 Risk and Reward

An inherent risk of our project is the assumption that changes in the neural coding of sounds by auditory cortical neurons in mice is an appropriate model for speech sound learning in humans. This risk is mitigated to an extent by observed commonalities in the perception of acoustic stimuli, including speech-like sounds, between these species[21,41].

The potential rewards of this research, however, are substantially greater than its risks. It is critically important to integrate insights from second language learning with a detailed understanding of learning-induced changes in neural coding, if we are to devise powerful models and efficient strategies for language learning. Our **research team**, along with our advisory board, are perfectly suited to bridge these levels of analysis. With complementary expertise in second language acquisition in humans (PI Baese-Berk) and the neural basis of sound-driven behavior in mice (PI Jaramillo), we are well-poised to take on this challenge. Further, our preliminary data from training mice in speech sound categorization suggest this animal model is appropriate for the research program proposed here. We anticipate that our work will not only yield key insights about the neural mechanisms of language learning, but also provide a solid framework for the integration of our distinct fields.

B. Background and preliminary studies

B.1 Speech sound learning

For several decades, studies have investigated how listeners can improve their ability to differentiate and categorize sounds from an unfamiliar language. In a laboratory setting, listeners can improve their perception of new speech sounds[48,35], and this improvement is long-lasting[47]. However, this training is quite taxing and time-consuming, as it requires that participants respond to a stimulus on each trial (over several weeks of daily sessions).

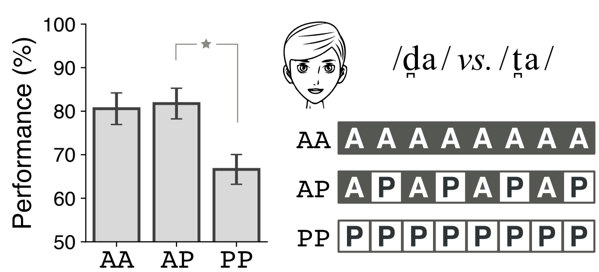

Fig. 1: Replacing some active training sessions with less-effortful passive exposure (AP) results in robust speech sound learning, comparable to more-effortful active alone (AA), and much better than passive alone (PP)[89,90].

Compelling recent evidence indicates that some of these ”active” sessions can be replaced with passive stimulus exposures, resulting in robust learning that is equivalent to active-only training[89,90]. Even when passive stimulus exposures do not result in robust learning on their own, when combined with active training listeners, they provide a benefit (**Fig. 1**). This work demonstrated that the all-active (AA) and active+passive (AP) schedules yielded equivalent amounts of robust learning, and that these effects could not be attributed solely to the number of active trials, as both groups performed better than a group in which passive sessions were replaced with periods of no stimulus. These results suggest that the taxing training traditionally required for novel speech sound learning could be less demanding and time-consuming for learners.

Two issues remain unresolved regarding the benefits of passive exposure during learning. First, what precise combinations of active training and passive exposure result in optimal learning is unknown. Second, the neural mechanisms by which these benefits arise are unclear, limiting development of detailed models that allow for efficient exploration of parameters influencing learning. The specific objectives proposed here will provide the groundwork necessary to address these questions.

B.2 A mouse model of speech learning

Understanding the neural mechanisms that underlie learning to categorize speech sounds from a new language, requires an experimental level of detail that is currently not feasible in humans. Relating changes in the neural coding of sounds to the behavioral changes that result from active practice or passive exposure requires animal models with two features: sufficient behavioral complexity to capture the process of learning speech sounds, and sufficient experimental accessibility to allow for precise monitoring and manipulation of individual neurons and neuron classes.

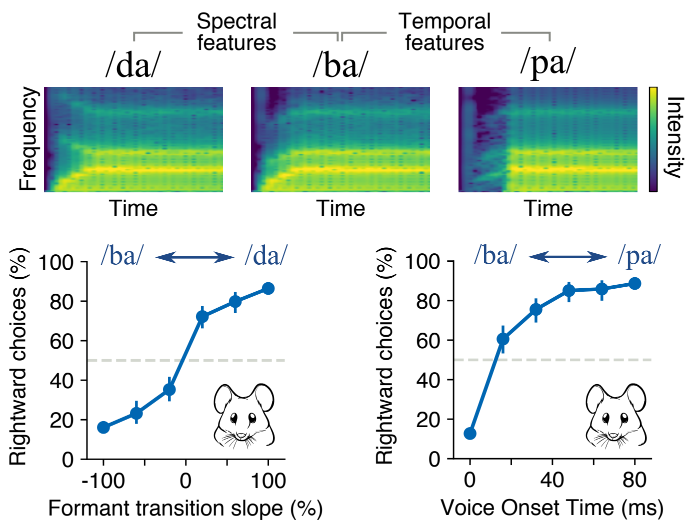

Fig. 2: Using a two-alternative choice task, mice can be trained to categorize human speech sounds (shifted to the mouse frequency range) according to spectral features (formant transitions) or temporal features (voice onset time).

The mouse provides unparalleled advantages regarding experimental access compared to other mammalian models, including the availability of thousands of transgenic lines, advanced methods for recording hundreds of neurons simultaneously across days, and techniques for precise manipulation of neural activity which can be much more challenging, when possible, in other species such as non-human primates. Yet, is the mouse a suitable model for human speech sound learning? While the mouse is not expected to accurately capture the full complexity of human behavior (a challenge in any use of animal models), much success about the neural basis of learning and memory has been achieved by capitalizing on common principles across species, taking into account the limitations of the model organism used. Given that the scope of our project is limited to the processing of speech sounds, rather than the interpretation of language or production of speech, the mouse has the potential to provide insights into the mechanisms of speech sound learning, given the similarities in anatomy and physiology between the auditory systems of mice and humans.

Mice have been used successfully in the study of auditory processing and auditory-driven behavior for several decades[86]. Our own work has demonstrated that mice can be trained to associate specific sounds with different actions, and rapidly adapt these associations several times within a single behavioral session[37,27,28]. It is important to note that while rodents use social calls as a common form of communication[77,46,31,68], more relevant to our proposed work is the observation that mice can be readily trained to categorize human speech sounds when these sounds are frequency-shifted to the appropriate hearing range[75]. Specific to the research proposed here, our preliminary data shows that mice can categorize speech sounds that vary in spectral features (formant transitions) as well as temporal features (voice onset time) (**Fig. 2**). It remains unknown, however, whether replacing active training sessions with passive exposure can have the same effects in mice as it is observed in humans. Objective 1 of this proposal addresses this gap in knowledge.

B.3 Neural coding of sounds by auditory cortical neurons

Measurement of single neurons along the auditory system have yielded great insights into the neural representation of sounds, and how signals are transformed from the cochlea to the cerebral cortex. Auditory cortical neurons show selectivity not only to the frequency of sounds, but also to computed features such as frequency modulations[53] and temporal structure[76], reflecting both subcortical and cortical processing. These cortical responses to sounds predict discrimination performance and spontaneous categorization of sounds in behaving animals, including mice[56,10]. These neurons, however, do not act in isolation; they are part of an interconnected network and act together to process sound-related signals[32,54]. Therefore, if we intend to understand how speech sounds are processed and circuits changed during learning, an analysis of simultaneously recorded neurons is necessary. The last decade has seen major advances in techniques for monitoring the activity of hundreds to thousands of neurons simultaneously from awake mice, via two-photon calcium imaging[2,30,79,61] and high-density electrophysiology[38]. These advances together with novel data analysis methods tailored for populations of neurons allow investigating how features that may not be apparent from the activity of individual neurons are key in the neural representation and processing of sensory stimuli[3,73,59,42].

Two-photon calcium imaging data from our laboratory (**Fig. 3**) illustrates our ability to record the sound responses of hundreds of neurons simultaneously from the auditory cortex. The response on each trial across neurons can be represented as a point in a high-dimensional space, with multiple trials defining a "cloud" of points as the neural representation for each sound. The right-most panel shows how these clouds (in this case focusing on just two neurons) capture the correlations across neurons (the orientation of the clouds) and the separability of clouds from different stimuli, which can be used by later stages in the neural pathway to categorize sounds as needed. We will use this type of analysis of neural population coding of sounds to investigate changes in coding that occur with active training and passive exposure in Objectives 2 and 3 of this proposal.

B.4 Learning-induced changes in auditory neural coding

Learning to detect or discriminate features of acoustic stimuli alters the responses of auditory cortical neurons in animals[70,25,65,66], including humans[36,57]. Additionally, auditory cortical responses to sounds also change after passive exposure to acoustic stimuli, during both development and adulthood[40,39,7]. Importantly, these changes from passive exposure are specific to features present in the stimulus ensemble, even when these features are not predictive of rewards or punishments[44], sug-

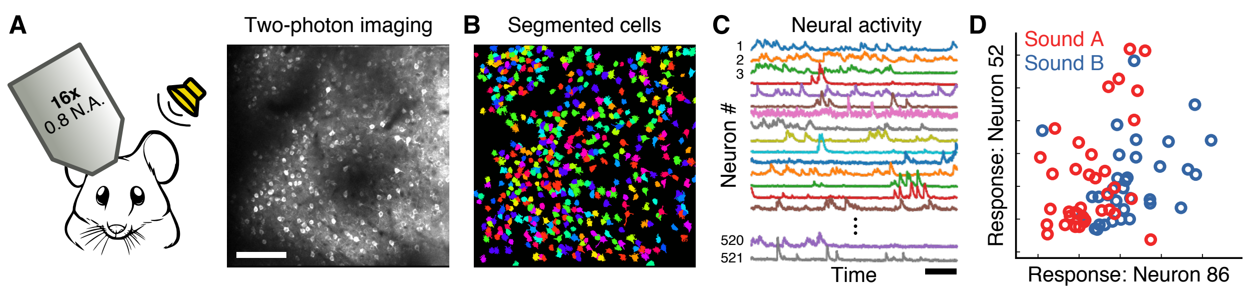

Fig. 3: (**A**) Two-photon calcium imaging measures the activity of hundreds of auditory cortical neurons simultaneously (scale=100 μm). (**B**) Neurons can be segmented automatically[61] (arbitrary coloring). (**C**) Change in fluorescence ($\Delta f/f$) associated with the activity of each neuron (scale=20s). (**D**) The evoked response ($\Delta f/f$ after sound onset) on each trial across all cells corresponds to a point in an N-dimensional space, where N is the number of neurons. This example shows the responses of two neurons (N=2) to two different sounds (red and blue) in a naive mouse, illustrating correlated variability across neurons, and the separability of the neural representation of these sounds.

gesting the nervous system constantly adapts to the statistics of the environment it is exposed to. The characterization of these changes, however, has relied primarily on analysis of one neuron at a time, and information about how the neural population code changes with sound learning is lacking.

Comparison of neural responses to sounds during active task performance and passive exposure have demonstrated clear differences in sound-evoked responses by auditory cortical neurons between these conditions[58,15,43,91]. However, much less is known about the relation between the consequences induced by each type of exposure. Specifically, it is largely unknown whether the changes that occur in the auditory cortex after passive exposure to sounds are similar in nature to those resulting from active training, how these conditions may influence one another, and under what conditions one could replace the other (**Fig. 1**). Taking advantage of the ability to record the same set of neurons across several days using two photon calcium imaging[33,39,19,78], we will address these gaps in knowledge in Objectives 2 and 3 of this proposal.

B.5 Theoretical framework to investigate changes in neural coding

The following theoretical framework guides our interpretation of the proposed experiments and hypotheses regarding changes in neural coding that occur with active training or passive exposure to speech sounds. When an organism undergoes categorization learning, its nervous system must change in such a way that future stimuli can be assigned to appropriate learned categories. As presented in **Fig. 4**, this goal can be achieved via the combination of two processes: the neural representation of stimuli from each category changes in order to make categories as separable as possible in a multidimensional representation space (**Fig. 4**, **top**), and categorization boundaries in this space are learned in order to assign the correct category to each future sample (**Fig. 4**, **bottom**). This description is akin to what occurs in machine learning systems such as kernel-based support vector machines[16] and artificial neural networks[11], in which the early stages of the system yield non-linear transformations of the inputs (often resulting in linearly separable representations), and the last stages (often a linear readout) establishes categorization boundaries for classification.

We propose that while active training takes advantage of both of these processes, passive exposure results in changes in neural coding without changes in the categorization boundary. Under the right conditions, these changes in neural coding from passive exposure could be sufficient to achieve high levels of categorization performance when mixed with the right amount of active training. This would suggest that periods of active training can be replaced by passive exposure and subjects would still achieve high levels of performance, as observed in our previous experiments in humans (**Fig. 1**). It remains unknown, however, whether changes in neural coding that occur during active training of speech sounds are of similar nature as those during passive exposure.

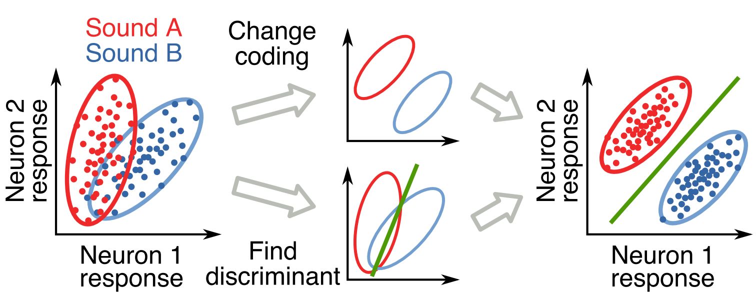

Fig. 4: Categorization learning consists of two processes: (1) a change in neural coding to make representations as separable as possible, and (2) finding a discriminant that best separates the neural representation of different categories. We hypothesize that active training involves both processes, while passive exposure results only in changes in coding.

We hypothesize that during passive exposure, the neural representation of sounds become as separable as possible to allow for arbitrary future categorizations (**Fig. 5**, top), analogous to the adaptation to stimulus statistics observed throughout the nervous system[4,83,50]. This adaptation, however, is only effective for categorization when combined with active training, which sets appropriate category boundaries. In contrast, we posit that during active training, changes in neural coding focus on separating the set of categories being learned, while not affecting (or sometimes decreasing) the separability of representations within a category (**Fig. 5**, bottom). As a consequence, categorization performance for untrained categories may be worse after extensive active training than after extensive passive exposure and brief training. We will test these hypotheses in objective 2.

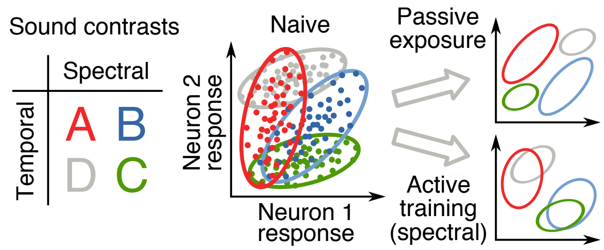

Fig. 5: Hypothesized changes in neural coding from passive exposure *vs.* active training to categorize spectral features. Separability for the untrained dimension (temporal) is better after passive exposure than after active training.

Furthermore, the effects of active training and passive exposure may interact in such a way that the final outcome depends on the order in which subjects are exposed to these conditions. In objective 3, we describe hypotheses for these interactions, their corresponding behavioral predictions, and experiments to test them.

C. General Methods

C.1 General methods: Human experiments

All human experiments will follow similar methodology to quantify changes in speech categorization performance after different training schedules.

C.1.1 Participants. Participants will be monolingual American English speakers between 18 and 35 years old, recruited from the Linguistics and Psychology subject pool at the University of Oregon. We will collect demographic and language background information using a standard questionnaire. All participants must pass a hearing screening. Exclusion criteria include previous experience with languages that use the speech contrasts described below or history of speech, language, or hearing disorder. We will aim to collect data from 20 participants per group (described below). This sample size is larger than that in previous studies and will provide appropriate power given effect sizes from our previous work[89,6,5].

C.1.2 Materials. Stimuli will be speech sounds that do not exist in the speaker's native language. Specifically, participants will be exposed to one of two contrasts: the Hindi dental-retroflex contrast /d̪/-/ɖ/ or /t̪/-/ʈ/ or the Hindi voiced-voiceless contrast /d̪/-t̪/ or /ɖ/-ʈ/. These stimuli vary in spectral features (formant transitions) and temporal features (voice onset time), and thus are analogous to the stimuli used in the mouse experiments. A 6-step continuum of sounds along one of these dimensions will be presented. Stimuli will be delivered via headphones (AKG-K-240-MKII), and will be presented using PsychoPy[63].

Stimuli will be synthesized using the software package Praat[12] from four naturally produced tokens from a native speaker. Vowel duration will be normalized to 270 ms, and amplitude normalized to 65 dB SPL. Stimuli for the dental-retroflex contrast are created by shifting the third formant (F3) transition from the consonant into the vowel (more shallow for /d̪/ and /t̪/ and steeper for /ɖ/ and /ʈ/). Stimuli for the voiced-voiceless contrast are created by manipulating the amount of prevoicing for the stop consonant (more prevoicing for /d̪/ and /ɖ/ and less for /t̪/ and /ʈ/). Having a stimulus space that allows for both spectral and temporal dimensions to be manipulated within the same acoustic space, enables us to investigate learning on trained *vs.* untrained dimensions (Objective 2).

C.1.3 Procedure. Participants will complete a test before and after each training session, over two consecutive days following previous work[89,6,5,20], with the same basic paradigm (*i.e.*, pre-test, learning, post-test) on both days. Sessions will include two types of exposure to the stimuli: active training and passive exposure.

Active training. These sessions will include a brief exposure phase during which participants hear a small number of exemplars from the training continua (but do not respond to them) to familiarize them with the sounds. Participants will then hear a training token drawn from the stimulus ensemble and categorize it by pressing one of two buttons on a button box connected to the computer. They will receive feedback for these categorizations (*i.e.*, "Correct" or "Incorrect").

Passive exposure. Participants will hear tokens from the stimulus ensemble, but will not respond to those tokens. Instead, they will complete a distractor task, designed to prevent them from performing the active task covertly. Participants will be presented with a mapping table made up of several characters from the font *Webdings*, each matched with a number. Below this table, they will see several rows of Webdings characters, each with a blank box above it. The task is for participants to translate each character into its respective number. Participants are required to fill in each box in line, completing the preceding square before moving to the next one[89].

Test. In the test protocol, participants will hear a token from the ensemble and will be asked to categorize it, as in the active training described above. However, unlike in the active training, participants will not receive feedback on their performance.

C.1.4 Quantification of categorization performance. Performance on this task is estimated using proportion of retroflex responses for each stimulus in the case of the spectral contrast and proportion of prevoiced responses in the case of the temporal contrast. We will characterize this performance using Bayesian mixed models[13] with performance on the test as the dependent variable. These models allow us to investigate which conditions are statistically different and which are statistically equivalent. Fixed factors will include: stimulus continuum step, test (pre *vs.* post training), day (Day 1 or 2), and training schedule (as described in Objective 1), and the interactions of these factors. Random effects will include the structure that is fully specified by the models. We will investigate changes from pre-test to post-test in the shape of the psychometric function (*e.g.*, the slope of this function) to determine under what conditions participants learn.

C.2 <u>General methods</u>: Mouse behavior and stimulus presentation

Behavioral experiments in mice of both sexes (same strain as in physiological experiments described below) will follow a similar procedure as those in humans, but adapted to a head-fixed two-alternative choice preparation. Before experiments, animals will undergo a surgical procedure in which a head-post is attached to the skull to allow for head fixation during experiments[29]. Water is used as reward throughout the experiments, and a water restriction schedule is used to maintain motivation[82]. All procedures are in accordance with protocols approved by the University of Oregon Institutional Animal Care and Use Committee.

C.2.1 Sounds. Mice will be presented with speech sounds that vary in either formant transitions (*e.g.*, /ba/ *vs.* /da/) or voice-onset time (*e.g.*, /ba/ *vs.* /pa/), which we have demonstrated are effective sound contrasts for mice (**Fig. 2**). Sounds along the continuum for each contrast are synthesized using Praat[12] (a software package for speech analysis in phonetics), and shifted up in frequency 8 times from the human hearing range to better match the mouse human range.

C.2.2 Procedure. In each experimental session, a mouse is placed in an apparatus that maintains the animal's head fixed while allowing them to run freely on top of a wheel. Two lick-ports placed in front of the animal (right and left of the midline) serve as reward delivery conduits and sensors of the animal's choice on each trial. Naive mice will undergo a habituation and behavioral shaping process for 4 days to become familiar with the setup and learn to lick right and left in response to sounds uninformative for the final task. During **active training** sessions, a speech sound will be presented every 4 seconds, and animals must respond by licking the correct port according to the category associated with the sound in order to obtain reward. For instance, during categorization according to formant transitions, the correct response is left for /ba/ or /pa/, and right for /da/ or /ta/. During **passive exposure** sessions, the same set and number of stimuli are presented, but the lick ports are moved away to make them unavailable to the mouse. To mirror the visual distractor task in humans, animals are also exposed to lights placed in the right and left hemifield, turned on and off independently from the sounds presented. **Test** sessions to evaluate final performance will require animals to respond as in the active sessions. Test sessions will use a continuum of 6 stimuli between /ba/ and /da/ or between /ba/ and /pa/ to estimate psychometric performance. Measurements of pupil diameter throughout the sessions are used to monitor the animals' state of arousal[71,52].

C.2.3 Quantification of categorization performance. Categorization accuracy for each sound will be estimated as the fraction of correct choices: $N_{correct}/(N_{correct} + N_{error})$. Similar to the analysis of human behavioral data, we will evaluate overall categorization performance using Bayesian mixed models[13] with accuracy as the dependent variable. Fixed factors in the models will include: stimulus continuum step, test (pre *vs.* post), and training schedule (as described in Objective 1), as well as the interactions of all of these factors. Using this model, we will quantify changes in the shape of the psychometric function (*e.g.*, the slope of this function) from pre- to post-learning in order to determine which conditions result in most effective learning. We will collect data from 16 mice for each condition, which is expected to provide appropriate statistical power given previous work[37,75].

C.3 General methods: Mouse physiology

We will use two-photon calcium imaging of neural activity in mice expressing a fluorescent calcium indicator in excitatory cells (Thy1-GCaMP6f mice[18]) to measure the sound evoked responses of auditory cortical neurons. From these data, we will quantify how this population of cells encode the speech sounds presented, and how this neural representation changes with learning. Because sound-evoked responses differ between periods of task engagement and passive listening[58,15], we will evaluate responses under both conditions during test sessions for all mice.

C.3.1 Two-photon calcium imaging of auditory cortex. We will perform calcium imaging of auditory cortical neurons in layer 2/3 from head-fixed mice implanted with a cranial window, using two-photon microscopy (16x 0.8 NA objective, Ti:Sapphire laser at 920 nm). The borders of primary and non-primary auditory cortex will be estimated from the responses to pure tone stimuli using one-photon excitation (470 nm), and a field of view for two-photon microscopy defined to cover a large portion of primary auditory cortex and a subregion of secondary auditory cortex.

C.3.2 Estimation of neural coding of sounds. We will estimate the sound-evoked response of each neuron on each trial by applying a spike deconvolution method[60] to the change in fluorescence measured during stimulus presentation. The response across all neurons on a given trial will define a point in an N-dimensional space (where N is the number of neurons). Each trial will generate a slightly different point in this space, even when the same stimulus is presented, according to the variability in neural responses (**Fig. 3D)**. We will quantify how well neurons encode differences between sound categories by calculating the *stimulus discriminability* of neural representations, via the performance of a linear classifier (a support vector machine[16] with cross-validation). Changes in stimulus discriminability, however, can result from multiple mechanisms, including a reduction in the size of the cloud of points representing each sound, the orientation of each cloud, or other factors. To investigate the nature of changes in neural coding that result from learning, we will estimate the following set of population coding metrics before and after each learning schedule, applying dimensionality reduction methods[17] when necessary to obtain reliable estimates:

- *Individual neuron variability*, as measured by the Fano Factor (variance over mean) of evoked responses for a given stimulus. Variability is expected to decrease with learning[55].
- *Correlated variability* (noise correlations), estimated as the correlation in evoked responses to the same stimulus across neurons. Noise correlation is expected to decrease with learning[55].
- *Population sparseness* of the representation, measured by the kurtosis of the distribution of responses to a stimulus across the population[85]. Population sparseness is expected to increase with learning[87].
- *Dimensionality* of the neural representation[51,22]. The number of dimensions occupied by the neural responses is expected to change with learning[9].

D. Specific objectives

Our general approach is to address each objective with a combination of experiments with humans and with mice. The aim of these studies is not to provide perfect symmetry between the experiments in the two species. Instead, we will capitalize on the relative advantages of each species to investigate various aspects of these objectives, and provide complementary support for or against our hypotheses.

D.1 Objective 1: Identify conditions in which periods of active training can be replaced by passive exposure without a major impact on final performance.

D.1.1 Measurements and comparisons for humans. To achieve this objective, we will compare speech sound categorization performance after participants complete one of several training "schedules" (**Fig. 6**) that combine active training with passive exposure. Sounds will vary in either spectral (formant transitions) or temporal (voice onset time) features as described in Section C.1.2, and each participant will be trained to categorize sounds according to only one of these features.

Learning will be divided into 8 blocks per day for two days, and participants will complete a test at the beginning and at the end of each day. Schedules will differ in both the amount and the order of active training and passive exposure blocks (**Fig. 6**). In addition to schedules that mix active and passive sessions, two control schedules will be included: a *short-active* condition that alternates blocks of active exposure with blocks of no exposure (where participants will complete the distractor task and will not hear stimuli from the continuum); and an *all-passive* condition that includes 8 blocks of stimuli while completing the distractor task.

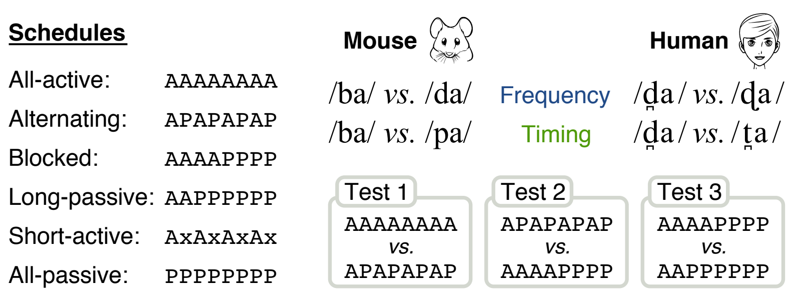

Fig. 6: Objective 1. We will test whether mice benefit from passive exposure as humans do. We will additionally test under which schedules passive exposure can benefit learning when combined with active training.

We will first compare *all-active* to *all-passive* to quantify the benefits of active training. We will then compare *alternating* to *short-active* to quantify benefits of passive mixed with active, and adjust the number of sessions and exposures as needed to obtain robust results. A comparison between *all-active* to *alternating* will be used to evaluate our previous results, and serve as a baseline for the novel schedules explored here. For the key comparisons (**Fig. 6**, right), we will evaluate performance in *alternating* compared to *blocked* to examine whether alternation is necessary for improved performance. Last, we will compare *blocked* to *long-passive* to evaluate whether equal amounts of active training and passive exposure are required for improved performance.

D.1.2 Measurements and comparisons for mice. Experiments in mice will use the head-fixed two-alternative choice task described in section C.2.2, using speech sounds that vary in spectral and temporal features, to quantify categorization performance after the training schedules described above (**Fig. 6**). The goal of these experiments is to evaluate to what extent passive exposure to sounds benefits categorization learning in mice, and determine under what conditions the mouse serves as a valid model for human speech sound learning, beyond our preliminary findings. Because the time scale of learning for mice is generally longer than that in humans, we will perform experiments across 6 days, where each daily session includes two blocks of 250 trials each. Each block will be either active training or passive exposure, depending on the schedule tested.

We will first quantify categorization performance after *all-active* compared to *short-active*, and verify that for the number of trials and sessions used, performance has not saturated after *short-active*. The length and number of sessions will be adjusted accordingly. We will then compare categorization performance between schedules as described for humans.

D.1.3 Expected results and interpretation. Beyond replication of previous results in which active training could be replaced with passive exposure and still achieve similar categorization performance (**Fig. 1**), differences and similarities in performance after *alternating*, *blocked* and *short-passive* schedules will provide insights into the timescales at which passive exposure is beneficial for learning. Given previous findings of implicit and perceptual learning in animals including rodents[49,14], we expect to find conditions in which categorization learning in the mouse replicates the advantages of mixing active and passive sessions in humans. Even if mouse behavior doesn't fully match that of humans (as expected with any animal model), our results will help identify common principles between these species which will guide the interpretation of neural mechanisms explored in objectives 2 and 3.

D.1.4 Potential limitations and solutions. All behavioral procedures in humans and mice are currently performed in our laboratories, and therefore we do not expect any major technical difficulties in these experiments. Because the parameter space for possible schedules is very large, the proposed experiments focus initially on a small number of variations to schedules that have been effective in the past[88]. Results from objectives 2 and 3 will inform appropriate strategies for future exploration of the space of parameters to find the strongest benefits from passive exposure to sounds.

Studies of passive exposure to sensory stimuli have found that attention influences the effects of this exposure[62]. Unlike in human experiments where performance on the visual task serves as a measure of attention during passive sessions, in mice, requiring shifts in attention is much more challenging. Instead, measurements of pupil diameter in mice will allow inclusion of arousal in our analysis.

A fundamental challenge in using any animal model is the extent to which that species serves as a suitable model for a human. Even if sound learning in mice does not fully capture results in humans, any observed similarities in combination with our characterization of neural coding changes due to learning are likely to provide insights into the mechanisms of speech sound learning in humans.

D.2 Objective 2: Quantify changes in the neural coding of sounds resulting from active training *vs.* passive exposure.

D.2.1 Measurements and comparisons for mice. To quantify changes in neural coding of sounds during learning, we will simultaneously record the activity of hundreds of auditory cortical neurons, via two-photon calcium imaging across experimental sessions. Using recently developed methods for the analysis of activity from neural populations, we will quantify changes that result from learning to categorize speech sounds during active training and compare these changes to those that result from passive exposure to the same sounds.

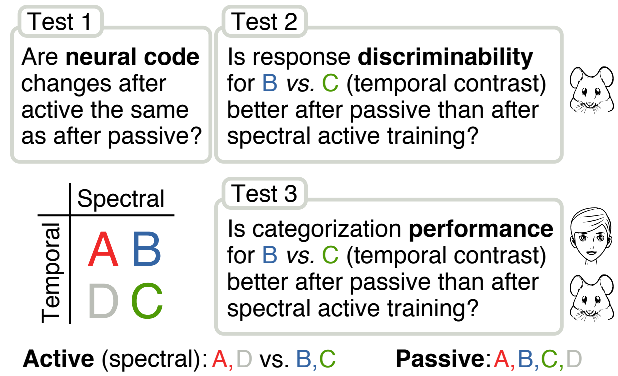

Fig. 7: Objective 2. In mice, we will evaluate whether changes in the population coding of sounds are similar between active training and passive exposure. We will relate these results to hypotheses about behavior in humans and mice, *e.g.*, that categorization of untrained categories (blue *vs.* green sounds) is better after passive exposure than active training.

Mice will be presented with synthesized speech sounds that vary in both spectral and temporal features (see C.2.1), but each cohort of mice will be trained to categorize stimuli according to only one feature. Each of the neural coding metrics described in section C.3.2 will be evaluated before and after active training to categorize these contrasts in one cohort, and after passive exposure to these sounds in another cohort. From these metrics, we will test: (1) whether changes in population neural coding by passive exposure are of the same nature as those by active training; and (2) the hypothesis that passive exposure results in better discriminability of neural responses for untrained contrasts compared to active training (section B.5 and **Fig. 5**).

D.2.2 Measurements and comparisons for humans. To test the impact that changes in coding resulting from active training *vs.* passive exposure may have on human behavior, we will compare categorization performance after an *all-active* and an *all-passive* schedule, but using speech sounds that vary in both spectral and temporal features. Participants will be tested in each of these dimensions separately, and the key comparison will evaluate post-test performance on the untrained dimension. These results will provide insights into changes from passive exposure that could benefit any future categorization, and/or a potential merge of stimulus representations within a learned category after active training, as predicted by our model.

D.2.3 Expected results and interpretation. Given previously observed effects of learning on the responses of sensory cortical neurons across sensory modalities in rodents[8,66,64,67], we expect to see changes in population coding as a result of speech sound learning. However, we are agnostic as to the precise nature of changes by active *vs.* passive sessions, *e.g.*, whether they rely more on a separation of representations, changes in neural correlations, or other coding features. Our population coding metrics will help determine the precise changes under each exposure condition.

Specifically, changes that result in improved neural discriminability (and better categorization performance) for untrained contrasts under passive exposure will support our hypothesis that the auditory system is influenced by the statistics of sensory stimuli in a way that enhances future categorization. Behavioral results on implicit, incidental, and statistical learning[69,26,72], suggest this may be the case. Moreover, changes that result in poorer neural discriminability (and reduced categorization performance) for different stimuli within a trained category will support our hypothesis that active training merges stimulus representations within a learned category, potentially helping the process of finding

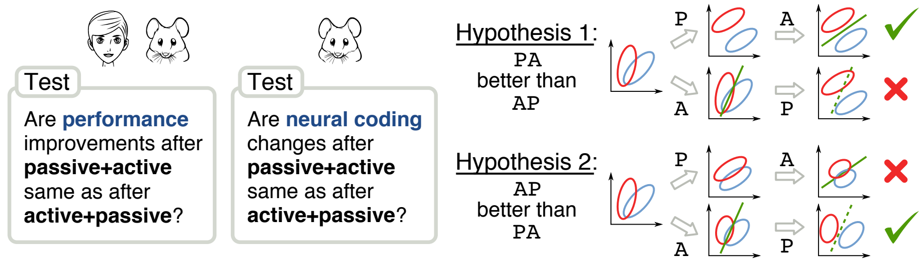

Fig. 8: Objective 3. Test whether the order of active and passive sessions influences learning. We propose two hypotheses on how active & passive interact, yielding different predictions (see text).

categorization boundaries for the given task. Observations that human subjects do not improve on untrained dimensions[62,90] hint at this possibility. Even if our hypotheses are not fully supported, our measurement of neural coding changes will provide major insights that can be used to update models of speech sound learning.

D.2.4 Potential limitations and solutions. While two-photon calcium imaging provides several key advantages for what our experiments require, it also has a few limitations that are relevant to our studies of speech sound coding. Calcium signals are slow compared to the action potentials, and it is not straightforward to estimate spike timing from these measurements, a factor that may be relevant for the representation of some speech sound features[23]. However, calcium imaging has been successfully used to determine neural selectivity to frequency modulations akin to those of the sounds we study[34], supporting the suitability of this technique. Our initial experiments are limited to measurements from layer 2/3 where two-photon measurements are most reliable. Because this layer of the auditory cortex displays stronger task-dependent plasticity compared to other layers[24], we consider it is an appropriate laminar location to start our investigation. Complementary electrophysiological techniques recently develop for high density recordings[38] (available in our laboratory) will be adopted for this study as needed. Last, there is evidence that the processing of sounds by auditory cortical circuits differs between cerebral hemispheres[84,45]. Our initial study will investigate neural coding by circuits from the right hemisphere, but control experiments in the left hemisphere will be performed to evaluate the generality of our results.

D.3 Objective 3: Quantify the interaction between active training and passive exposure.

D.3.1 Measurements and comparisons for humans. We will manipulate the order in which active training and passive exposure blocks are presented to evaluate whether and how these condition interact with each other. Each exposure condition will consist of three sections. The final section in all cases will be a test (as described in Objective 1). Participants will be assigned to one of two conditions. In the active-first condition, participants will complete a training schedule identical to that of the *blocked* condition in Objective 1. In the passive-first condition, participants will complete a similar schedule but with passive exposure section followed by an active training section and then the test. We will compare performance in the test block across the two conditions.

D.3.2 Measurements and comparisons for mice. To complement the experiments in humans, we will evaluate whether the changes in neural coding of sounds depend on the order in which active training and passive exposure are experienced. Analogous to the human experiments, mice will be exposed to two conditions: one in which passive exposure occurs first, followed by active training, and one in which active training occurs first followed by passive exposure. We will evaluate whether changes in population coding (quantified using the metrics described in Section C.3.2) and categorization behavior in mice differ between these training schedules.

D.3.3 Expected results and interpretation. Differences in performance between the two schedules (`AP` *vs.* `PA`) will indicate an interaction between active training and passive exposure, which we hypothesize could take one of two forms (**Fig. 8**): If the active session sets the discriminator in a position that will not be effective for subsequent changes from passive exposure, performing passive first would be advantageous (Hypothesis 1). Alternatively, if the system is able to capitalize on the coding changes from active training, which are then enhanced by passive exposure, performing the active sessions first would be better (Hypothesis 2). Our measurements of changes in population coding of sounds in mice will provide support for or against these hypotheses. Even if neither hypothesis is fully supported, the combination of behavioral and physiological experiments proposed here will inform models of the interaction between active training and passive exposure.

D.3.4 Potential limitations and solutions. We propose using the *blocked* schedule from Objective 1, because it maximizes the effect of the order of active training and passive exposures, to most clearly examine interaction. However, if we do not see learning in the *blocked* schedule, we will determine which schedules from Objective 1 do result in learning, and will examine the effect of order (*i.e.*, active or passive first) in those schedules. If this is the case, we will include outcome measures throughout the schedule, instead of just at the beginning and end of the day.

E. Results from NSF Support in the Prior 5 Years

Dr. Jaramillo has no previous NSF support to report. Dr. Baese-Berk holds one NSF grant as a PI: *Interactions between speech perception and production during learning* (2017-2020; BCS-1734166, total award $413,379). This grant is not directly related to the work proposed here. **Intellectual Merit**: the project has demonstrated that many linguistic factors (*e.g.*relationship of target language and native language) and non-linguistic factors (*e.g.*, timing of stimuli) can positively and negatively impact the relationship between speech perception and production during learning. The project has resulted in 7 conference presentations, 4 journal articles, and 1 peer-reviewed proceedings paper. Two additional articles are under review. **Broader Impacts**: We opened one museum exhibit with our partners at the Eugene Science Center, with another currently under construction. We piloted a new undergraduate course aimed at broadening participation in science. We have also continued partnerships with other area partners to pursue outreach, including a TEDx talk and "Science Pub" talks. Dr. Baese-Berk has also served as senior personnel on two REU supplements (both to BCS-1500714; $10,250 and $15,000). These two projects are focused on language revitalization and are unrelated to the current project. Dr Baese-Berk is also the PI on a Doctoral Dissertation Research Improvement Grant (BCS-1941739; $10,303), which was funded on 2/15/19.

- Baese-Berk, M. and Morrill, T. H. (2019). Perceptual consequences of variability in native and non-native speech. *Phonetica, 76*(2-3), 121-141.
- Baese-Berk, M. (2019). Interactions between speech perception and production during learning of novel phonemic categories. *Attention, Perception, Psychophysics, 81*(4), 981-1005.
- Jaggers, Z. and Baese-Berk, M. (2019). Moments of moments: Acoustic phonetic character and within-category variability of the Basque three-place sibilant contrast. *Proceedings of the 19th International Congress of Phonetic Sciences.*
- Kato, M. and Baese-Berk, M. (2020) The effect of input prompts on the relationship between perception and production of non-native sounds. *Journal of Phonetics, 79*, 1-20.
- Vaughn, C. R., Baese-Berk, M., and Idemaru, K. (2019). Re-examining phonetic variability in native and non-native speech. *Phonetica, 76*(5), 327-358.

F. Broader Impacts and Outreach Objectives

F.1 Outreach Objective 1: Integration with education

We will conduct two activities to integrate our proposed research with the educational mission of the University of Oregon. **(1)** We will pilot a program for first-year students using the existing First-Year Interest Group (FIG) structure at the University of Oregon (see letter of collaboration from Amy Hughes Giard). Activity: We will design a year-long program targeting a class of 25 first-year students per year to bridge language and neuroscience. Outcome: Students will participate in the year-long course and will complete a capstone project on research to give them experience conducting experiments and disseminating these findings broadly (including both in academic and non-academic settings). Assessment: We will rely on strategies developed by the University specifically for the FIG program, including immediate post-surveys and tracking within the university system. **(2)** We will promote participation in cross-disciplinary colloquia and symposia. Activity: We will promote cross-disciplinary engagement via a yearly symposium conducted when our advisory board members (Holt, McCormick, and Shea-Brown) attend our annual project meeting. Outcome: Faculty and trainees from Linguistics, the Institute of Neuroscience and other relevant departments on campus (*e.g.*, Psychology) will gain interdisciplinary perspectives on the topics of the current grant and related topics in the field. Assessment: We will conduct surveys of participants after each annual symposium in order to improve the symposium for the next year.

F.2 Outreach Objective 2: Broadening participation in STEM

We will participate in several programs for broadening participation in STEM by promoting involvement of underrepresented populations. **(1)** We will continue to participate in the Science Program to Inspire Creativity and Excellence (SPICE), a summer camp for middle-school girls which creates a learning environment where girls can thrive in science, technology, engineering, and mathematics. Activity: We provide an interactive tour of a neuroscience lab with hands-on stations (slicing brains, imaging, etc) to 40-50 middle school girls each summer. Outcome: Participants will gain interest in science, attitudes toward science, and their science identity. Assessment: Gains will be assessed via pre- and post-program surveys and interviews as previously described[80,81]. **(2)** Our labs will continue to participate in the Summer Program for Undergraduate Research at UO, which focuses on students from underrepresented minorities. Activity: We will host students for mentored undergraduate research. Outcome: Participants will increase confidence and preparation for careers in science, and present their research at national conferences (ABRCMS[1] or SACNAS[74]). Assessment: The program includes measurements of success in entering graduate school. **(3)** The PIs will continue to serve as research advisors in UO programs designed to prepare future educators. Activity: Participate as mentor in the "Experiencing Science Practices through Research to Inspire Teaching" (ESPRIT) program at UO, designed to recruit, prepare, and support science majors for K-12 science teaching careers in high-need school districts. Outcome: Highly qualified K-12 science educators with direct research experience who will serve groups that are typically underrepresented in STEM fields. Assessment: The program assesses recruitment, retention, and teaching effectiveness of participants.

F.3 Outreach Objective 3: Wider dissemination of science

We will disseminate our work to a broad audience. **(1)** We will collaborate with the Eugene Science Center (ESC) (`eugenesciencecenter.org`), a hands-on science museum and planetarium, serving children ages 0-14, their families, caregivers, and teachers. Activity: We will expand existing exhibits and special events about acoustics, neuroscience, language science and language learning, further developing our existing relationship with the museum (see letter of collaboration from Tim Scott, Director of the ESC). Through a previous NSF project, Dr. Baese-Berk designed two speech-science exhibits, one focusing on how sound works (i.e., acoustics) and the other focusing on language learning. One exhibit is open and the second will open later this year. With this project, we plan to update these exhibits and expand these offerings by designing a new neuroscience exhibit. We will also participate in the annual "Meet a Scientist" day and the National Living Laboratory Day, two ongoing programs at the museum, and in the Language Outreach Day, a new program piloted by MMBB. Outcome: Children in the greater Eugene community will gain familiarity with the basic principles of our fields. Assessment: The impact of these programs will be assessed via surveys of museum-goers, conducted by the ESC staff. **(2)** Activity: The PIs will participate in public facing outreach talks, including the Oregon Museum of Science and Industry Pub Talk series, held in both Eugene and Portland, and the University of Oregon Quack Chat series, designed to present science content to a general audience. Assessment: Surveys of participants collected by event organizers will help assess the impact of these events in the community. **(3)** Activity: Each year, the PIs will author an article for an online or print venue (*e.g.*, *The Conversation*) designed to communicate the basic topics of this grant to a general audience. Assessment: We will use readership numbers and feedback from the communications team at the UO to improve our performance for this activity.

F.4 Outreach Objective 4: Bridging theory and practice (second language theory and teaching)

Traditionally, the fields of second language teaching and theoretical linguistics do not communicate their insights well to one another. **(1)** We will work with the Language Teaching Studies (LTS) Master's program (housed in the Linguistics department) and the Second Language Acquisition and Teaching Certificate Program (directed by MMBB) to include current research findings in the curriculum for the students in this program. Activity: We will partner with University of Oregon colleagues, Dr. Julie Sykes, director of the Center for Applied Second Language Studies (CASLS), a Title VI Language Resource Center, and Dr. Keli Yerian, director of the LTS program. With them, we will determine the best ways to integrate our work into the existing curriculum for their programs and other programs focusing on applied linguistics at the UO and Lane Community College (LCC; see letters of collaboration from Drs. Sykes and Yerian). Outcome: Language teachers will receive training in how the results of the current project could be translated into classroom practice. Assessment: Participants will be surveyed to determine effectiveness of this program. **(2)** We will expand our involvement in the applied linguistics field more broadly. Activity: We will contribute articles to applied journals, newsletters, and conferences, *e.g.*, the annual Teaching English to Speakers of Other Languages [TESOL] convention, and the Speech, Pronunciation, and Listening Interest Section (SPLIS) Newsletter. Outcome: The broader language-teaching community will be included in discussions of how our findings may be relevant for their practice. Assessment: We will assess success via surveys to students.

TIMELINE		**Year 1**	**Year 2**	**Year 3**
Objective 1:	Human	Collect	Analyze	Write
	Mouse	Collect/Analyze	Analyze/Write	-
Objective 2:	Human	Pilot	Collect	Analyze/Write
	Mouse	Pilot	Collect	Analyze/Write
Objective 3:	Human	Design	Pilot/Collect	Analyze/Write
	Mouse	-	Collect	Analyze/Write
Broad Impact 1:	Education	Design	Run	Run
Broad Impact 2:	Participation	Participate	Participate	Participate
Broad Impact 3:	Dissemination	Design/Outreach	Implement/Outreach	Implement/Outreach
Broad Impact 4:	Bridge to practice	Design	Present	Present

G. Collaboration and Coordination Plan

G.1 Collaboration between PIs and cross-discipline scientific integration

The PIs' expertise is perfectly complementary for this project. Dr. Jaramillo has expertise in systems neuroscience, specifically focusing on the study of auditory cognition using rodents. Dr. Baese-Berk's work similarly focuses on auditory cognition but from a human behavioral standpoint, with an expertise in second language acquisition. The PIs' offices are located within a short (less than 5 min) walk from each other on the same campus, facilitating in-person collaboration.

The PIs have a history of collaboration. Specifically, they have received a University of Oregon Incubating Interdisciplinary Awards grant which provided the funding for the pilot data presented in the current proposal. While preparing that proposal, and since having received that award, the PIs meet weekly, either in person or via Skype to discuss each aspect of the project from conceptualization to design to analysis. The project is truly a joint effort, with both PIs contributing to the design of both human and mouse experiments.

Our history of working together is evidence that we will successfully collaborate on the research proposed here. In addition to the continuation of weekly meetings of senior personnel, monthly meetings will include all trainees involved in the project across our laboratories. We expect presentations and publications from this work will take place not only in subfield-specific venues to bring a new perspective to each subfield, but also in more general venues for dissemination of the science of learning, providing a true cross-discipline integration (see Outreach Objectives 3 and 4).

G.2 Specific roles and project management

Dr. Baese-Berk will manage the everyday aspects of human experiments, Dr. Jaramillo those of experiments in mice, and both will document any decisions and findings in a shared wiki platform accessible to all members of the project. Both PIs will coordinate hiring staff, managing budget, writing scientific manuscripts, and submitting required reports.

Procedures for resolving possible conflicts: Any substantial deviation from the funded specific objectives will be discussed by the PIs. If conflicts arise regarding budgets or fund allocation, these will be discussed and decided by consensus. In general, Dr. Baese-Berk will make final decisions regarding the implementation and direction of human experiments, while Dr. Jaramillo will make final decisions regarding the implementation and direction of mouse experiments. The strong collaboration between the PIs minimizes the possibility that there will be any conflicts that cannot be resolved between the two principal investigators. However, in the unlikely event that any differences cannot be reconciled, the Ombuds program at the University of Oregon will act as a mediator for conflict resolution.

G.3 Composition and plans for convening advisory board

We will convene a three-person advisory board, consisting of: Dr. Lori Holt, Professor of Psychology and the Center for the Neural Basis of Cognition at Carnegie Mellon University, Dr. David McCormick, Professor of Biology and the Director of the Institute of Neuroscience at the University of Oregon, and Dr. Eric Shea-Brown, Professor of Applied Mathematics at the University of Washington, all of whom have agreed to participate as advisors.

Each of these individuals brings a unique perspective to our board, including language learning and human behavior, neural circuits and systems in animal models, and theoretical neuroscience. Our budget includes funds for our advisory board to travel to Eugene each year for an advisory board meeting, and a symposium about our interdisciplinary research focus.

References

[1] ABRCMS (2020). Annual Biomedical Research Conference for Minority Students. https://www.abrcms.org/.

[2] Andermann, M. L., Kerlin, A. M., and Reid, R. C. (2010). Chronic cellular imaging of mouse visual cortex during operant behavior and passive viewing. *Frontiers in Cellular Neuroscience*, 4(MAR):1–16.

[3] Averbeck, B. B., Latham, P. E., and Pouget, A. (2006). Neural correlations, population coding and computation. *Nature reviews. Neuroscience*, 7(5):358–66.

[4] Baccus, S. A. and Meister, M. (2002). Fast and slow contrast adaptation in retinal circuitry. *Neuron*, 36(5):909–919.

[5] Baese-Berk, M. and Samuel, A. (2016). Listeners beware: Speech production may be bad for learning speech sounds. *Journal of Memory and Language*, 89:23–36.

[6] Baese-Berk, M. M. (2019). Interactions between speech perception and production during learning of novel phonemic categories. *Attention, Perception, and Psychophysics*, 81(4):981–1005.

[7] Bao, S. (2015). Perceptual learning in the developing auditory cortex. *European Journal of Neuroscience*, 41(5):718–724.

[8] Bao, S., Chang, E. F., Woods, J., and Merzenich, M. M. (2004). Temporal plasticity in the primary auditory cortex induced by operant perceptual learning. *Nature Neuroscience*, 7(9):974–981.

[9] Bartolo, R., Saunders, R. C., Mitz, A., and Averbeck, B. B. (2019). Dimensionality, information and learning in prefrontal cortex. *bioRxiv*, (October 29).

[10] Bathellier, B., Ushakova, L., and Rumpel, S. (2012). Discrete Neocortical Dynamics Predict Behavioral Categorization of Sounds. *Neuron*, 76(2):435–449.

[11] Bishop, C. M. (1995). *Neural Networks for Pattern Recognition*. Oxford University Press, Inc., New York, NY.

[12] Boersma, P. and van Heuven, V. (2001). Speak and unSpeak with Praat. *Glot International*, 5(9-10):341–347.

[13] Bürkner, P. (2018). Advanced Bayesian Multilevel Modeling with the R Package brms. *The R Journal*, 10(1):395–411.

[14] Caras, M. L. and Sanes, D. H. (2017). Top-down modulation of sensory cortex gates perceptual learning. *Proceedings of the National Academy of Sciences of the United States of America*, 114(37):9972–9977.

[15] Carcea, I., Insanally, M. N., and Froemke, R. C. (2017). Dynamics of auditory cortical activity during behavioural engagement and auditory perception. *Nature Communications*, 8:1–12.

[16] Cortes, C. and Vapnik, V. (1995). Support-vector networks. *Machine Learning*, (20):273–297.

[17] Cunningham, J. P. and Yu, B. M. (2014). Dimensionality reduction for large-scale neural recordings. *Nature Neuroscience*, 17(11):1500–1509.

[18] Dana, H., Chen, T. W., Hu, A., Shields, B. C., Guo, C., Looger, L. L., Kim, D. S., and Svoboda, K. (2014). Thy1-GCaMP6 transgenic mice for neuronal population imaging in vivo. *PLoS ONE*, 9(9).

[19] Driscoll, L. N., Pettit, N. L., Minderer, M., Chettih, S. N., and Harvey, C. D. (2017). Dynamic Reorganization of Neuronal Activity Patterns in Parietal Cortex. *Cell*, 170(5):986–999.

[20] Earle, F. S. and Myers, E. B. (2015). Overnight consolidation promotes generalization across talkers in the identification of nonnative speech sounds. *The Journal of the Acoustical Society of America*, 137(1):EL91–EL97.

[21] Ehret, G. and Riecke, S. (2002). Mice and humans perceive multiharmonic communication sounds in the same way. *Proceedings of the National Academy of Sciences of the United States of America*, 99(1):479–482.

[22] Engel, T. A. and Steinmetz, N. A. (2019). New perspectives on dimensionality and variability from large-scale cortical dynamics. *Current Opinion in Neurobiology*, 58:181–190.

[23] Engineer, C. T., Perez, C. A., Chen, Y. T. H., Carraway, R. S., Reed, A. C., Shetake, J. A., Jakkamsetti, V., Chang, K. Q., and Kilgard, M. P. (2008). Cortical activity patterns predict speech discrimination ability. *Nature Neuroscience*, 11(5):603–608.

[24] Francis, N. A., Elgueda, D., Englitz, B., Fritz, J. B., and Shamma, S. A. (2018). Laminar profile of task-related plasticity in ferret primary auditory cortex. *Scientific Reports*, 8(1):1–10.

[25] Fritz, J., Shamma, S., Elhilali, M., and Klein, D. (2003). Rapid task-related plasticity of spectrotemporal receptive fields in primary auditory cortex. *Nature Neuroscience*, 6(11):1216–1223.

[26] Gabay, Y., Dick, F. K., Zevin, J. D., and Holt, L. L. (2015). Incidental auditory category learning. *Journal of Experimental Psychology: Human Perception and Performance*, 41(4):1124–1138.

[27] Guo, L., Walker, W. I., Ponvert, N. D., Penix, P. L., and Jaramillo, S. (2018). Stable representation of sounds in the posterior striatum during flexible auditory decisions. *Nature Communications*, 9(1):1534.

[28] Guo, L., Weems, J. T., Walker, W. I., Levichev, A., and Jaramillo, S. (2019). Choice-selective neurons in the auditory cortex and in its striatal target encode reward expectation. *Journal of Neuroscience*, 39(19):3687–3697.

[29] Guo, Z. V., Hires, S. A., Li, N., O'Connor, D. H., Komiyama, T., Ophir, E., Huber, D., Bonardi, C., Morandell, K., Gutnisky, D., Peron, S., Xu, N. L., Cox, J., and Svoboda, K. (2014). Procedures for behavioral experiments in head-fixed mice. *PLoS ONE*, 9(2).

[30] Hamel, E. J., Grewe, B. F., Parker, J. G., and Schnitzer, M. J. (2015). Cellular level brain imaging in behaving mammals: An engineering approach. *Neuron*, 86(1):140–159.

[31] Hammerschmidt, K., Radyushkin, K., Ehrenreich, H., and Fischer, J. (2009). Female mice respond to male ultrasonic 'songs' with approach behaviour. *Biology Letters*, 5(5):589–592.

[32] Harris, K., Bartho, P., Chadderton, P., Curto, C., de la Rocha, J., Hollender, L., Itskov, V., Luczak, A., Marguet, S., and Renart, A. (2011). How do neurons work together? Lessons from auditory cortex. *Hearing Research*, 271(1):37–53.

[33] Huber, D., Gutnisky, D. A., Peron, S., O'Connor, D. H., Wiegert, J. S., Tian, L., Oertner, T. G., Looger, L. L., and Svoboda, K. (2012). Multiple dynamic representations in the motor cortex during sensorimotor learning. *Nature*, 484(7395):473–478.

[34] Issa, J. B., Haeffele, B. D., Young, E. D., and Yue, D. T. (2017). Multiscale mapping of frequency sweep rate in mouse auditory cortex. *Hearing Research*, 344:207–222.

[35] Iverson, P., Hazan, V., and Bannister, K. (2005). Phonetic training with acoustic cue manipulations: A comparison of methods for teaching English /r/-/l/ to Japanese adults. *Citation: The Journal of the Acoustical Society of America*, 118(5):3267–3278.

[36] Jäncke, L., Gaab, N., Wüstenberg, T., Scheich, H., and Heinze, H. J. (2001). Short-term functional plasticity in the human auditory cortex: an fMRI study. *Cognitive Brain Research*, 12(3):479–485.

[37] Jaramillo, S. and Zador, A. M. (2014). Mice and rats achieve similar levels of performance in an adaptive decision-making task. *Frontiers in Systems Neuroscience*, 8(September):1–11.

[38] Jun, J. J., Steinmetz, N. A., Siegle, J. H., Denman, D. J., Bauza, M., Barbarits, B., Lee, A. K., Anastassiou, C. A., Andrei, A., Aydin, , Barbic, M., Blanche, T. J., Bonin, V., Couto, J., Dutta, B., Gratiy, S. L., Gutnisky, D. A., Häusser, M., Karsh, B., Ledochowitsch, P., Lopez, C. M., Mitelut, C., Musa, S., Okun, M., Pachitariu, M., Putzeys, J., Rich, P. D., Rossant, C., Sun, W. L., Svoboda, K., Carandini, M., Harris, K. D., Koch, C., O'Keefe, J., and Harris, T. D. (2017). Fully integrated silicon probes for high-density recording of neural activity. *Nature*, 551(7679):232–236.

[39] Kato, H. K., Gillet, S. N., and Isaacson, J. S. (2015). Flexible Sensory Representations in Auditory Cortex Driven by Behavioral Relevance. *Neuron*, 88(5):1027–1039.

[40] Keuroghlian, A. S. and Knudsen, E. I. (2007). Adaptive auditory plasticity in developing and adult animals. *Progress in Neurobiology*, 82(3):109–121.

[41] King, J., Insanally, M., Jin, M., Martins, A. R., D'amour, J. A., and Froemke, R. C. (2015). Rodent auditory perception: Critical band limitations and plasticity. *Neuroscience*, 296:55–65.

[42] Kriegeskorte, N. and Diedrichsen, J. (2019). Peeling the Onion of Brain Representations. *Annual Review of Neuroscience*, 42(1):407–432.

[43] Kuchibhotla, K. V., Gill, J. V., Lindsay, G. W., Papadoyannis, E. S., Field, R. E., Sten, T. A. H., Miller, K. D., and Froemke, R. C. (2017). Parallel processing by cortical inhibition enables context-dependent behavior. *Nature Neuroscience*, 20(1):62–71.

[44] Kurkela, J. L., Lipponen, A., Hämäläinen, J. A., Näätänen, R., and Astikainen, P. (2016). Passive exposure to speech sounds induces long-term memory representations in the auditory cortex of adult rats. *Scientific Reports*, 6(November):1–8.

[45] Levy, R. B., Marquarding, T., Reid, A. P., Pun, C. M., Renier, N., and Oviedo, H. V. (2019). Circuit asymmetries underlie functional lateralization in the mouse auditory cortex. *Nature Communications*, 10(1).

[46] Liu, R. C., Linden, J. F., and Schreiner, C. E. (2006). Improved cortical entrainment to infant communication calls in mothers compared with virgin mice. *European Journal of Neuroscience*, 23(11):3087–3097.

[47] Lively, S. E., Pisoni, D. B., Yamada, R. A., Tohkura, Y., and Tsuneo, Y. (1994). Training Japanese listeners to identify English/r/and/l/. III. Long-term retention of new phonetic categories. *The Journal of the Acoustical Society of America*, 96(4):2076–2087.

[48] Logan, J. S., Lively, S. E., and Pisoni, D. B. (1991). Training Japanese listeners to identify English/r/and/l/: A first report. *The Journal of the Acoustical Society of America*, 89(2):874–886.

[49] Loonis, R. F., Brincat, S. L., Antzoulatos, E. G., and Miller, E. K. (2017). A Meta-Analysis Suggests Different Neural Correlates for Implicit and Explicit Learning. *Neuron*, 96(2):521–534.

[50] Maravall, M., Petersen, R. S., Fairhall, A. L., Arabzadeh, E., and Diamond, M. E. (2007). Shifts in coding properties and maintenance of information transmission during adaptation in barrel cortex. *PLoS Biology*, 5(2):0323–0334.

[51] Mazzucato, L., Fontanini, A., and La Camera, G. (2016). Stimuli reduce the dimensionality of cortical activity. *Frontiers in Systems Neuroscience*, 10(FEB).

[52] McGinley, M. J., Vinck, M., Reimer, J., Batista-Brito, R., Zagha, E., Cadwell, C. R., Tolias, A. S., Cardin, J. A., and McCormick, D. A. (2015). Waking State: Rapid Variations Modulate Neural and Behavioral Responses. *Neuron*, 87(6):1143–1161.

[53] Mendelson, J. and Cynader, M. (1985). Sensitivity of cat primary auditory cortex (Al) neurons to the direction and rate of frequency modulation. *Brain Research*, 327(1-2):331–335.

[54] Mizrahi, A., Shalev, A., and Nelken, I. (2014). Single neuron and population coding of natural sounds in auditory cortex. *Current Opinion in Neurobiology*, 24(1):103–110.

[55] Ni, A. M., Ruff, D. A., Alberts, J. J., Symmonds, J., and Cohen, M. R. (2018). Learning and attention reveal a general relationship between population activity and behavior. *Science*, 359(6374):463–465.

[56] Niwa, M., Johnson, J. S., O'Connor, K. N., and Sutter, M. L. (2012). Active engagement improves primary auditory cortical neurons' ability to discriminate temporal modulation. *Journal of Neuroscience*, 32(27):9323–34.

[57] Ohl, F. W. and Scheich, H. (2005). Learning-induced plasticity in animal and human auditory cortex. *Current opinion in neurobiology*, 15(4):470–7.

[58] Otazu, G. H., Tai, L.-H., Yang, Y., and Zador, A. M. (2009). Engaging in an auditory task suppresses responses in auditory cortex. *Nat Neurosci*, 12(5):646–654.

[59] Pachitariu, M., Lyamzin, D. R., Sahani, M., and Lesica, N. A. (2015). State-dependent population coding in primary auditory cortex. *Journal of Neuroscience*, 35(5):2058–2073.

[60] Pachitariu, M., Stringer, C., and Harris, K. D. (2018). Robustness of spike deconvolution for neuronal calcium imaging. *Journal of Neuroscience*, 38(37):7976–7985.

[61] Pachitariu, M., Stringer, C., Schröder, S., Dipoppa, M., Rossi, L. F., Carandini, M., and Harris, K. D. (2016). Suite2p: beyond 10,000 neurons with standard two-photon microscopy. *bioRxiv*, page 061507.

[62] Pederson, E. and Guion-Anderson, S. (2010). Orienting attention during phonetic training facilitates learning. *The Journal of the Acoustical Society of America*, 127(2):EL54–EL59.

[63] Peirce, J., Gray, J. R., Simpson, S., MacAskill, M., Höchenberger, R., Sogo, H., Kastman, E., and Lindeløv, J. K. (2019). PsychoPy2: Experiments in behavior made easy. *Behavior Research Methods*, 51(1):195–203.

[64] Peron, S. P., Freeman, J., Iyer, V., Guo, C., and Svoboda, K. (2015). A Cellular Resolution Map of Barrel Cortex Activity during Tactile Behavior. *Neuron*, 86(3):783–799.

[65] Polley, D. B., Heiser, M. A., Blake, D. T., Schreiner, C. E., and Merzenich, M. M. (2004). Associative learning shapes the neural code for stimulus magnitude in primary auditory cortex. *Proceedings of the National Academy of Sciences of the United States of America*, 101(46):16351–16356.

[66] Polley, D. B., Steinberg, E. E., and Merzenich, M. M. (2006). Perceptual Learning Directs Auditory Cortical Map Reorganization through Top-Down Influences. *Journal of Neuroscience*, 26(18):4970–4982.

[67] Poort, J., Khan, A. G., Pachitariu, M., Nemri, A., Orsolic, I., Krupic, J., Bauza, M., Sahani, M., Keller, G. B., Mrsic-Flogel, T. D., and Hofer, S. B. (2015). Learning Enhances Sensory and Multiple Non-sensory Representations in Primary Visual Cortex. *Neuron*, 86(6):1478–1490.

[68] Portfors, C. V. and Perkel, D. J. (2014). The role of ultrasonic vocalizations in mouse communication. *Current Opinion in Neurobiology*, 28:115–120.

[69] Reber, A. S. (1989). Implicit Learning and Tacit Knowledge. *Journal of Experimental Psychology: General*, 118(3):219–235.

[70] Recanzone, G. H., Schreiner, C. E., and Merzenich, M. M. (1993). Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys. *Journal of Neuroscience*, 13(1):87–103.

[71] Reimer, J., Froudarakis, E., Cadwell, C. R., Yatsenko, D., Denfield, G. H., and Tolias, A. S. (2014). Pupil Fluctuations Track Fast Switching of Cortical States during Quiet Wakefulness. *Neuron*, 84(2):355–362.

[72] Romberg, A. R. and Saffran, J. R. (2010). Statistical learning and language acquisition. *Wiley Interdisciplinary Reviews: Cognitive Science*, 1(6):906–914.

[73] Rothschild, G., Nelken, I., and Mizrahi, A. (2010). Functional organization and population dynamics in the mouse primary auditory cortex. *Nature Neuroscience*, 13(3):353–360.

[74] SACNAS (2020). Society for Advancement of Chicanos/Hispanics and Native Americans in Science. https://www.sacnas.org/.

[75] Saunders, J. L. and Wehr, M. (2019). Mice can learn phonetic categories. *The Journal of the Acoustical Society of America*, 145(3):1168–1177.

[76] Schreiner, C. E. and Urbas, J. V. (1988). Representation of amplitude modulation in the auditory cortex of the cat. II. Comparison between cortical fields. *Hearing Research*, 32(1):49–63.

[77] Sewell, G. (1970). Ultrasonic Communication in Rodents Models for the Brain. *Nature*, 227:1970.

[78] Sheintuch, L., Rubin, A., Brande-Eilat, N., Geva, N., Sadeh, N., Pinchasof, O., and Ziv, Y. (2017). Tracking the Same Neurons across Multiple Days in Ca2+ Imaging Data. *Cell Reports*, 21(4):1102–1115.

[79] Sofroniew, N. J., Flickinger, D., King, J., and Svoboda, K. (2016). A large field of view two-photon mesoscope with subcellular resolution for in vivo imaging. *eLife*, 5(JUN2016):1–20.

[80] Todd, B. (2015). *Little Scientists: Identity, Self-Efficacy, and Attitude Toward Science in a Girls' Science Camp*. PhD thesis, University of Oregon. Eugene, OR.

[81] Todd, B. and Zvoch, K. (2019). Exploring Girls' Science Affinities Through an Informal Science Education Program. *Research in Science Education*, 49(6):1647–1676.

[82] Toth, L. A. and Gardiner, T. W. (2000). Food and Water Restriction Protocols: Physiological and Behavioral Considerations. *Contemporary Topics in Laboratory Animal Science*, 39(6):9–17.

[83] Ulanovsky, N., Las, L., and Nelken, I. (2003). Processing of low-probability sounds by cortical neurons. *Nature Neuroscience*, 6(4):391–398.

[84] Wetzel, W., Ohl, F. W., and Scheich, H. (2008). Global versus local processing of frequency-modulated tones in gerbils: An animal model of lateralized auditory cortex functions. *Proceedings of the National Academy of Sciences of the United States of America*, 105(18):6753–6758.

[85] Willmore, B. and Tolhurst, D. J. (2001). Characterizing the sparseness of neural codes. *Network: Computation in Neural Systems*, 12(3):255–270.

[86] Willott, J. F., editor (2001). *Handbook of Mouse Auditory Research: From Behavior to Molecular Biology*. CRC, Boca Raton, FL.

[87] Woloszyn, L. and Sheinberg, D. L. (2012). Effects of Long-Term Visual Experience on Responses of Distinct Classes of Single Units in Inferior Temporal Cortex. *Neuron*, 74(1):193–205.

[88] Wright, B. A., Baese-Berk, M. M., Marrone, N., and Bradlow, A. R. (2013). Enhancing speech learning by combining task practice with periods of stimulus exposure without practice. *The Journal of the Acoustical Society of America*, 138(2):928–937.

[89] Wright, B. A., Baese-Berk, M. M., Marrone, N., and Bradlow, A. R. (2015). Enhancing speech learning by combining task practice with periods of stimulus exposure without practice. *The Journal of the Acoustical Society of America*, 138(2):928–937.

[90] Wright, B. A., Sabin, A. T., Zhang, Y., Marrone, N., and Fitzgerald, M. B. (2010). Enhancing Perceptual Learning by Combining Practice with Periods of Additional Sensory Stimulation. *Journal of Neuroscience*, 30(38):12868–12877.

[91] Xin, Y., Zhong, L., Zhang, Y., Zhou, T., Pan, J., and Xu, N. l. (2019). Sensory-to-Category Transformation via Dynamic Reorganization of Ensemble Structures in Mouse Auditory Cortex. *Neuron*, 103(5):909–921.